Autumn and Winter 2021-2022: potential COVID-19 epidemic trajectories

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A. Summary

This report summarises potential COVID-19 epidemic trajectories until March 2022 based on the recent data and assumptions around changes in contact rates, vaccine effectiveness (VE) and coverage, cross-protection between variants, and waning of natural and vaccine-induced protection.

1. Based on the latest data available to 8 October 2021 on the UK Coronavirus Dashboard, 85% of the population aged 12+ in England have received one vaccine dose and 79% have received two doses.
2. The projected scale of the winter wave is sensitive to small changes in assumptions about vaccine effectiveness including boosters, cross-protection from prior non-Delta infections, and waning of natural- and vaccine-induced protection. It is also sensitive to the assumed level of social mixing reached by 1 December 2021.
3. In the most optimistic scenario we have considered ("central" VE, cross protection, waning of natural- and vaccine-induced protection, effectiveness of boosters, and lower contact rates), current levels of protection in the population combined with the delivery of boosters should maintain the epidemic at levels similar to or lower than currently observed.
4. However, under more pessimistic assumptions around contact patterns or underlying assumptions around the extent and duration of immunity (see Table 1), we project a substantial wave of total infections, hospitalisations and deaths, totalling 9,900 (95% CrI: 6,000, 14,200) deaths by 31 March 2022. In this scenario with more pessimistic assumptions, the current booster programme and vaccination of 12-15 year olds would thus not be sufficient to maintain the epidemic at low levels
5. Given the difference in epidemic dynamics between boosters being rolled out or not (Figure 2), any delay departing from the assumed booster scheduled could result in a much larger epidemic.
6. *Importantly, boosters were not included in model fitting, therefore we may be underestimating current contact rates and over-estimating the impact of boosters.*
7. Note that we have not considered other winter pressures such as influenza here, the potential emergence of future variants of concern, the reimplementation of measures, or the expansion of the booster programme to the under 50s. Emphasis on, and good adherence to, baseline NPIs such as handwashing and case isolation if symptomatic will be important.
8. It will be important to continue to closely monitor the trends in real-time and re-evaluate the need to re-implement interventions if necessary.

B. Potential epidemic trajectories

The UK government has set out an Autumn and Winter plan for 2021-2022 with contingency plans ("Plan B"), should the NHS face unsustainable winter pressures, including re-introduction of some non-pharmaceutical interventions (NPIs) such as mask wearing and advice to work from home. Note that we do not model this potential reintroduction of measures here.

Based on the trends observed in latest available data, in this report we explore the potential COVID-19 epidemic trajectory to March 2022 under different assumptions around i) potential changes in mixing patterns; ii) implementation of mRNA booster doses (50+ years); and iii) first dose mRNA vaccination of 12-15 year olds.

We make the following assumptions about key determinants of the epidemic trajectory:

1. The level of social mixing and transmissibility of the Delta variant as we return to a "new normal" with and without "Plan B" NPIs. We formulate this in terms of Delta's reproduction number in the absence of natural- and vaccine-induced immunity ($R_{excl\_immunity}$).
2. Future vaccination programme progress including booster doses for 50+ year olds (at least 6 months after their second dose) and first dose vaccination of 12-15 year olds.
3. We do not consider the reintroduction of interventions.
4. We do not consider the emergence of new variants of concern.

1. Characteristics of the Delta variant

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

We consider two scenarios (central and pessimistic) with respect to: i) the level of cross-protection from prior infection with non-Delta variants; ii) waning infection-induced immunity; iii) waning vaccine-induced immunity; and iv) vaccine effectiveness against Delta (Table 1).

2. Vaccine Effectiveness (VE)

Table 1 summarises our assumptions regarding the effectiveness of the Pfizer, AstraZeneca, and Moderna vaccines for Alpha and Delta variants.

We now allow for waning of vaccine-induced immunity for each outcome based on PHE data [1] followed by a boosting of VE upon receiving a booster dose (for 50+ years and vulnerable adults, modelled here as a fraction of other age groups, informed by ONS) [2, 3]. We assumed that all booster doses were mRNA vaccines [4] resulting in the same boosted VE levels regardless of first and second dose vaccine type (see Methods). Note that we currently assume that all 50+ years wane before receiving a booster dose.

3. Vaccination Coverage

Data on vaccine uptake by age and product over time and for each NHS region in England were provided by PHE. For the forward projections, future vaccine rollouts follow a Cabinet Office Scenario with an average of 1.3 million mRNA booster doses administered per week for the vulnerable and over 50-year olds and an average of 200,000 first doses offered per

week for those aged between 12 and 15. Currently 12-15 year olds are included as part of the vaccine eligible age groups with a 50% uptake.

We assume that booster doses are administered 6 months after dose two, and that booster dose coverage will be the same as that reached for doses 1 and 2.

4. Estimating contact rates following lifting of all NPIs (step 4)

We fitted a multi-variant model to data including cases reported in the Variant And Mutation (VAM) data in each England NHS region between 8 March - 8 October 2021 to account for the joint transmission dynamics of the Alpha and Delta variant. We estimated the current effective reproduction numbers (R_{eff}) and the corresponding reproduction number excluding immunity ($R_{excl\_immunity}$) separately for Alpha and Delta, which were used to inform assumptions about transmission in the future, $R_{excl\_immunity}$ for Delta. We assume transmission is lower during school holidays due to lower contact rates between children (-0.25 in terms of $R_{excl\_immunity}$ for Delta). We assumed an average school holiday pattern across England until March 2022.

Table 1: Vaccine effectiveness assumptions for three two-dose vaccines licensed for use in England: Oxford-AstraZeneca ChadOx1 nCov-19 AZD1222 (AZ), Pfizer-BioNTech COVID-19 vaccine BNT162b2 (PF) and Moderna mRNA-1273*

			Central	Pessimistic	Informed by
Average duration of natural immunity⁺			6 years	3 years	[5] and sensitivity
Infection with VOC resulting in protection vs Alpha			100%	100%	[6] and sensitivity
Infection with Alpha or earlier variants resulting in protection vs Delta^	Infection/ mild disease		85%	75%	[6] and sensitivity
	Hospitalisation		95%^	90%^	[6] and sensitivity
Vaccine effectiveness	**Vaccine (dose)**	**Alpha**	**Delta (Central/Waned[1]/Booster)**	**Delta (Pessimistic/Waned[1]/Booster)**	**Informed by**
Against death	AZ (1)	80%	80%/NA	75%/NA	[7, 8]
	AZ (2)	95%	95%/85%/99%	95%/85%/95%	[7–9]
	PF (1)	85%	85%/NA	80%/NA	[7, 8]
	PF (2)	95%	95%/89%/99%	95%/89%/95%	[7, 8]
Against severe disease	AZ (1)	80%	80%/NA	75%/NA	[10, 11]
	AZ (2)	90%	90%/77%/99%	85%/73%/90%	[10–12] assumed greater than mild disease
	PF (1)	85%	85%/NA	80%/NA	[13]
	PF (2)	95%	95%/89%/99%	90%/86%/90%	[12, 14] assumed greater than mild disease
Against mild disease or infection⁺	AZ (1)	50%	33%/NA	20%/NA	[12, 15, 16]
	AZ (2)	74%	58%/43%/92%	45%/34%/78%	[15–18]
	PF (1)	50%	33%/NA	20%/NA	[11, 14, 15, 18]
	PF (2)	93%	85%/67%/92%	78%/62%/78%	[14, 15, 18, 19]
Against infectiousness if infected	All vaccines (1 and 2)	45%	40%//40%	35%/35%	[7], assumed

*We assumed that Moderna had the same vaccine effectiveness as PF for first and second doses. ⁺VE against infection was assumed equal to VE against mild disease. ^Assumed same as PF two dose effectiveness. [1]Waned VE at 20 weeks after second dose. VE is capped so that VE vs deaths > severe > mild.

5. Projected changes in population contact rates for Winter 2021-22

Table 2 summarises our assumptions for the level of mixing over winter 2021-22 for England. To capture the continued "return to the new normal", we explored 3 scenarios where $R_{excl\_immunity}$ continues to gradually increase (from 8 October) to i) 120%; ii) 130%; and iii) 140% of current levels by 1 December 2021. Note that given recent observed epidemics trends, under the pessimistic assumptions regarding the extent and duration of immunity, we estimate a lower current $R_{excl\_immunity}$ as a lower level of transmissibility is required to explain the current trends. Therefore the $R_{excl\_immunity}$ reached by 1 December is also lower.

Table 2: Relative gradual increase in contact rates from 8 October to 1 December 2021. Values are given with school open.

Increase in contacts by 1 Dec 2021	**Corresponding $R_{excl\_immunity}$ (95% CI)**	
	"Central" VE and immunity*	"Pessimistic" VE and immunity*
120%	4.2 (3.5-5.0)	3.5 (2.9-4.3)
130%	4.6 (3.9-5.4)	3.8 (3.2-4.6)
140%	4.9 (4.2-5.7)	4.1 (3.5-4.8)

*see Table 1

6. Results

The magnitude of the potential winter 2021-22 wave is highly uncertain, depending on the assumed extent and duration of protection following infection and vaccination (including boosters), and the level of mixing reached.

Cumulative admissions and deaths by 31 March 2022 reach 42,800 (95% CrI: 23,500, 71,900) and 5,300 (95% CrI: 3,200, 7,700) respectively in the most optimistic scenario (higher immunity assumptions, booster campaign and 120% mixing reached by 1 December), and go up to 100,300 (95% CrI: 60,000, 145,800) and 9,900 (95% CrI: 6,000, 14,200) respectively in the most pessimistic scenario with boosters (lower immunity assumptions and 140% mixing reached by 1 December) scenario explored, illustrating the high uncertainty across all scenarios (Table 4).
If vaccine and immunity assumptions are on the lower end of what we have modelled, or if the booster programme slows down, then the booster programme and vaccination of 12-15 year olds may not be sufficient to prevent a substantial winter wave (see Figure 2-3 and Table 3).

As we have not modelled booster doses in the model fitting and assume an immediate protective effect upon boosting, we may be overestimating the impact of boosters.

We have assumed that contact rates remain constant from 1 December at 120-140% of current levels until 31 March 2022. This is a simplifying assumption, and we anticipate that contacts will continue to change especially in the lead up to the Christmas holidays.

Note that we have not modelled the potential impact of re-implementing interventions or expansion of the booster programme to under the 50s, or the emergence of a new variant of concern. Careful and continued monitoring of the epidemic trends will be critical over the winter particularly in context of other winter pressures such as influenza which we do not consider here.

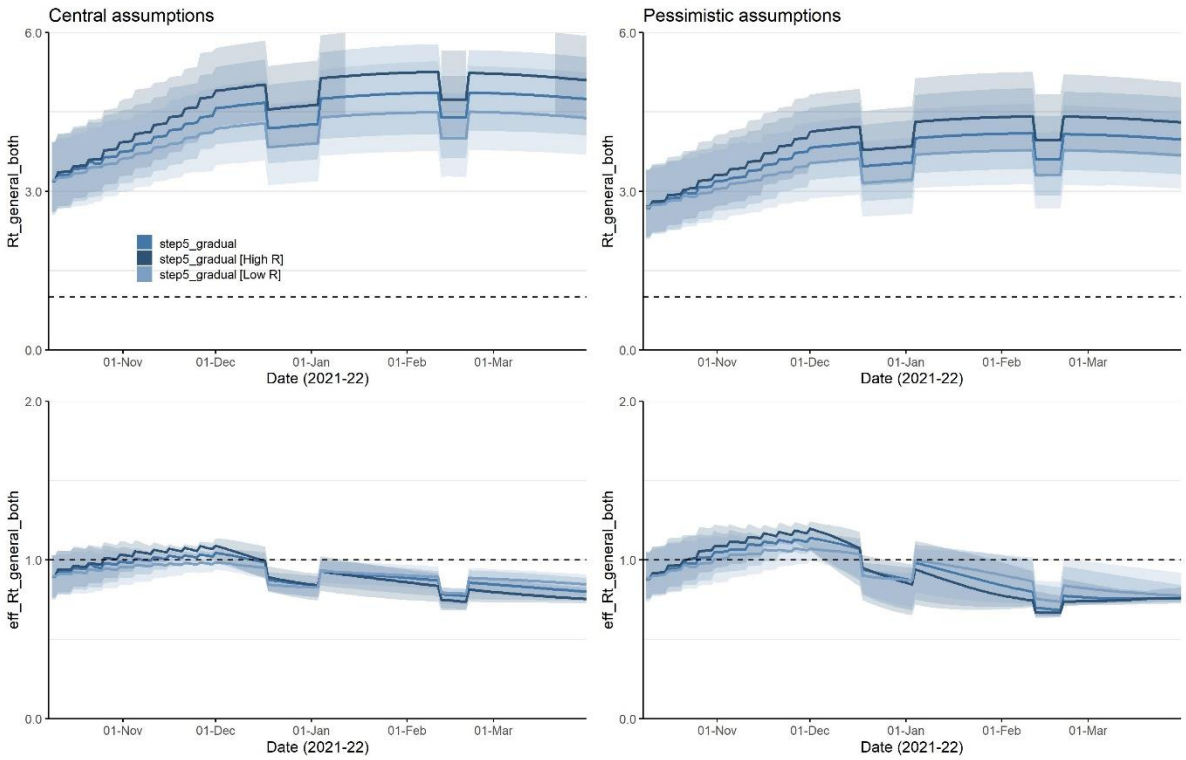

Figure 1: Reproduction number excluding immunity (top row) and the effective reproduction number R_{eff} (bottom row) accounting for natural- or vaccine-induced immunity in England assuming contact rates gradually increase from 8 October to 120% (light blue), 130% (blue), and 140% (dark blue) of current levels by 1 December 2021 with no further interventions (see Table 2 for corresponding $R_{excl\_immunity}$ values) and with booster campaign and vaccination of 12-15 year olds. We consider VE, cross-protection from prior infection, and waning immunity to be (left) central or (right) pessimistic (see Table 1). The horizontal dashed lines show the $R_{excl\_immunity} = 1$ or $R_{eff} = 1$ thresholds. The y-axis limits differ in the top and bottom panels. Note that given recent observed epidemics trends, under the pessimistic assumptions regarding the extent and duration of immunity, we estimate a lower current $R_{excluding\_immunity}$ as a lower level of transmissibility is required to explain the current trends.

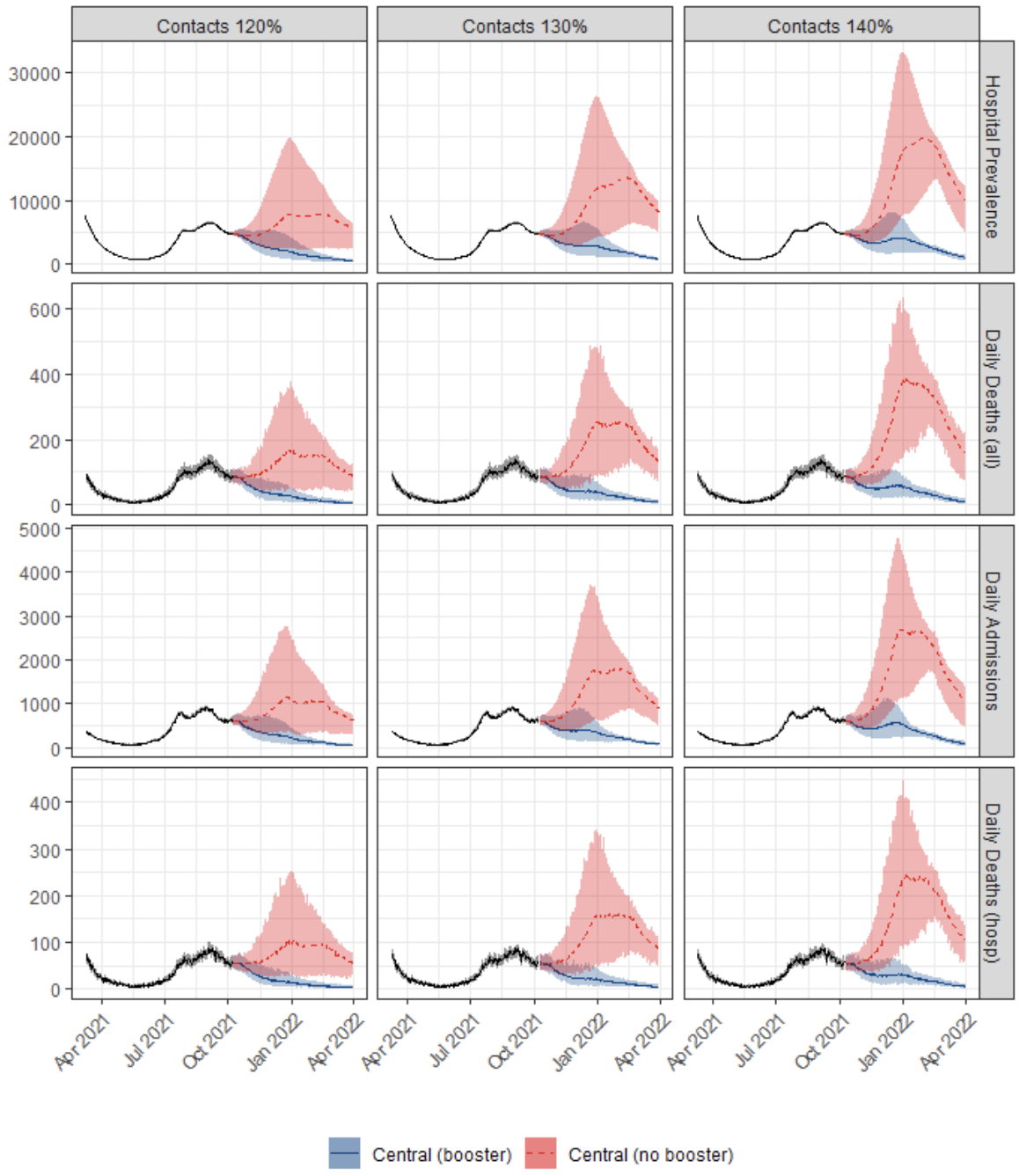

Figure 2: COVID-19 England daily (top row) hospital occupancy, (second row) all daily deaths, (third row) daily admissions, and (bottom row) daily hospital deaths over time under our "*central*" VE and immunity assumptions with (blue) and without (pink) booster doses (see Table 1). Both set of simulations include vaccination of 12-15 year olds. The black line and grey shaded area shows the model fit and 95% CrI to the past data, the blue solid line the median projection for the central scenario with boosters and blue shaded area the 95% CrI, and the red dashed line the median projection for the central scenario without boosters and the red shaded area the 95% CrI. From left to right assuming contacts increase gradually between 8 October to 1 December 2021 to (left) 120%, (middle) 130%, and (right) 140% of current levels.

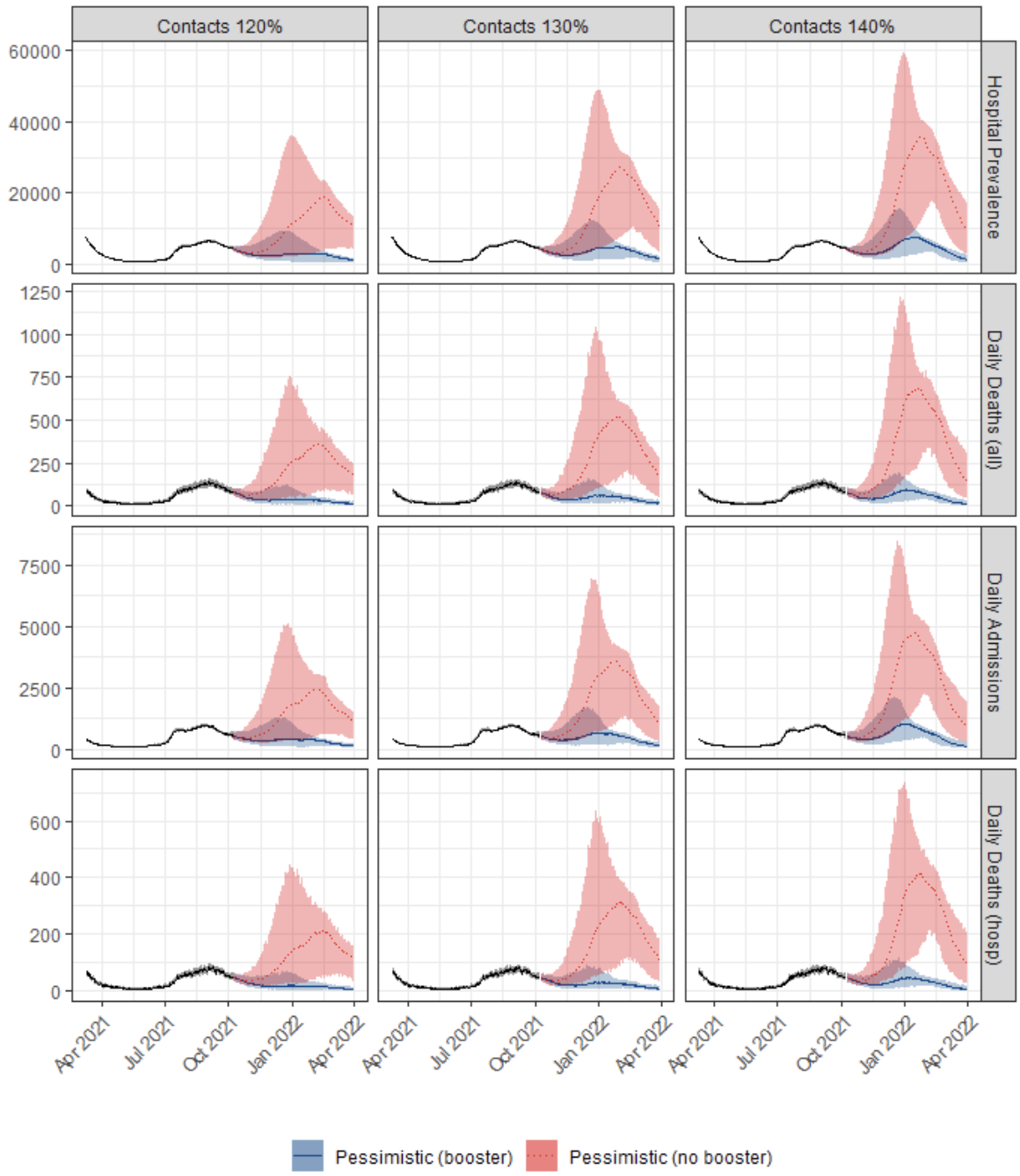

Figure 3: COVID-19 England daily (top row) hospital occupancy, (second row) all daily deaths, (third row) daily admissions, and (bottom row) daily hospital deaths over time under our "*pessimistic*" VE and immunity assumptions with (blue) and without (pink) booster doses (see Table 1). Both set of simulations include vaccination of 12-15 year olds. The black line and grey shaded area shows the model fit and 95% CrI to the past data, the blue solid line the median projection for the central scenario with boosters and blue shaded area the 95% CrI, and the red dashed line the median projection for the central scenario without boosters and the red shaded area the 95% CrI. From left to right assuming contacts increase gradually between 8 October to 1 December 2021 to (left) 120%, (middle) 130%, and (right) 140% of current levels.

Table 3: Median cumulative deaths, hospital admissions, and incidence in England (95% CrI, nearest 100) between 8 October 2021 and 31 December 2021.

Analysis type			Cumulative deaths (95%CrI)	Cumulative hospital admissions (95%CrI)	Cumulative incidence (95%CrI)
VE vs Delta, waning immunity, cross protection[1]	**Contacts by 1 December[2]**	**Boosters**	**Up to 31 December 2021**		
Central	120%	Yes	4,000 (2,600, 6,100)	31,300 (18,900, 54,800)	3,042,800 (1,330,300, 6,109,600)
	120%	No	9,200 (4,900, 17,100)	66,300 (33,300, 138,200)	3,619,700 (1,535,600, 7,700,700)
	130%	Yes	4,500 (2,900, 6,800)	36,200 (21,100, 63,300)	3,849,500 (1,770,800, 7,324,500)
	130%	No	11,200 (5,700, 20,400)	83,600 (40,700, 167,300)	4,692,100 (2,069,300, 9,232,800)
	140%	Yes	5,000 (3,200, 7,500)	42,500 (24,700, 72,200)	4,876,500 (2,352,800, 8,601,400)
	140%	No	13,900 (7,400, 23,700)	107,100 (54,300, 195,600)	6,056,800 (2,938,300, 10,682,800)
Pessimistic	120%	Yes	3,700 (1,900, 8,100)	32,400 (14,500, 80,700)	3,726,400 (1,137,900, 9,861,700)
	120%	No	9,600 (3,900, 27,700)	69,600 (25,200, 207,500)	4,454,100 (1,273,600, 11,958,300)
	130%	Yes	4,200 (2,100, 9,200)	39,000 (16,600, 95,000)	4,996,300 (1,550,700, 11,640,300)
	130%	No	12,400 (4,900, 33,500)	94,500 (33,900, 261,000)	6,283,700 (1,947,100, 14,488,700)
	140%	Yes	5,000 (2,400, 10,200)	49,000 (21,300, 109,700)	6,761,700 (2,415,600, 13,559,100)
	140%	No	15,800 (6,000, 39,600)	125,000 (43,600, 310,500)	8,279,400 (2,724,200, 16,561,300)

[1]See Table 1 for details on cross-protection and VE. [2]Relative increase in contacts compared to current estimate as of 8 October 2021.

Table 4: Median cumulative deaths, hospital admissions, and incidence in England (95% CrI, nearest 100) between 8 October 2021 and 31 March 2022.

Analysis type			Cumulative deaths (95%CrI)	Cumulative hospital admissions (95%CrI)	Cumulative incidence (95%CrI)
VE vs Delta, waning immunity, cross protection[1]	**Contacts by 1 December[2]**	**Boosters**	**Up to 31 March 2022**		
Central	120%	Yes	5,300 (3,200, 7,700)	42,800 (23,500, 71,900)	4,831,400 (2,138,700, 8,323,000)
	120%	No	21,700 (9,100, 35,600)	150,900 (62,800, 263,000)	6,924,800 (2,827,000, 11,672,200)
	130%	Yes	6,600 (4,100, 9,100)	54,700 (31,500, 83,800)	6,594,000 (3,516,100, 9,855,600)
	130%	No	31,500 (15,900, 43,300)	223,000 (110,700, 320,600)	9,695,000 (4,999,400, 13,680,900)
	140%	Yes	7,900 (5,300, 10,300)	68,500 (42,700, 96,400)	8,438,900 (5,271,600, 11,330,400)
	140%	No	41,700 (27,100, 51,000)	298,400 (194,500, 375,900)	12,238,700 (8,197,500, 15,408,100)
Pessimistic	120%	Yes	6,300 (2,700, 11,400)	60,400 (22,100, 112,200)	7,972,700 (2,612,500, 13,018,400)
	120%	No	37,300 (12,000, 59,200)	252,100 (73,800, 398,000)	11,743,100 (3,895,200, 17,178,800)
	130%	Yes	8,000 (4,000, 12,700)	79,700 (35,300, 127,800)	10,480,500 (4,902,100, 14,655,400)
	130%	No	49,700 (22,500, 66,700)	342,700 (145,700, 460,200)	14,912,500 (7,337,000, 19,133,600)
	140%	Yes	9,900 (6,000, 14,200)	100,300 (60,000, 145,800)	12,772,633 (8,277,300, 16,498,200)
	140%	No	59,900 (36,900, 73,700)	418,200 (248,500, 516,200)	17,406,900 (11,298,900, 21,011,700)

[1]See Table 1 for details on cross-protection and VE. [2]Relative increase in contacts compared to current estimate as of 8 October 2021.

C. Appendix

Key assumptions

a. We do not allow for administration of booster doses before vaccine-induced immunity has waned. Individuals with ongoing full effect of second dose cannot receive increased protection (*pessimistic)* but boosters are given to less protected (optimistic).
b. We assume an exponential waning of vaccine-induced immunity based on PHE data [1] with a mean of 20 weeks.
c. We assume that all booster doses are mRNA vaccines and post-booster VE will be the same regardless of first and second dose vaccine type.
d. We assume that booster effectiveness does not wane over the timescale of our analyses (*optimistic*)
e. The booster roll out schedule used (from Cabinet Office roll out assumptions) may be overly optimistic for the early period. If that is the case the early trajectory of the epidemic is likely to be closer to the no booster scenario (*optimistic*)
f. We account for booster doses and vaccines administered to 12-15 year olds in the past by assuming these all occur in the first week of the simulation.
g. All scenarios incorporate seasonality in transmission with a 20% peak to trough variation in transmissibility throughout the year.
h. There is considerable uncertainty in the level of contacts that may occur in the coming months.
i. We assumed infection with the Delta variant was more severe than Alpha with a 1.85x hospitalisation risk.
j. We estimate the relative transmissibility of Delta over Alpha by fitting a two-variant model to Delta and Alpha cases over time.
k. We assume vaccines provide protection against infection in addition to protection from severe disease and death *(optimistic).*
l. We assume vaccines prevent to a certain extent, an infected person who is vaccinated from transmitting the virus.
m. We model school holidays by assuming an average decrease in $R_{excl\_immunity}$ for Delta of 0.25 whilst schools are closed.
n. We assume Moderna has the same VE as Pfizer.
o. We assume no correlation between vaccine uptake and risk of severe infection. If uptake is 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)*.
p. We do not model differential infectivity or susceptibility by age.
q. We assume no dynamic replenishment of the care-home population *(optimistic).*
r. We do not model the reintroduction of interventions, or the potential expansion of the booster programme to the under 50s *(pessimistic).*
s. We do not consider the emergence of new variants of concern *(optimistic)*.

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 [20]. The model

was extended to include vaccination where each compartment in the model is further stratified to account for vaccination status [21]. We used parameter values calibrated to data from 8 October 2021. The model was fitted with vaccination (both first and second doses) as reported by PHE to SPI-M. The model is further fitted to variant and mutation data to explicitly model the emergence of the Delta variant and estimate its transmission advantage over Alpha. Full details are described in [21, 22].

Definitions of the relative contact rate and 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.
- **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 are immune (because of infection- or vaccine-induced immunity) p_{immune}, with $R_{eff} = R_{excl\_immunity} * (1-p_{immune})$.

Transmissibility associated with potential changes in contact rates over Winter 2021-22

The level of transmissibility associated with the potential re-introduction of NPIs (as set out in "Plan B") is highly uncertain.

We modelled 3 scenarios for Winter 2021-22 with a gradual linear increase of $R_{excl\_immunity}$ from the current estimated level up to:

1. 120% of current levels by 1 December 2021
2. 130% of current levels by 1 December 2021
3. 140% of current levels by 1 December 2021

We additionally assumed that school holidays will decrease transmissibility in terms of $R_{excl\_immunity}$ by an average of -0.25.

Vaccine roll out and waning of vaccine-induced immunity

We assume first doses were delivered in England between 8 December 2020 and 8 October 2021 as reported in data received from PHE via SPI-M. We then assume an average vaccine dose roll-out of 1.3 million booster doses administered per week for the vulnerable and over 50-year olds and an average of 200,000 first doses offered per week for those aged between 12 and 15. We assume uptake amongst 12-15 year olds will be 50%. 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 8 October onwards, we assumed doses are split between NHS regions in proportion to their population size. We assumed that a mixture of Pfizer and AstraZeneca vaccines as observed thus far in each age group continue to be distributed to individuals 40+ years and <40 years will receive Pfizer or Moderna only.

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

1. Care home workers and residents
2. Individuals 50 or over by decreasing 5-year age band priority as well as health care workers (we assume a fraction of the working age population to be within this group) and vulnerable individuals (also modelled as a fraction of the population)
3. Individuals under 50
4. One dose of Pfizer or Moderna to individuals 50+ years at least 6 months after their second dose
5. One dose of Pfizer to children 12-15 years

Children under 12 years are not vaccinated in our analyses. As our model is stratified using 5-year age classes, we model the vaccination of individuals aged 12-14 by assuming homogeneous eligibility in 60% (3/5 individual ages in the age class) of the 10-14 age group.

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

There are 6 successive vaccination stages (duration of each stage and effectiveness of vaccine in each stage are shown below) associated with each compartment in the model:

- Unvaccinated
- Vaccinated with 1st dose before onset of vaccine effectiveness
- Vaccinated with 1st dose with full effectiveness from 1st dose – this includes individuals having received the second dose before the onset of effectiveness of the second dose
- Vaccinated with 2nd dose with full effectiveness from 2nd dose
- Waning vaccine-induced immunity
- Vaccinated with booster dose with effectiveness described in Table 1

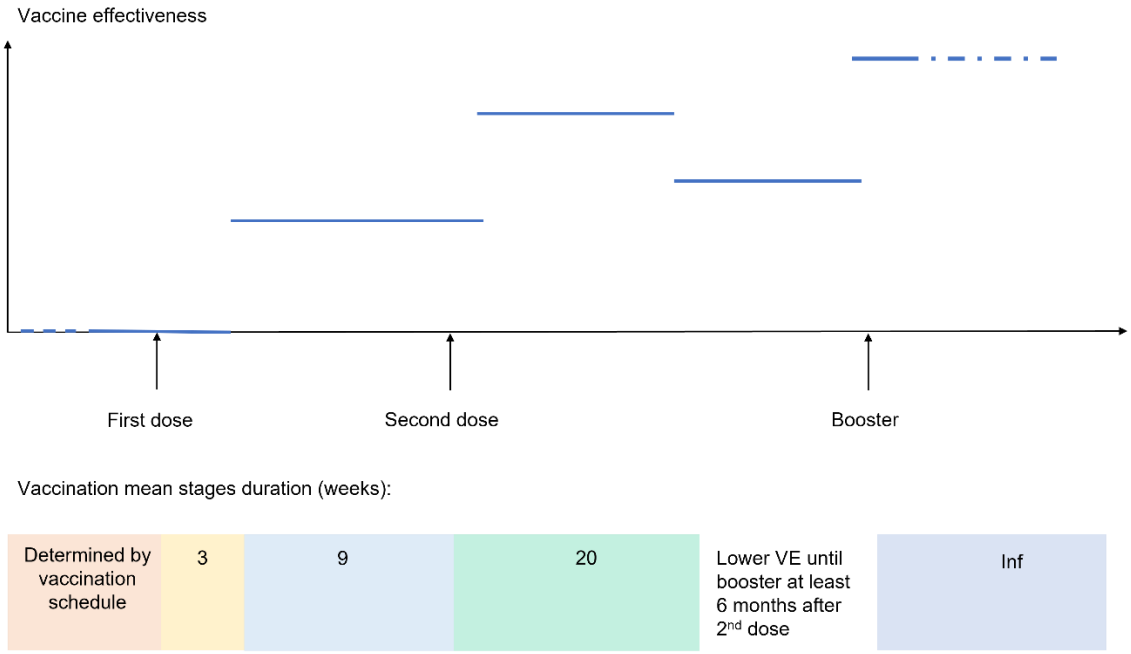

Figure S1: Vaccination stage duration and associated vaccine effectiveness. The lower panel depicts mean duration of vaccination stages in weeks (numbers denote number of weeks in each stage). The top panel shows the associated vaccine effectiveness and delays to protection over time.

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

- No effectiveness in the 21 days following the first dose
- Immediate effectiveness of the second dose following dose 2 in our forward simulations
- An exponential waning of vaccine-induced immunity based on PHE data [1] with a mean of 20 weeks
- Immediate effectiveness of the booster dose (see Table 1)

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 effectiveness in the fits, but assumed immediate second dose effectiveness in our forward simulations.

We fit a daily multiplicative VE reduction factor for two vaccines (AZ and PF) across three disease severity tiers (mild, severe, and death) to recent PHE data [1]. We assumed that vaccine-induced immunity waned from 42 days post dose two and extrapolated to 200 days (Figure S2). We then assumed an 11.3-fold and 19.5-fold increase in PF VE upon receiving a booster dose at least 6 months post-dose two for mild and severe disease respectively based on Israeli Ministry of Health data [2]. Due to all UK booster shots being PF or Moderna vaccines, we assumed that VE for those initially administered with AZ would have the same VE post-booster as those initially vaccinated with PF/Mod, based upon effectiveness results for AZ primers and PF boosters [25].

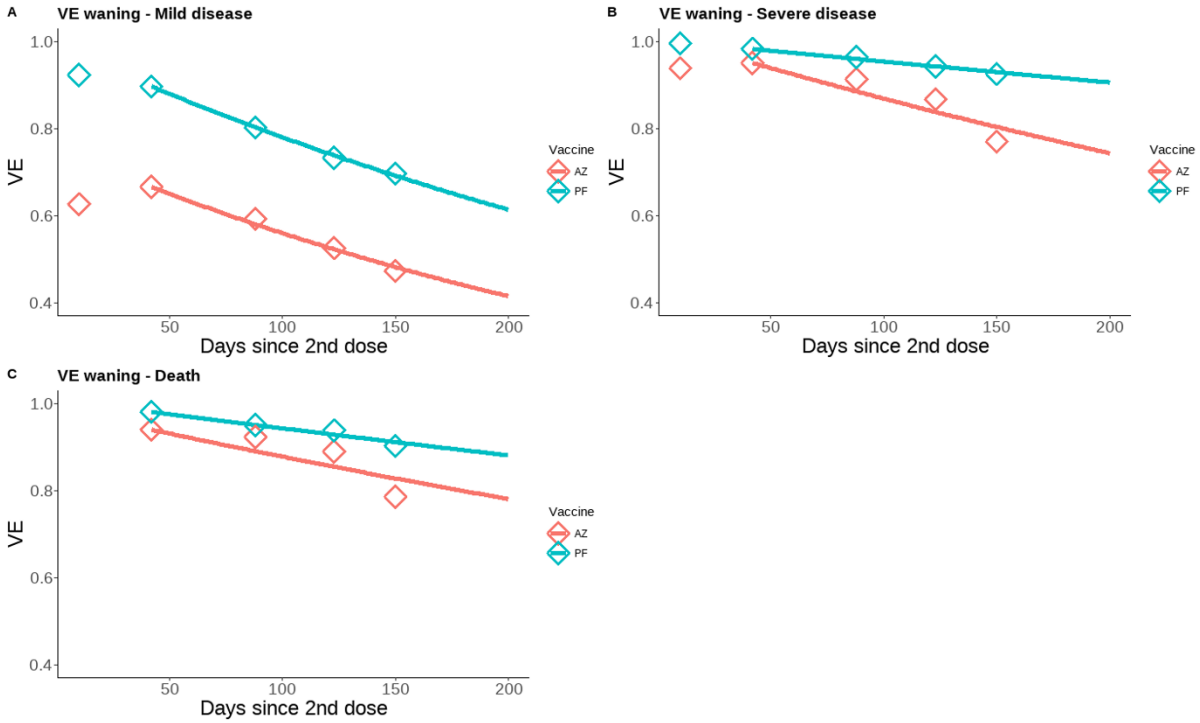

Figure S2: Waning vaccine effectiveness against A) mild disease, B) severe disease, and C) death for AZ (pink; bottom in each panel) and PF (blue; top in each panel) vaccines from 42 days post dose two. The points show the PHE data [1] **and the line the model fit.**

Vaccine effectiveness

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

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

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

infection ("Effectiveness *against severe infection,* e_{hosp}", non-conditional on symptomatic infection) in vaccinated individuals, compared to those not vaccinated.

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

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

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

Similarly, the reduction in the risk of death (e_{death}), as listed in Table 1, is determined by the reduction in the risk of being infected (e_{inf}), and of severe disease warranting hospitalisation (e_{hosp}), the reduction in risk of becoming symptomatic if infected ($e_{sympt \mid inf}$), the reduction in risk of developing severe symptoms if infected and symptomatic ($e_{hosp \mid sympt}$), and the reduction in risk of death if displaying severe symptoms ($e_{death \mid hosp}$) as follows:

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

D. Supplementary Results

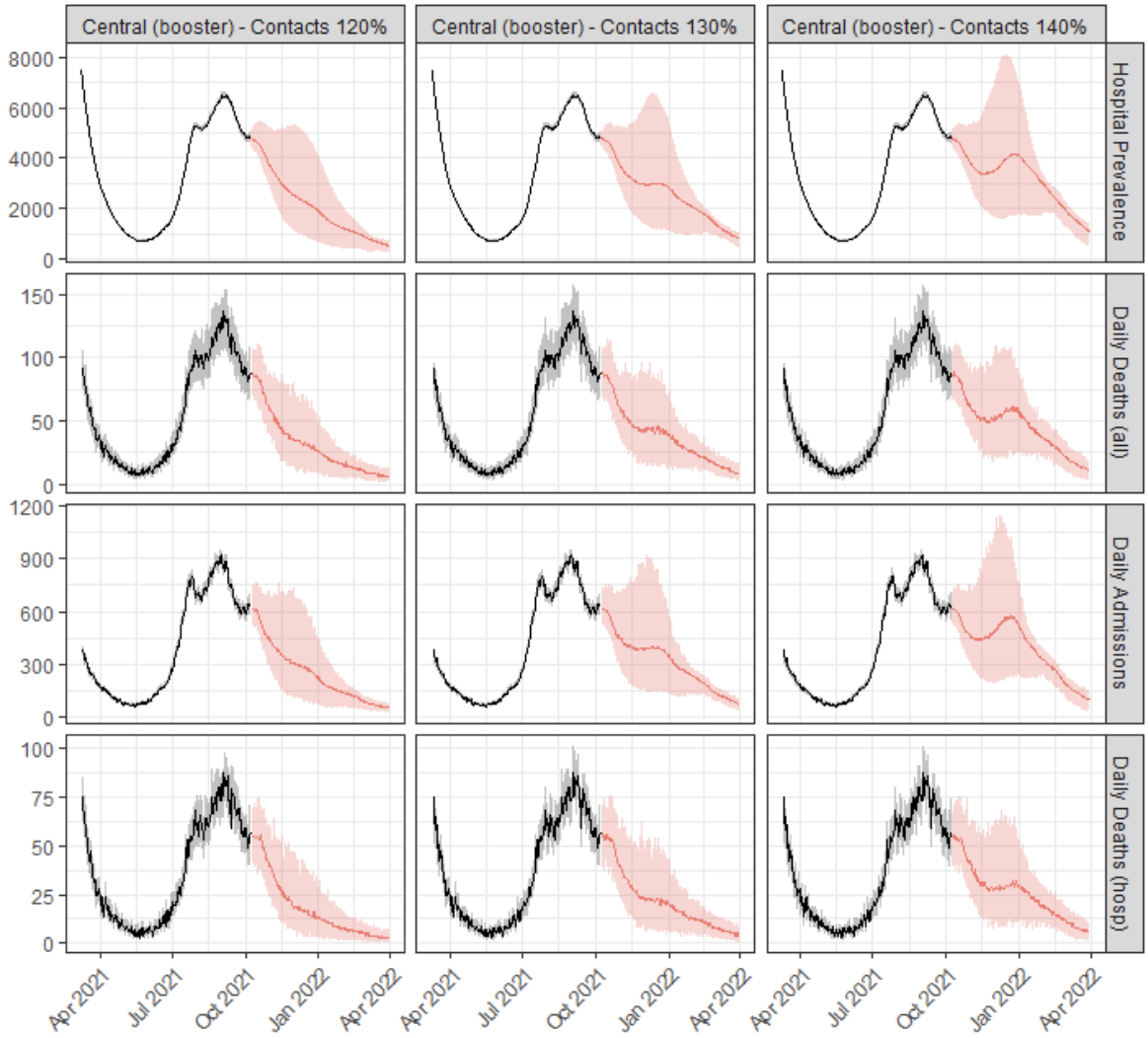

Figure S3: COVID-19 England daily (top row) hospital occupancy, (second row) all daily deaths, (third row) daily admissions, and (bottom row) daily hospital deaths over time under our "*central*" VE and immunity assumptions with booster doses and vaccination of 12-15 year olds (see Table 1). The black line and grey shaded area shows the model fit and 95% CrI to the past data, the red solid line the median projection, and the red shaded area the 95% CrI. From left to right assuming contacts increase gradually between 8 October to 1 December 2021 to (left) 120%, (middle) 130%, and (right) 140% of current levels.

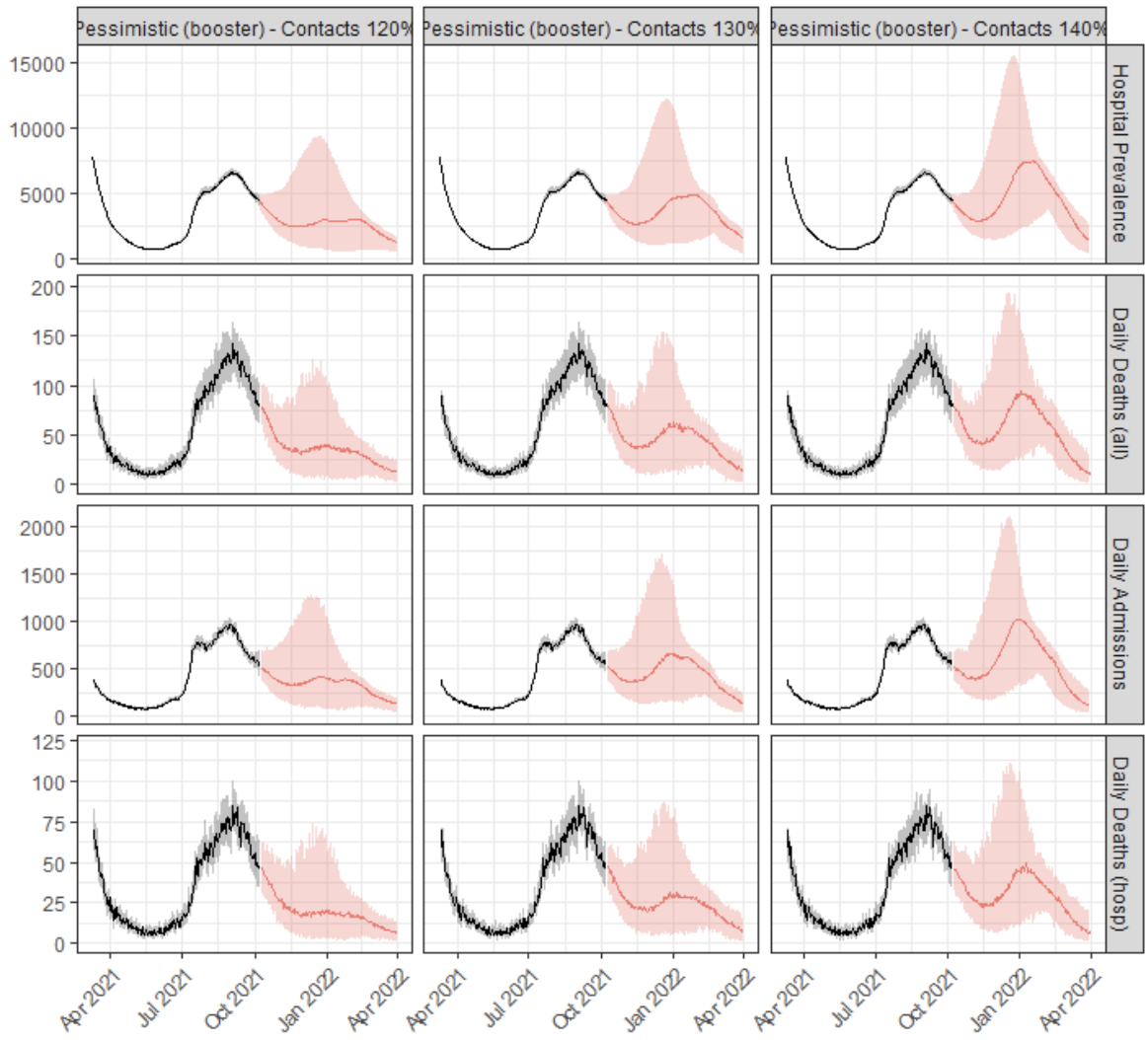

Figure S4: COVID-19 England daily (top row) hospital occupancy, (second row) all daily deaths, (third row) daily admissions, and (bottom row) daily hospital deaths over time under our "*pessimistic*" VE and immunity assumptions with booster doses and vaccination of 12-15 year olds (see Table 1). The black line and grey shaded area shows the model fit and 95% CrI to the past data, the red solid line the median projection, and the red shaded area the 95% CrI. From left to right assuming contacts increase gradually between 8 October to 1 December 2021 to (left) 120%, (middle) 130%, and (right) 140% of current levels.

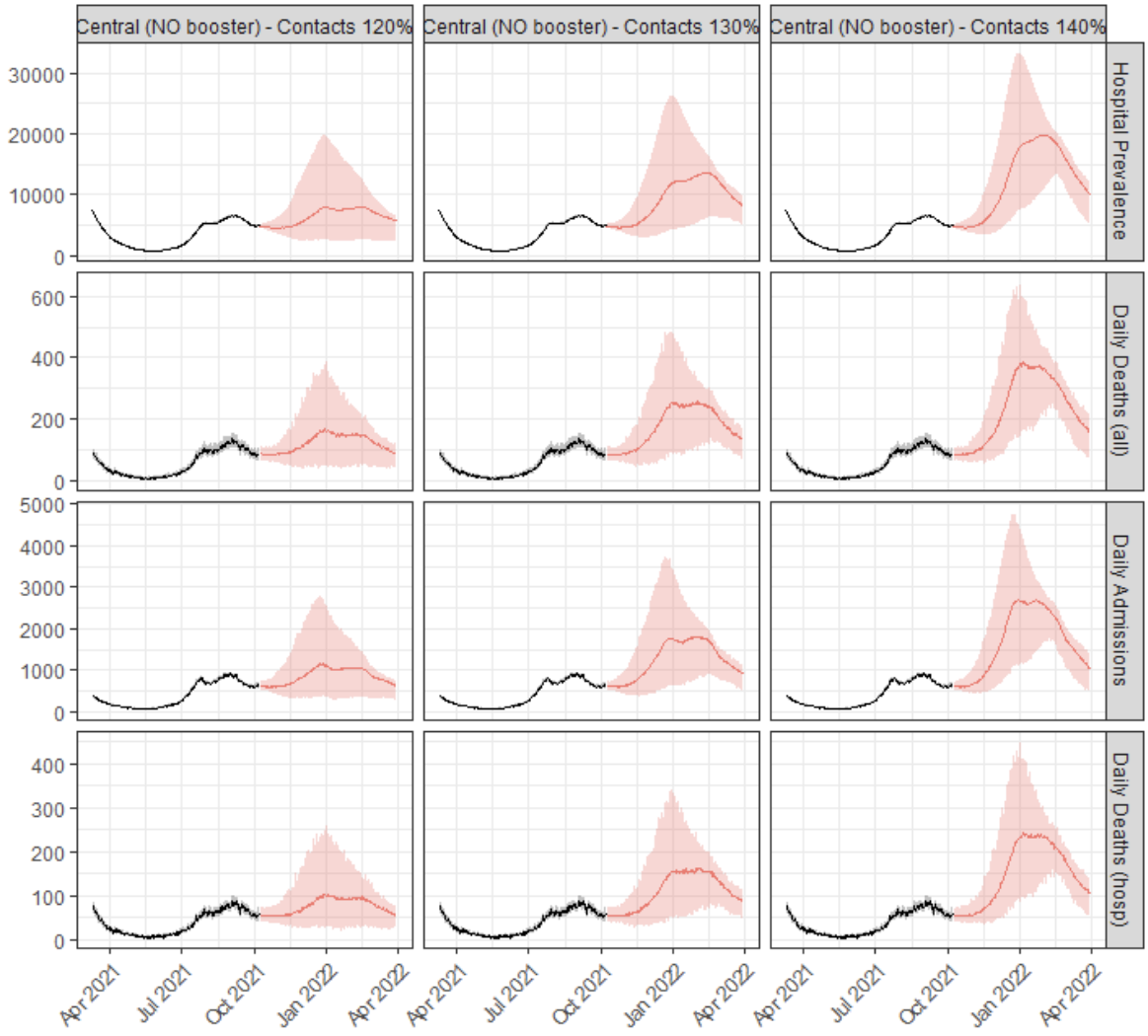

Figure S5: COVID-19 England daily (top row) hospital occupancy, (second row) all daily deaths, (third row) daily admissions, and (bottom row) daily hospital deaths over time under our "central" VE and immunity assumptions with vaccination of 12-15 year olds but *without* booster doses (see Table 1). The black line and grey shaded area shows the model fit and 95% CrI to the past data, the red solid line the median projection, and the red shaded area the 95% CrI. From left to right assuming contacts increase gradually between 8 October to 1 December 2021 to (left) 120%, (middle) 130%, and (right) 140% of current levels. Note this plot is based on 100 particles rather than 200 used for all other plots.

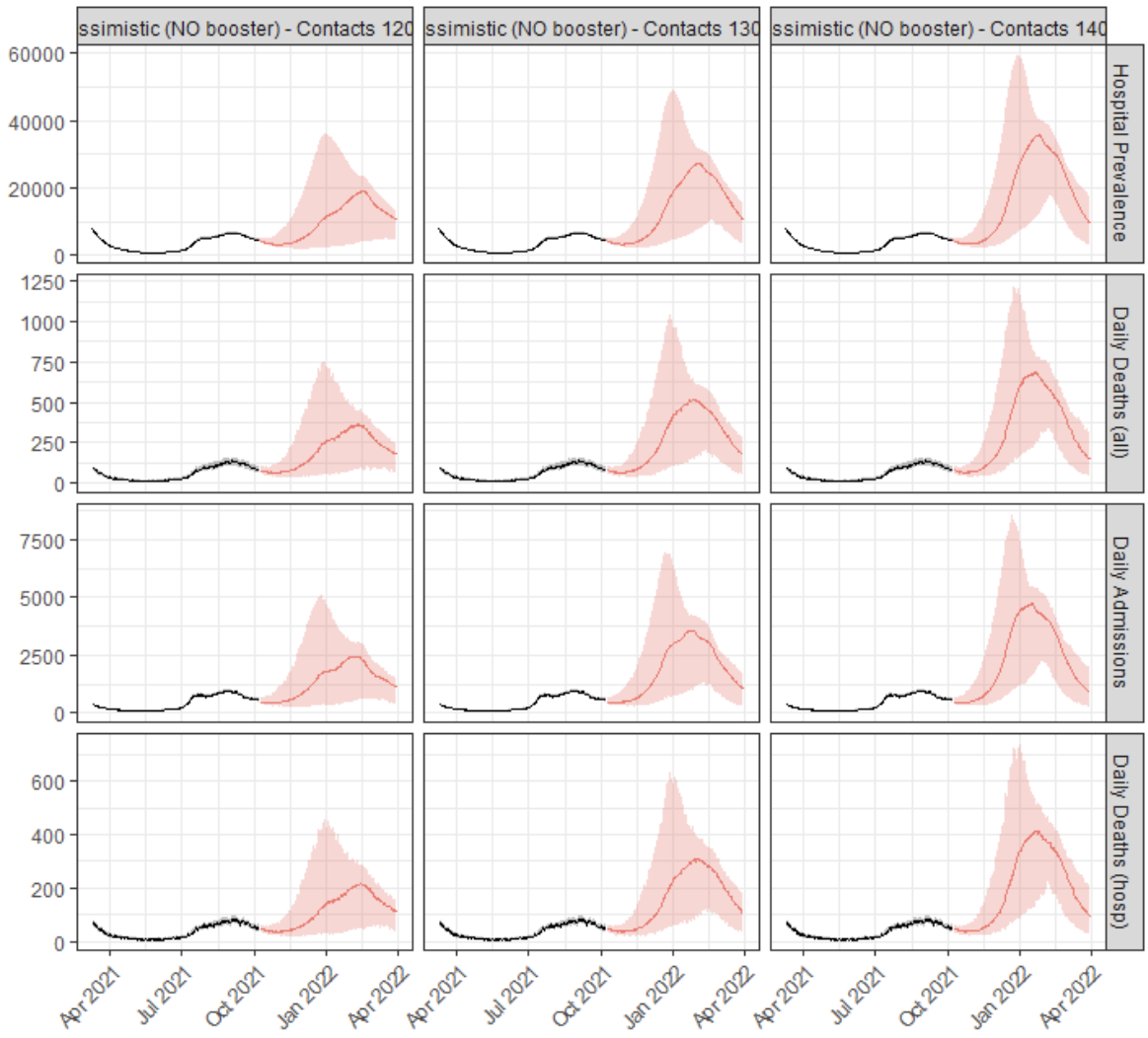

Figure S6: COVID-19 England daily (top row) hospital occupancy, (second row) all daily deaths, (third row) daily admissions, and (bottom row) daily hospital deaths over time under our "pessimistic" VE and immunity assumptions with vaccination of 12-15 year olds but *without* booster doses (see Table 1). The black line and grey shaded area shows the model fit and 95% CrI to the past data, the red solid line the median projection, and the red shaded area the 95% CrI. From left to right assuming contacts increase gradually between 8 October to 1 December 2021 to (left) 120%, (middle) 130%, and (right) 140% of current levels. Note this plot is based on 100 particles rather than 200 used for all other plots.

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