# Projections of SARS-CoV-2 transmission and COVID-19 disease until June 2022: the action of waning efficacy and boosters

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## Executive Summary

1. We consider the likely epidemic trajectory into the first half of 2022, using data up to 8th October. This is modelled for the seven NHS regions of England and then the data are combined, although regional heterogeneities are also considered.

2. We find that further waves of infection cannot be excluded and there remains considerable uncertainty about the long-term dynamics.

    (a) Most of the scenarios considered project a slow decline in hospital admissions and deaths throughout the remainder of 2021.

    (b) A continuation in the observed decline in vaccine efficacy can generate very large-scale waves of hospital admissions in the next four to eight months, which can be further exacerbated by high levels of seasonal forcing. These could be tempered by either giving boosters to younger age groups hence pushing the population closer to herd immunity, or by giving additional boosters to older age groups to maintain high efficacy.

    (c) In contrast, vaccine efficacies that remain at a high asymptotic level of protection result in a continual decline in hospital admissions between now and June 2022.

    (d) A more gradual return to pre-COVID mixing patterns pushes the epidemic waves to later in 2022.

3. We highlight three key uncertainties that impact the projected dynamics.

    (a) Data from a number of sources highlights the waning of vaccine efficacy over the medium term, especially for older individuals, but data on longer-term protection (6 months post second dose) is limited. Here we have used three sets of assumptions that capture the medium term behaviour but differ over longer time-scales. Similarly, while trial data on third doses (boosters) highlight their immunological benefit, the resultant vaccine efficacy and period of waning is again unknown and hence we consider two extremes of potential behaviour.

(b) The future behaviour of the population is largely unknown and forms one of our key uncertainties. The massive impact of gatherings associated with the EURO 2020 football, the subsequent "pingdemic" and summer music festivals, all highlight the sensitivity of infection levels to changes in behaviour. We model a gradual return to pre-COVID mixing levels, but note that individual events or national perturbations can overwhelm this pattern for short periods.

(c) Finally, we still have limited information on seasonality - here modelled by a sine-wave based change in transmission with a peak of transmission in February and a minimum in August. The amplitude of this variation has not been quantified and may depend on a range of external factors.

4. Four major changes have been made to the model structure since the previous assessment of the roadmap (12th July 2021):

(a) vaccine efficacy is assumed to wane over time, dropping to a lower asymptotic level with three assumptions (high, medium and low) considered;

(b) booster doses are included for the over 50s, with two assumptions (repeated waning of efficacy and long-term immunity as pessimistic and optimistic extremes) used for the action of booster vaccines;

(c) the model now allows different levels of precautionary behaviour in the younger and older population, corresponding to different hesitancy in returning to pre-COVID mixing;

(d) vaccination of 12-15 year olds is included, but is modelled separately from the normal program due to the within-school delivery mechanism.

In keeping with the previous roadmap document, we again recognise the uncertainty in human behaviour and consider a range of times for population mixing to return to pre-COVID levels (from December 2021 to June 2022).

5. The model does not account for multiple factors which could impact the projections:

(a) waning immunity after infection is not included, which affects our ability to make very long-term predictions;

(b) vulnerable risk groups are not explicitly modelled. Risks, behaviour and vaccine uptake are an average across all individuals in the 5-year age-groups that are the foundations of the population structure;

(c) although we recognise that there is likely to be spatial heterogeneity at relatively small scales during the third wave, the model operates and is parameterised with information from the seven NHS regions. Vulnerable areas may exist where vaccine uptake has been low, although identifying these is contingent on accurate population estimates;

(d) our methodology is formulated around deterministic differential equations which work well for large populations and significant levels of infection, but a stochastic approach may be needed if we approach exceedingly low levels of infection;

(e) finally, the model is unable to address either changing patterns in individual behaviour with changes in perceived risk or the finer nuances of control measures, as both of these are translated into a single parameter that captures the impact of NPIs and precautionary behaviour at the population scale.

# 1 General Methodology and Key Uncertainties

This work uses the model that has been developed in Warwick over the past 18 months [1, 2] and matched to a variety of epidemiological data [3]. The model operates and is fitted to data from the seven NHS regions in England and the three devolved nations; here we mainly present results for England (aggregating output from the seven NHS regions) but similar analyses for the devolved nations are given in the appendices. The results of this model have been presented to SPI-M and SAGE on a number of occasions, and the model has been used to examine short-term and medium-term projections as well as reasonable worst-case scenarios. Key to the fitting of the model to epidemiological data is the temporarily varying level of precautionary behaviour which modulates the population level mixing. The model has previously been extended to include vaccination, initially to investigate priority ordering and has subsequently increased in complexity to include two-dose schedules and multiple actions of vaccine protection [2]. It also used the ratio of S-gene positive to S-gene negative PCR results to infer the spread of the Alpha (B.1.1.7) variant (which is S-gene negative on TaqPath system) at the end of 2020, and the more recent spread of the Delta (B.1.617.2) variant (which is S-gene positive) during April and May in 2021.

Four substantial changes have been made to the model structure since the last roadmap document in July 2021. Firstly, we now allow differential precautionary behaviour between older (over 60) and younger individuals (under 40) from May 2021 onwards. This mimics the observation that those attending secondary school and in their 20s and 30s are likely to be less cautious in their mixing behaviour than individuals over the age of 60. For those aged 40-59, transition between lower and higher levels of precautionary behaviour is gradual and monotonic with age. The second major change is that vaccine efficacies are now allowed to wane over time, this is performed by moving vaccinated / recovered individuals to a new category with lower levels of protection. (It is possible for immunity due to natural infection to wane within the model but this waning is set to zero throughout this document due to lack of data; when both infection and vaccination has occurred the protection due to infection takes precedence.) Figure 1 (and Table 1) shows three examples of lower vaccine efficacy that were chosen together with the resultant dynamics since vaccination, in comparison to recent PHE results. To counteract this waning, we now include the on-going booster programme which elevates protection in those offered their third dose of vaccine, described in more detail in section 3. We also include vaccination of school pupils aged 12-15, matching recent changes. Finally, parameters describing risk of hospitalisation from Delta and the distribution of length of stay are updated in keeping with the latest data.

**Table 1:** Vaccine efficacy assumptions. (∗=assumption to due lack of available data, † measures the reduction in onward transmission conditional on infection.)

| Efficacy | Pfizer 2nd Dose | AstraZeneca 2nd Dose | Waning VE Assumption 1 | Waning VE Assumption 2 | Waning VE Assumption 3 |
|---|---|---|---|---|---|
| **Infection** | 85% | 70%∗ | 50%∗ | 30%∗ | 0%∗ |
| **Symptoms** | 90% | 70% | 55%∗ | 35%∗ | 10%∗ |
| **Hosp Adm** | 95% | 95% | 85%∗ | 79%∗ | 70%∗ |
| **Mortality** | 98% | 98% | 85%∗ | 79%∗ | 70%∗ |
| **Transmission†** | 30%∗ | 30%∗ | 20%∗ | 20%∗ | 20%∗ |

Vaccine uptake within the model to date mirrors the recorded data in terms of dose and age of those vaccinated (although data on booster doses is not yet available). Projecting forwards, we now include: the first dose vaccination of 16 and 17 year olds as part of the national roll-out; the first dose vaccination of pupils age 12-15 as a school-based programme; and the delivery of booster vaccines to the over 50s and vulnerable in line with the latest JCVI guidance. It is worth noting that while the model

explicitly captures age-structure within the population, it is not structured in terms of vulnerability (which would double the model dimensionality), therefore the impact on hospital admissions due to boosting the vulnerable group will be greater than predicted by the model.
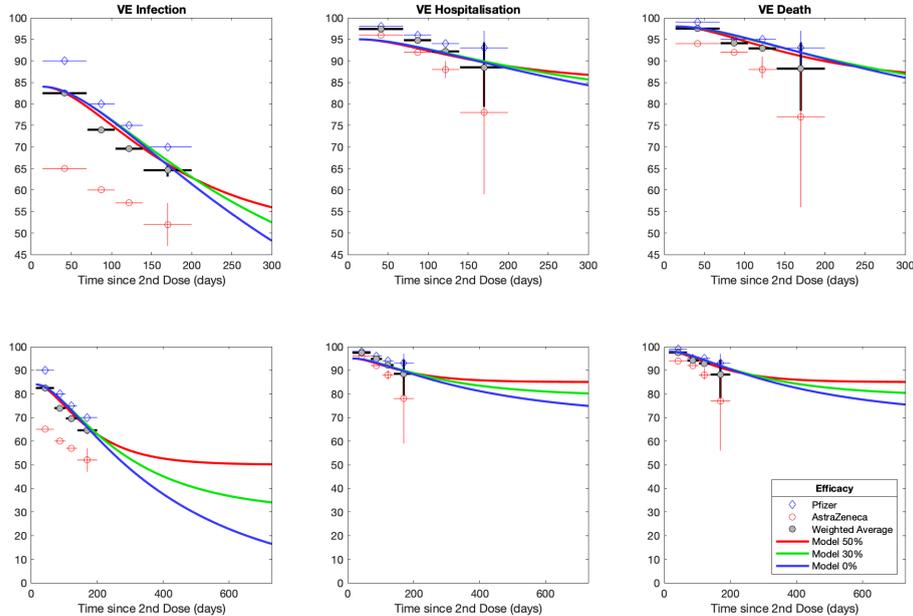


**Fig. 1:** Assumptions about waning vaccine efficacy. The markers show preliminary data from PHE (Vaccine effectiveness update, Pillar 2 data – Test Negative method) : blue diamond, Pfizer vaccine; red circle, AstraZeneca; grey circle, weighted average based on doses administered. The horizontal lines around each point show the time-scale of the data samples, vertical lines are the 95% confidence intervals. The three lines show three exemplar fits to the weighted average that are used throughout this document which, from top to bottom, asymptote to 50% (red), 30% (green) and 0% (blue) vaccine efficacy against infection (we note that the first 14 days post second dose is not shown as the model assumes it may take this long for the maximal level of protection to establish). We give asymptotic vaccine efficacy against Symptoms, Hospital Admissions and Mortality in Table 1. The upper row of figures are plotted over a shorter time-scale and a reduced y-scale to better illustrate the fit to the data.

Future vaccine rollouts follow a Cabinet Office Scenario with an average 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 who are being vaccinated through schools. In addition we assume a low level of first doses (approximately 10,000 a day) continue to be administered. We have assumed that 75% of pupils age 12-15 will accept the offer of a vaccine, and that 90% of those that received a second dose of vaccine will accept a booster. In keeping with JCVI recommendations, those aged 12-17 are only being given a single dose initially and booster doses are only given 6 months after the second dose.

We have accounted for changes in behaviour and restrictions over time, by inferring the effective level of protective behaviour (e.g. social distancing, mask use, avoiding high-risk settings, working from home) acting at the population scale (and hence capture changes to population-level mixing): we term this precautionary behaviour, $\phi$. We stress that the level of precautionary behaviour is actually a combination of restrictions, recommendations and behavioural changes that reduce the amount of population mixing relevant for transmission; this is scaled such that $\phi = 1$ corresponds to highly restrictive lockdown controls and $\phi = 0$ corresponds to a return to pre-pandemic behaviour. However, as shown in Fig. 2, changes in policy do not generate immediate changes in behaviour (with the notable exception of lockdowns which seem to precipitate larger and faster changes); for example, relaxation over the summer of 2020 was gradual and may have begun before the official end of the first lockdown,

while the dynamics in June and July of 2021 (Step 3 and 4 of relaxing restrictions) are impacted by gatherings to watch the EURO 2020 football and the subsequent "pingdemic".
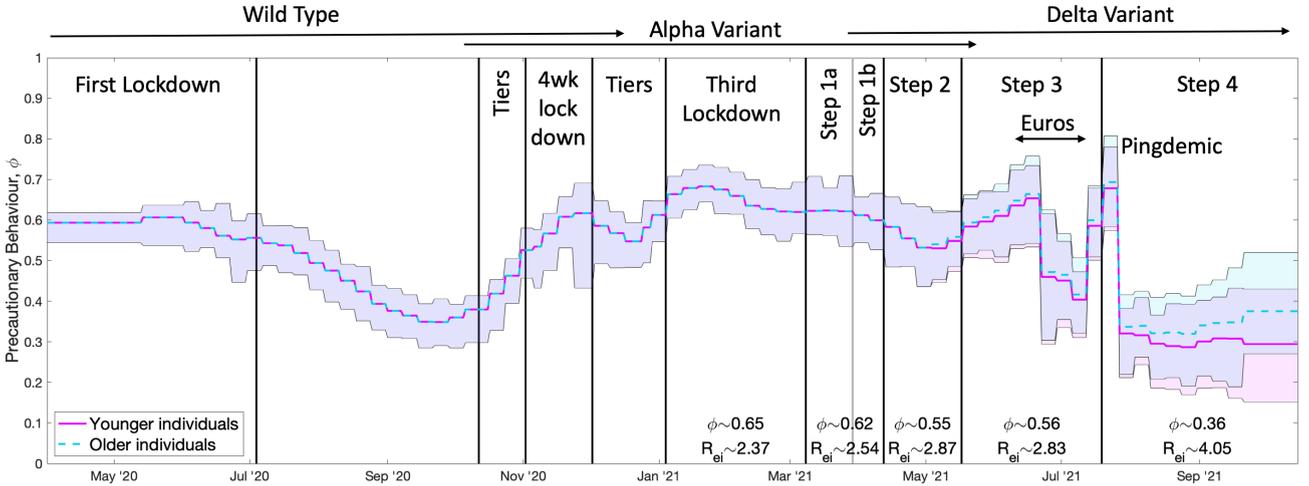


**Fig. 2:** Inferred precautionary behaviour, $\phi$, over time together with the different periods of restrictions and the variants in circulation. Solid lines show the mean values while shaded areas cover the 95% credible intervals (amalgamated over all three waning vaccine efficacy assumptions); mean values of $\phi$ and the associated value of $R_{ei}$ for the Delta variant over the different periods in 2021 are written on the lower part of the graph. Where $R_{ei}$ the value of $R$ excluding immunity is calculated from the growth rate with a given level of precautionary mixing but assuming everyone is susceptible to infection (see Fig. 3). The pink line shows the inferred values for the younger population (less than 40) while the light-blue dashed line shows the inferred values for the older population (over 60), with the two assumed equal before May 2021. (Ages between 40 and 60 take values between the two inferred levels, increasing with age.) Values of $\phi$ are generally assumed to vary slowly (exceptions are set based on observed behaviour such as the EURO 2020 football tournament and subsequent pingdemic) and remain constant over a week.

In general there has been a gradual decline in the level of precautionary behaviour since the 2021 lockdown (January-March 2021), dropping from around $\phi = 0.65$ to $\phi = 0.36$ over around six months
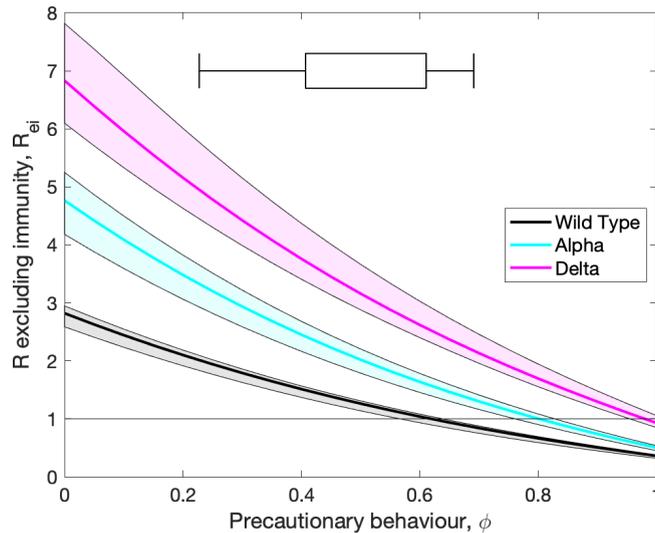


**Fig. 3:** Inferred values of $R$ excluding immunity $R_{ei}$ against the level of precautionary behaviour, $\phi$, for the wild type virus and two main variants of concern: Alpha and Delta. The line is the mean value while the shaded regions show 95% prediction intervals. The horizontal error bar shows the 95% and 50% interval on values of $\phi$ since 23rd March 2020.

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(Fig. 2), although the inferred drop for older individuals is less. We expect this trend of gradual decline to continue (especially if there are no further large spikes in hospital admissions or deaths), however the speed of decline is unknown. In the simulations that follow we consider a range of declines where the level of precautionary behaviour hits zero (and therefore mixing returns to pre-COVID levels) between December 2021 and June 2022. (We note that the values of precautionary behaviour shown in Fig. 2 are an amalgamation of inferred values for the three different assumptions about waning vaccine efficacy shown in Fig. 1. The waning assumptions naturally affect the predicted infection dynamics, and therefore different levels of precautionary behaviour are required to match the observed behaviour to date; waning to lower efficacy (blue line) requires more precautionary behaviour to maintain the same epidemic profile. The effects of the waning efficacy assumptions on the inferred levels of precautionary behaviour are shown in Appendix 1.)

School holidays are modelled by changing the mixing patterns for school-aged children, and we include all school holidays (half terms, Christmas, Easter and Summer holidays) over the simulation period. It is assumed that during school holidays pupil's precautionary behaviour matches that of adults, but during school terms this is reduced to 20% of the adult value due to the greater level of mixing that occurs within the school setting.

We measure the degree of behavioural relaxation within the population as both a change in the relative level of precautionary behaviour ($\phi$), and by computing the instantaneous growth rate ($r$) and the reproduction number excluding immunity ($R_{ei}$, Fig. 3), which can be conceptualised as the theoretical reproduction number at the start of the epidemic if such controls were in place.

## 2    Assessment of previous roadmap

The roadmap document published on the 12th July 2021 was based on data up to 2nd July 2021. Figures 3 and 4 of the roadmap document considered a range of behaviour post Step 4; these were characterised as an initial drop in the level of precautionary behaviour followed by a decline to pre-COVID levels of mixing. This generated a large envelope of projections (shown in grey) from which we selected eight scenarios (shown by coloured lines). The roadmap document also focused on three different assumptions about vaccine efficacy (default, cautious and optimistic). Here we compare these roadmap scenario projections against the available data up to 8th October 2021 (Fig. 4, default efficacy assumptions only). In this figure, the data that were used to infer model parameters are shown in blue, while the subsequent data are shown in yellow. From these graphs it is clear that the data fall below the worst case scenarios considered in the Roadmap, suggesting that any change in mixing has been gradual.
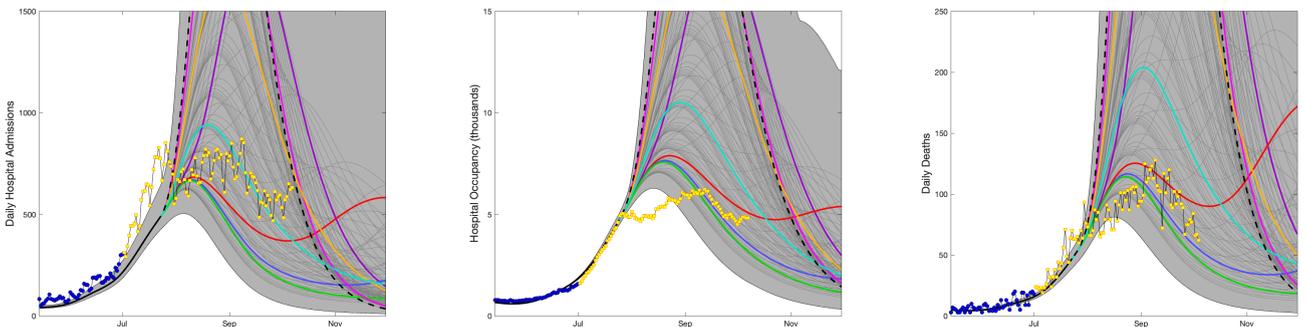


**Fig. 4:** Projections from the July Roadmap document using the default vaccine efficacy assumptions, together with the corresponding data (blue for data using in parameter inference for the roadmap, yellow for data since that time). The graphs show daily hospital admissions (left), hospital occupancy (middle) and daily deaths (right) for the whole of England.

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*Hospital Admissions* (left hand graph of Fig. 4): Hospital admissions show an unexpected rise in July followed by a sharp drop; this inversely correlated with the inferred precautionary behaviour (as in Fig. 2) but lagged by 7-10 days and therefore likely linked to large gatherings during the EURO 2020 football championships and the subsequent pingdemic. Throughout August and September, the data lie between the red and cyan curves, which correspond to a moderate decline in precautionary behaviour over the time period. We expect the data to continue to lie within the envelope of predicted behaviour for the next 2-3 months.

*Hospital Occupancy* (centre graph of Fig. 4): The roadmap projections significantly overestimated hospital occupancy in August. This is attributable to the observed shorter average length of stay for younger individuals and those infected with the Delta variant, neither of which was included in the original model projections, but are included within the most recent version of the model. Including these factors reduces the projections of hospital occupancy, in line with observations.

*Deaths* (right hand graph of Fig. 4): The previous roadmap projections again perform reasonably well at capturing deaths due to COVID-19, although the data during August generally lies within the lower envelope of scenarios, corresponding to a slow return to full social mixing (at least by those subject to the highest rates of mortality).

We clearly have not seen the very large-scale outbreaks that were considered feasible in the Step 4 scenarios (pink and dashed black lines); precautionary behaviour has not dropped as dramatically as was considered possible and the population has not returned to pre-COVID mixing. Given the large number of infections that have occurred during the summer months of 2021 and the additional amount of vaccine that has been delivered, it is now impossible to reach the highest levels that were projected as worst-case scenarios in the roadmap (without waning immunity or waning vaccine efficacy).

# 3 Exploration of Future Dynamics

We now project the fitted model forwards until June 2022, and focus on the number of hospital admissions across the seven NHS regions of England. We perform this calculation across the posterior set of parameters and for three assumptions about waning vaccine efficacy, two assumptions about booster vaccination and seven assumptions about declining precautionary behaviour (Fig. 5). The three waning vaccine efficacy assumptions are illustrated in Fig. 1, with asymptotic vaccine efficacy against infection set to 50% (red), 30% (green) or 0% (blue) - such that the red curves are associated with the highest levels of long-term vaccine efficacy. The two booster assumptions are that either: (i) the booster vaccine generates elevated levels of protection (VE against infection ∼90%, slightly higher than after the second dose) which wanes in a similar manner and over a similar time-scale to two doses of vaccine, this is shown in the central column of Fig. 5; or (ii) the booster vaccine generates complete protection (VE=100%) which does not wane over the time-scale of the scenarios considered, shown in the right-hand column of Fig. 5. Finally, we force the level of precautionary behaviour, $\phi$, to drop from its current value to the pre-COVID level of zero between October 2021 and dates between December 2021 and June 2022 (left-hand column in Fig. 5).

We gain four main insights from this analysis:
Firstly, that the asymptotic waning of immunity is potentially the key uncertainty (colours in Fig. 5). Waning to just 50% vaccine efficacy against infection (red lines) never generates large waves of hospital admissions in any of the scenarios considered; in contrast waning (over longer time scales) to 0% efficacy against infection (although still 70% efficacy against hospitalisation, blue lines) can generate large-scale outbreaks with considerable pressure on hospitals if there is either a rapid return to pre-COVID mixing (top row) or the action of boosting also wanes (central column).
Secondly, the action of boosters plays an important longer-term role (columns 2 and 3). While there
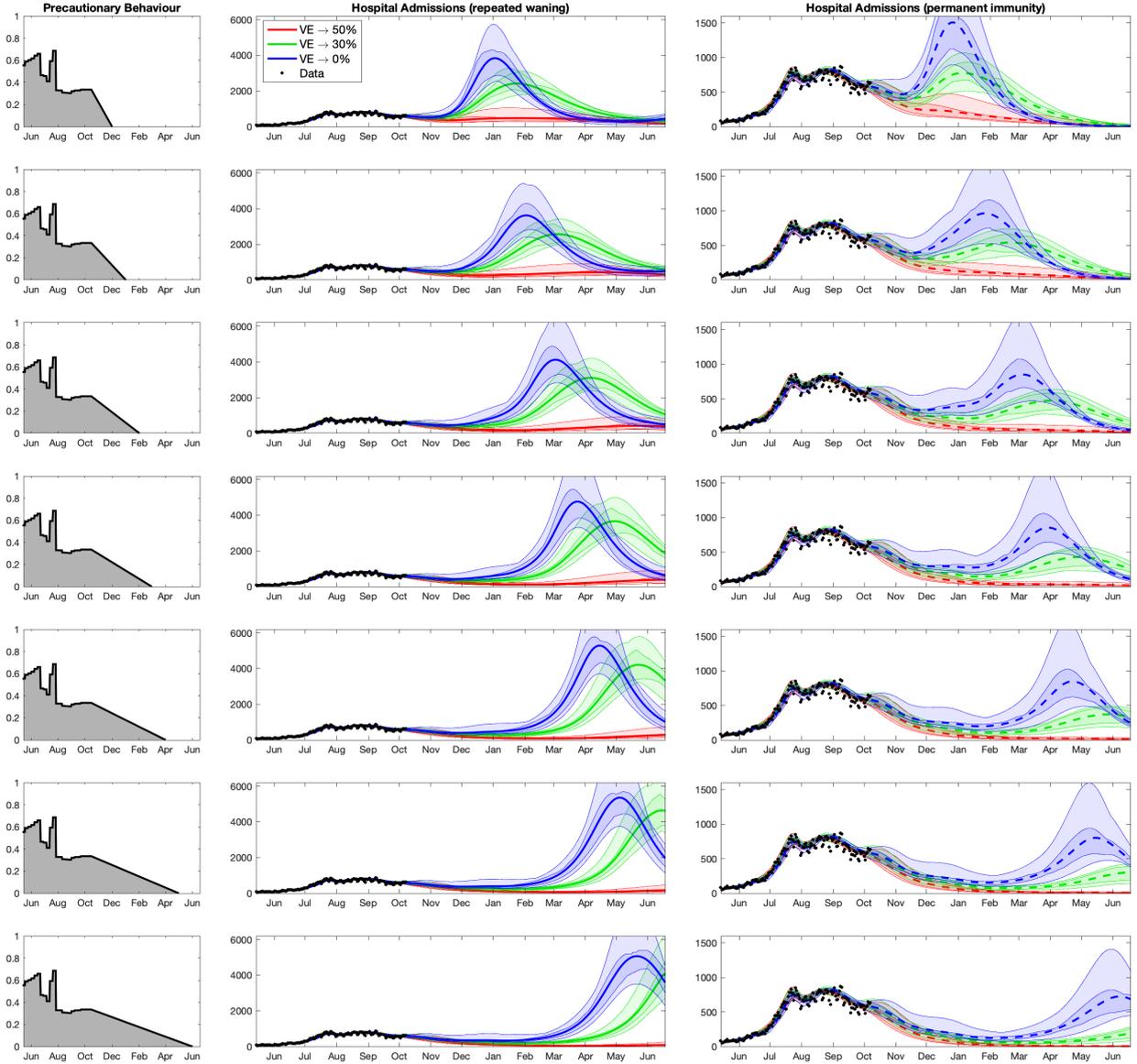
**Fig. 5:** Projected dynamics of hospital admissions with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows). Simulations include waning vaccine efficacy, booster vaccination, vaccination of children and seasonality at 10%. Left-hand column shows the level of inferred precautionary behaviour and the assumed decline, which is the same for all projections in a given row. Central column assumes that following the booster vaccine protection is raised to approximately 90% VE against infection, but this efficacy then wanes over similar time-scales to those assumed following second doses. Right-hand column makes the optimistic assumption that the booster vaccine provides 100% VE against infection, which does not wane over the time-scales being considered. Results are for the whole of England from combining projections for the seven NHS regions, shaded areas give the 50% and 95% prediction interval while the lines correspond to the mean value; black dots show the data to 8th October 2021. (Note that the central and right hand columns have different y scales to better illustrate the dynamics.)

exists immunological assessments of the impact of booster doses (which suggest high levels of protection) there are no corresponding estimates of vaccine efficacy nor the duration of protection. A situation in which the action of boosters again wanes (in a similar way to initial doses) leads to a perpetual cycle (central column, Fig. 5), whereas if boosters provide stronger and more long-lasting

protection then they will offer longer-term suppression of future waves (right-hand column, Fig. 5). As expected and echoing the results of the last roadmap document, a slow decline in precautionary behaviour (lower rows in Fig. 5) has a pronounced impact on the dynamics, pushing any possible peaks to later times and therefore providing more time for additional measures if necessary. In the model we have now split our precautionary behaviour into two age-based values; if the observed slower decline in the precautionary behaviour of the elderly continues for longer it could reduce some of the highest hospitalisation peaks by around 15% but does little to reduce the level of infection which is driven by younger ages.

Finally, there is a surprising interaction between booster assumptions and the decline in precautionary behaviour. When there is repeated waning of efficacy after boosting (central column), the later waves caused by a slower decline in precautionary behaviour (lower rows) are larger than earlier waves (upper rows). This is due to the increase in population susceptibility over time, such that later outbreaks have more susceptible 'fuel' compared to earlier outbreaks. However, a more rapid decline in precautionary behaviour coupled with repeated waning (top row, central column) will generate additional subsequent waves potentially before the end of 2022 (see Appendix 2). Tabulated cumulative numbers of projected deaths and hospital admissions are also given in Appendix 2. Comparable results for hospital occupancy, deaths and the number of new infections are given in Appendices 3-5; hospital admissions projections for the devolved nations are given in Appendices 7-9.

These results suggests that very careful monitoring of vaccine protection following boosters is required to better understand long-term patterns of protection. In part this should be achievable through monitoring of the age-structure and vaccine status of hospital admissions and cases (although noting that cases are biased by testing behaviour). The large waves projected under the pessimistic assumption for boosters (central column, Fig. 5) could be reduced by either giving boosters to younger age groups (e.g. those 18-49) hence pushing the population closer to herd immunity, or by giving additional boosters to older age groups to maintain high efficacy in the most vulnerable.

To gain a better understanding of the drivers of the patterns, we consider the age-structured dynamics (Fig. 6) for four extremes of behaviour and waning assumptions (corresponding to the top and bottom row and red and blue lines in Fig. 5), and assuming waning of vaccine efficacy after boosting (central column in Fig. 5). (Similar results for the situation where immunity after boosting is permanent are given in Appendix 10.) In all scenarios considered, it is the youngest age-group (0-9, darkest blue) that dominate infection, but the older age-groups (70+, yellow, orange and red) that dominate hospital admissions, although the proportions are subtly different between scenarios. For the assumption where the asymptotic level of vaccine efficacy is high (red lines in Fig. 5, columns 1 and 2 in Fig. 6), a more rapid decline in precautionary behaviour (comparing column 1 to column 2) leads to a slightly protracted wave of infections into early 2022 but a more notable wave of hospital admissions. The more rapid decline leads to a greater dominance by older individuals particularly in terms of hospital admissions, with the 2022 wave predominantly in the over 60s.

When vaccine efficacy can wane to zero (blue lines in Fig. 5, columns 3 and 4 in Fig. 6) then a large wave in 2022 is projected, with its timing related to the decline in precautionary behaviour. When the decline in precautionary behaviour is rapid (hitting zero in December 2021, column 3 of Fig. 6) then we project a large peak of infections and hospital admissions in late 2021 and early 2022. Infections in this wave are increasingly in older age groups (compared to the wave in July-August 2021) due to waning vaccine efficacy, although those under 40 still account for more than half of all infections. Hospital admissions show an even more pronounced peak in early 2022; this is generally dominated by older age groups, as expected, but there is a slight rise in hospitalisation of intermediate age-groups (50-69). The patterns for when precautionary behaviour declines slowly (column 4 of Fig. 6) are similar although the peaks are later, with the hospital admissions peak being substantially larger and with a greater proportion in the older age groups – the later timing of the wave has given more time
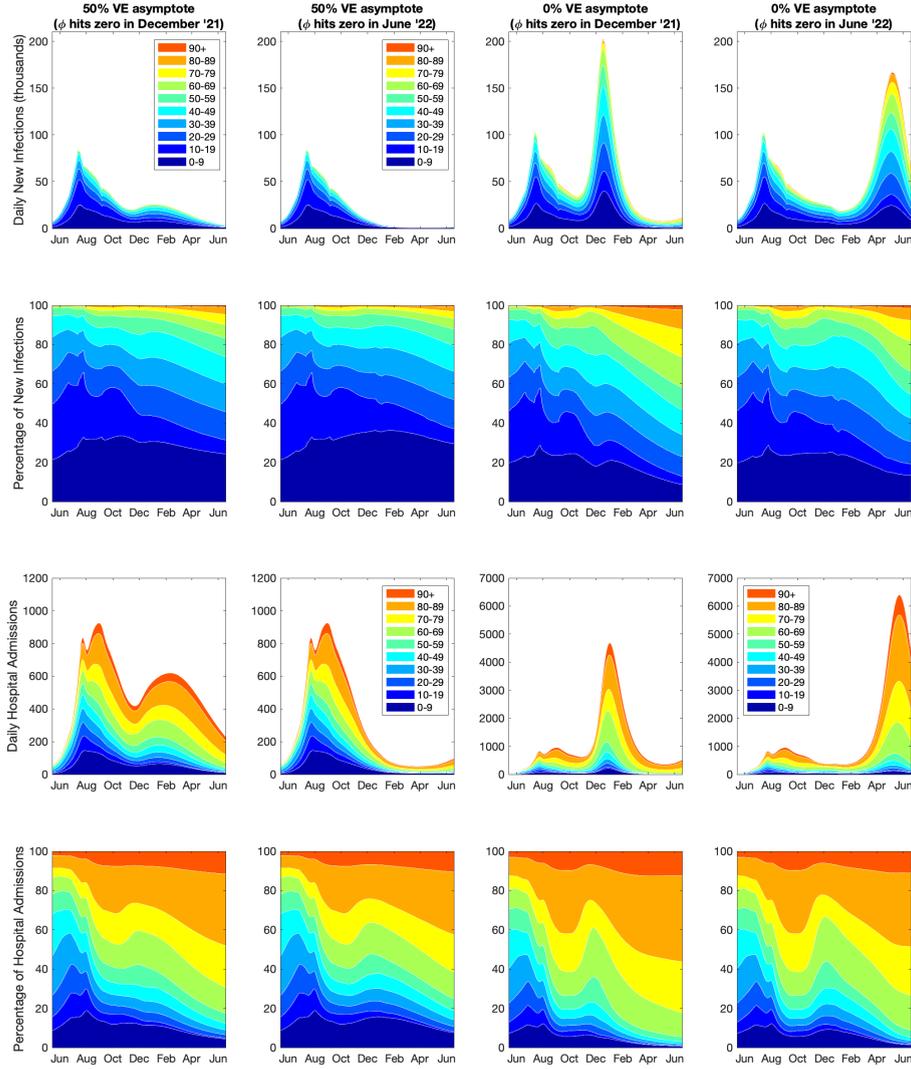
**Fig. 6:** Age structured dynamics of infection and hospital admissions under the assumption that vaccine efficacy wanes after boosting. Columns 1 and 2 correspond to optimistic assumptions about waning efficacy with the asymptotic level of vaccine efficacy against infection set at 50%; columns 3 and 4 are more pessimistic assumptions in which vaccine efficacy eventually reaches 0%. In columns 1 and 3 we force the precautionary behaviour, $\phi$, to decline to zero by December 2021, whereas in columns 2 and 4 $\phi$ does not reach zero until June 2022. Row 1 is the number of new daily infections; row 2 is the percentage of new infections in each age group; row 3 is the number of daily hospital admissions (notice the different y-scales to capture the full dynamics); while row 4 is the percentage of admissions in each age group. Colours scale from blue (bottom) to red (top) in increasing 10-year age bands.

for vaccine efficacy to wane, even after boosting.

## 4  Implications of Seasonality

The Warwick model has generally set seasonality at 10%, which we have taken to mean that the trough in transmission (in mid August) is 10% lower than the peak of transmission (in mid-February). This is in agreement with assessments from other coronaviruses, but a range of assumptions exist in the literature. Here we consider sensitivity to alternative assumptions, where seasonality smoothly increases from the current time onwards.
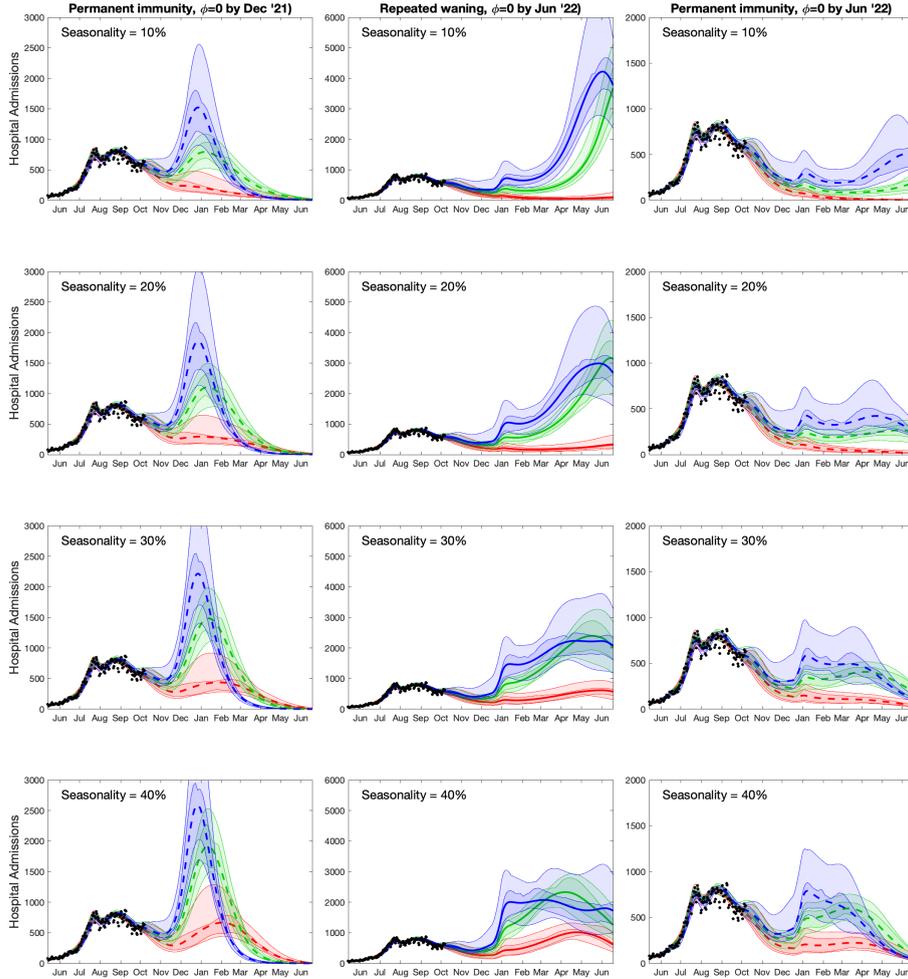
**Fig. 7:** Implications of seasonality on the number of daily hospital admissions. The colours are the same as in Fig. 5: red corresponds to an asymptotic VE of 50%, green an asymptotic VE of 30% and blue an asymptotic VE of 0%; dashed lines refer to highly protective boosters that do not wane over the time-scales considered whereas solid lines refer to boosters that wane in a similar manner to second doses. Column 1 is when the precautionary behaviour decays to zero by December 2021 (comparable to the top row of Fig. 5), columns 2 and 3 are when precautionary behaviour decays to zero by June 2022 (comparable to the bottom row of Fig. 5). Seasonality increases from 10% to 40% moving down the rows; in these projections we also assume that during a two-week period around Christmas mixing returns to pre-COVID levels.

We consider seasonality levels from 10% (our default) to 40% (the maximum in the literature) (shown as rows in Fig. 7) for three different assumptions about boosters and precautionary behaviour (left-hand column: boost to 100% VE over long time-scales and return to pre-COVID mixing by December 2021; central column: boost to 90% VE with decay of efficacy and return to pre-COVID mixing by June 2021; right-hand column boost to 100% VE over long time-scales and return to pre-COVID mixing by June 2021). In these simulations we also include additional mixing over the Christmas period, such that mixing returns to pre-COVID levels for 2 weeks, which is reflected by the rise in hospital admissions in January 2021. The interaction between seasonality, precautionary behaviour and booster behaviour is again complex. For an early decline in precautionary behaviour (left-hand column), increased seasonality, modelled as increased transmission during the winter peak, leads to a greater number of hospital admissions. When precautionary behaviour declines more slowly (centre and right-hand column) greater seasonality generates an earlier peak in hospital admissions which often leads to a lower but more prolonged outbreak in 2022 with more admissions.

# 5  Summary of Sensitivity

Here we bring together the impact of seasonality with assumptions about waning vaccine efficacy and boosting, and show the number of hospital admissions each month (October - December 2021, January-May 2022). In keeping with previous figures red, green and blue bars correspond to different levels of asymptotic waning of vaccine efficacy (50%, 30% and 0% respectively), while solid and hashed bars correspond to solid and dashed lines in previous graphs relating to waning of efficacy after boosting (solid) and permanent efficacy after boosting (hashed). Each of these six assumptions is shown for a set of declines in precautionary behaviour (hitting $\phi = 0$ which corresponds to pre-COVID mixing by December 2021 to June 2022) and seasonal forcing (10% to 40%) as shown by the description below the x-axis (Fig. 8). Similar projections for the total number of deaths are given in Appendix 6.
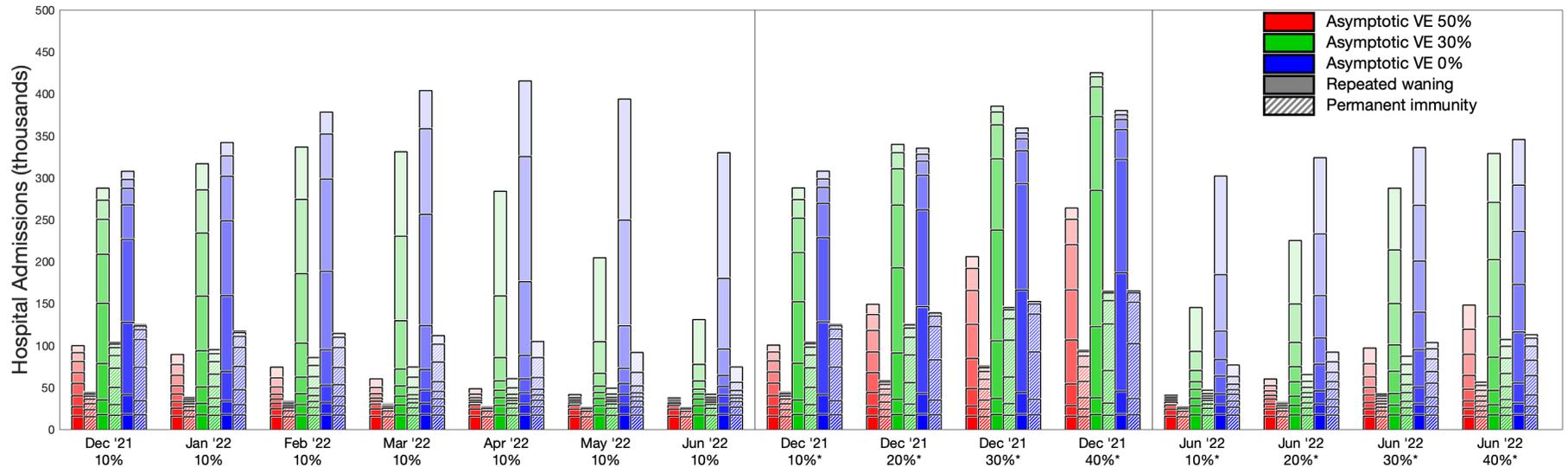


**Fig. 8:** Stacked bar graph showing the mean number of hospital admissions over the next eight months (October-December 2021, January-May 2022; each block corresponds to one month, with earliest months at the bottom). Colours refer to the level of asymptotic waning; solid or hashed refers to the action of boosting - hence each group of bars is ordered from left to right: VE→50% repeated waning then permanent immunity; VE→30% repeated waning then permanent immunity; VE→0% repeated waning then permanent immunity. The label on the x-axis gives the date when precautionary behaviour declines to zero and the strength of seasonal forcing, those with an asterisk include a return to pre-COVID mixing over a 2-week Christmas period.

These results echo and re-enforce the behaviour we have seen previously in this document. High levels of seasonality, complete waning of vaccine efficacy (blue - asymptotic level of 0%) and repeated waning following boosting (solid bars) all lead to higher levels of hospital admissions. However, the interaction with precautionary behaviour is complex, for 50% asymptotic vaccine efficacy (red bars) the total number of hospital admissions over the period declines as relaxation to pre-COVID mixing is slower, however for complete waning of vaccine efficacy (blue bars) an intermediate rate of relaxation is worst due to greater waning of immunity that has occurred by the time a late outbreak is generated.

Taken together in their worst combination, these four unknowns can lead to around 300,000 hospitalisations over the next six months (October 2021 to March 2022, Appendix 2) – greater than has been seen in any six-month period during this pandemic, although obviously such a rise in hospital admissions would not be allowed to go unchecked. In contrast, for the most optimistic combination of these unknowns we could expect less than 30,000 hospitalisations over the next nine months (October 2021 to June 2022).

# 6    Implications of Novel Variant

The UK remains vulnerable to any novel variant that can overcome existing immunity. The two major invasive variants in the UK over the past 12 months were successful due to their greater transmission potential, but as we approach high levels of immunity the advantage favours any variant that can escape from vaccine immunity and/or natural immunity. The types of large outbreak that can develop from invasion of a novel variant have already been well documented [4], and their scale is critically dependent on the degree of vaccine escape, their transmission potential and the timing (and location) of their arrival in the UK. We therefore adopt a simpler approach here, and focus on the early growth (as measured by the reproduction number, $R$) of a new variant with the same transmission rate (and other characteristics) as Delta, but with a level of (partial) vaccine escape (Fig. 9).

We calculate the reproduction number ($R$) of a novel variant arriving in the UK in early November, assuming that levels of precautionary behaviour (and testing) are maintained at current levels. The degree of vaccine escape (x-axis) is measured as the reduced level of vaccine efficacy compared to that of the Delta variant, such that a value of zero implies complete escape and a value of 100% implies the same vaccine efficacy as Delta (see Table 1). Vaccine efficacy against infection, symptoms, hospitalisation and death are all assumed to scale by the same proportion. The reproduction number
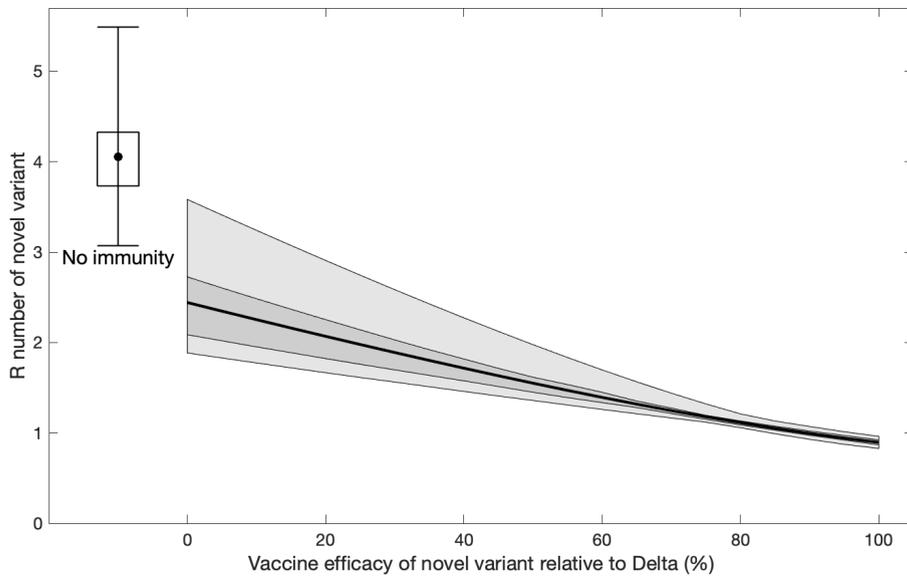


**Fig. 9:** Implications of a vaccine escape variant on the estimated $R$ number. Assuming a novel variant with partial vaccine escape properties invades the UK in November 2021, we calculate the reproductive number of this variant (under the assumption that there is repeated waning of immunity after boosting, and combining all three assumptions for the asymptotic level of vaccine efficacy). The x-axis gives the level of vaccine efficacy against the new variant compared to the Delta variant. Solid line shows the mean values, while the shaded regions are the 50% and 95% prediction intervals. For comparison, the single error bar shows the implications of a variant that completely escapes both infection-derived and vaccine-derived immunity.

increases with increasing vaccine escape (decreasing relative efficacy) such that when there is complete escape from vaccine-derived immunity $R = 2.44$ (PI 1.88-3.58), comparable to the reproduction number of $\sim 2.8$ at the start of the pandemic in March 2020. As a comparison, we also show the reproduction number for a variant which has complete escape from both infection-derived and vaccine-derived immunity ($R = 4.06$ (PI 3.07-5.49)).

The characteristics of any novel variant of concern are high-dimensional (with a range of transmission and severity parameters linked to each variant). A variant with the same transmission potential (and other characteristics) as Delta, that can also escape vaccine efficacy, will naturally invade the population and will pose a danger to those whose protection is derived solely from the vaccine (about 50% of the population, although approximately 85% of those over sixty). However, even a variant with lower transmission but a degree of vaccine escape could have a competitive advantage over Delta and generate additional cases, especially in the older more vulnerable population where vaccine-derived protection is greatest.

# Appendix 1: Inferred Precautionary Behaviour for the Three Waning Efficacy Assumptions

In the main text and Fig. 2, we considered the level of precautionary behaviour $\phi$ as the amalgamation of all inferred values for the three different waning efficacy assumptions. However, as the assumptions about vaccine efficacy change, so do all the inferred parameters - as the model must still match to the same epidemiological data. Here we separate the inferred values of $\phi$ by the underlying assumption about waning vaccine efficacy ($VE \rightarrow 50\%$ red, $VE \rightarrow 30\%$ green and $VE \rightarrow 0\%$ blue; Fig. 10)). Although we maintain the same pattern as observed for the amalgamated behaviour, there is increasing divergence during August and September 2021 as difference in population-level immunity driven by waning begin to affect the model dynamics. Higher levels of waning (blue compared to red) require higher levels of precautionary behaviour to generate a match to the observed epidemic to date.
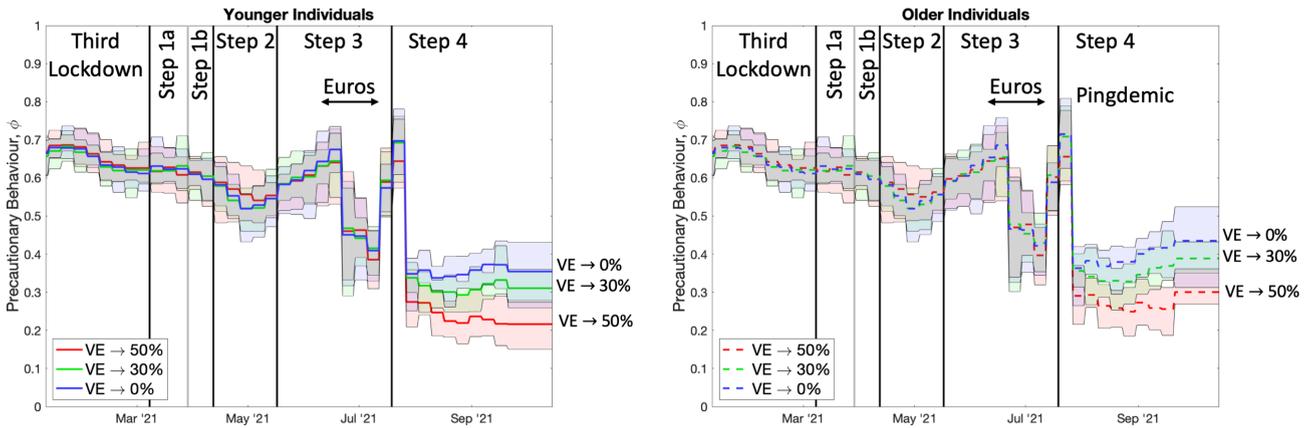


**Fig. 10:** Inferred precautionary behaviour, $\phi$, over time together with the different periods of restrictions and the variants in circulation. Lines show the mean values while shaded areas cover the 95% credible intervals; estimates are separated by the underlying assumption about waning vaccine efficacy. Solid lines on the left-hand figure correspond to $\phi$ in the younger age-groups, while dashed lines on the right (which are generally higher) correspond to $\phi$ in the older age-groups.

# Appendix 2: Longer Term Projections

Although projections over longer time scales are inherently less robust, here we extend the projections to December 2022 to illustrate the differences in dynamics due to different declines in precautionary behaviour. In extending these projections into late 2022, we also include repeat boosting of the over 50s, which may be necessary to prevent further large waves of hospital admissions. These graphs correspond to the top and bottom row in Fig. 5 but over a long time scale. Most notably for the model in which there is repeated waning of efficacy (centre column), although a slower decline leads to a larger peak of hospital admissions in mid 2022, a faster decline is projected to generate two waves in this same period.
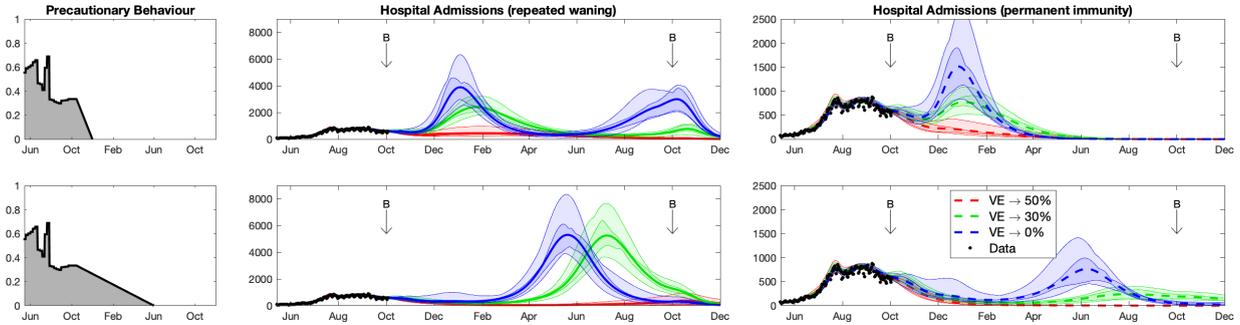


**Fig. 11:** Projected dynamics of hospital admissions with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows); these show simulations over a longer time-scale than in the main text. Simulations include waning vaccine efficacy, booster vaccination (as shown with arrows) and vaccination of children; black dots show the data to 8th October 2021.

On the following page, we also provide a table of projections over different periods and for different assumptions about booster action (repeated waning from a VE $\sim 90\%$ or permanent immunity with a VE assumed to be 100%, providing a pessimistic and optimistic view of boosters), asymptotic vaccine efficacy (matching to available data but assuming that VE eventually asymptotes to 0%, 30% or 50%) and different assumptions about precautionary behaviour (with mixing returning to pre-COVID levels by December 2021, March 2022 or June 2022). For each assumption we show cumulative hospital admissions and cumulative deaths (means and 95% prediction intervals) over three time frames.

| Assumptions | Cumulative Hospital Admissions | | | Cumulative Deaths | | |
|---|---|---|---|---|---|---|
| | Oct'21 - Dec'21 | Oct'21 - Mar'22 | Oct'21 - Jun'22 | Oct'21 - Dec'21 | Oct'21 - Mar'22 | Oct'21 - Jun'22 |
| Repeated waning, VE → 0%, $\phi = 0$ in December '21 | 124,000 (94,700-164,000) | 287,000 (212,000-376,000) | 319,000 (226,000-417,000) | 16,300 (9590-28,500) | 54,700 (31,900-80,300) | 59,900 (34,100-86,500) |
| Repeated waning, VE → 0%, $\phi = 0$ in March '22 | 46,700 (37,700-72,100) | 252,000 (184,000-341,000) | 422,000 (294,000-564,000) | 5800 (4550-10,400) | 44,700 (23,900-76,300) | 95,100 (49,700-158,000) |
| Repeated waning, VE → 0%, $\phi = 0$ in June '22 | 40,700 (33,000-62,700) | 94,700 (73,600-139,000) | 431,000 (302,000-599,000) | 5240 (4020-9120) | 11,600 (8530-22,600) | 102,000 (52,600-180,000) |
| Repeated waning, VE → 30%, $\phi = 0$ in December '21 | 77,000 (57,100-89,900) | 250,000 (200,000-310,000) | 297,000 (252,000-362,000) | 8960 (5930-11,000) | 43,700 (25,400-65,500) | 53,400 (36,100-79,800) |
| Repeated waning, VE → 30%, $\phi = 0$ in March '22 | 39,700 (29,500-48,300) | 127,000 (91,800-166,000) | 384,000 (313,000-481,000) | 5040 (3680-6080) | 17,000 (9910-24,100) | 90,100 (49,700-153,000) |
| Repeated waning, VE → 30%, $\phi = 0$ in June '22 | 36,300 (27,000-44,300) | 57,700 (39,700-71,300) | 230,000 (167,000-332,000) | 4740 (3500-5700) | 7150 (4720-9080) | 43,200 (21,200-76,600) |
| Repeated waning, VE → 50%, $\phi = 0$ in December '21 | 40,100 (28,800-62,000) | 81,000 (54,900-146,000) | 105,000 (75,100-178,000) | 5680 (4010-8430) | 12,100 (7920-19,900) | 17,000 (11,100-26,600) |
| Repeated waning, VE → 50%, $\phi = 0$ in March '22 | 30,200 (22,200-45,700) | 42,800 (29,800-66,600) | 70,700 (44,600-134,000) | 4650 (3400-7230) | 6240 (4330-9450) | 11,200 (6860-19,500) |
| Repeated waning, VE → 50%, $\phi = 0$ in June '22 | 29,000 (21,400-44,200) | 34,600 (24,600-53,600) | 40,200 (27,700-60,800) | 4520 (3330-7060) | 5260 (3730-8390) | 6060 (4200-9290) |
| Permanent immunity, VE → 0%, $\phi = 0$ in December '21 | 73,100 (57,900-97,800) | 124,000 (94,300-175,000) | 126,000 (96,800-176,000) | 8660 (6340-14,300) | 16,500 (10,600-24,000) | 16,900 (10,900-24,300) |
| Permanent immunity, VE → 0%, $\phi = 0$ in March '22 | 36,700 (30,100-53,300) | 79,900 (61,300-117,000) | 115,000 (90,000-164,000) | 4880 (3840-7890) | 8960 (6550-13,900) | 13,800 (9680-19,500) |
| Permanent immunity, VE → 0%, $\phi = 0$ in June '22 | 33,400 (27,600-48,300) | 46,700 (38,700-69,100) | 92,800 (69,800-139,000) | 4600 (3560-7300) | 5820 (4410-10,100) | 10,300 (7310-14,700) |
| Permanent immunity, VE → 30%, $\phi = 0$ in December '21 | 49,800 (38,100-58,500) | 97,700 (75,800-125,000) | 105,000 (85,000-134,000) | 5910 (4330-6870) | 11,800 (7850-14,700) | 12,700 (8920-15,600) |
| Permanent immunity, VE → 30%, $\phi = 0$ in March '22 | 32,100 (24,900-38,600) | 50,200 (37,500-61,400) | 81,900 (61,600-103,000) | 4330 (3340-5150) | 5910 (4380-6990) | 9410 (6320-11,400) |
| Permanent immunity, VE → 30%, $\phi = 0$ in June '22 | 30,200 (23,500-36,600) | 36,400 (27,000-44,100) | 47,000 (34,400-58,900) | 4170 (3230-4980) | 4750 (3530-5690) | 5630 (4160-6740) |
| Permanent immunity, VE → 50%, $\phi = 0$ in December '21 | 30,800 (22,900-45,000) | 42,600 (30,600-71,800) | 45,200 (32,300-77,800) | 4640 (3450-6610) | 5980 (4250-8150) | 6310 (4440-8830) |
| Permanent immunity, VE → 50%, $\phi = 0$ in March '22 | 25,600 (19,400-36,400) | 29,600 (21,800-42,000) | 31,800 (23,200-46,900) | 4140 (3150-6030) | 4550 (3390-6660) | 4770 (3520-6900) |
| Permanent immunity, VE → 50%, $\phi = 0$ in June '22 | 24,900 (18,900-35,600) | 27,100 (20,200-39,200) | 27,700 (20,500-40,000) | 4070 (3100-5930) | 4320 (3240-6360) | 4370 (3280-6460) |

# Appendix 3: Hospital Occupancy
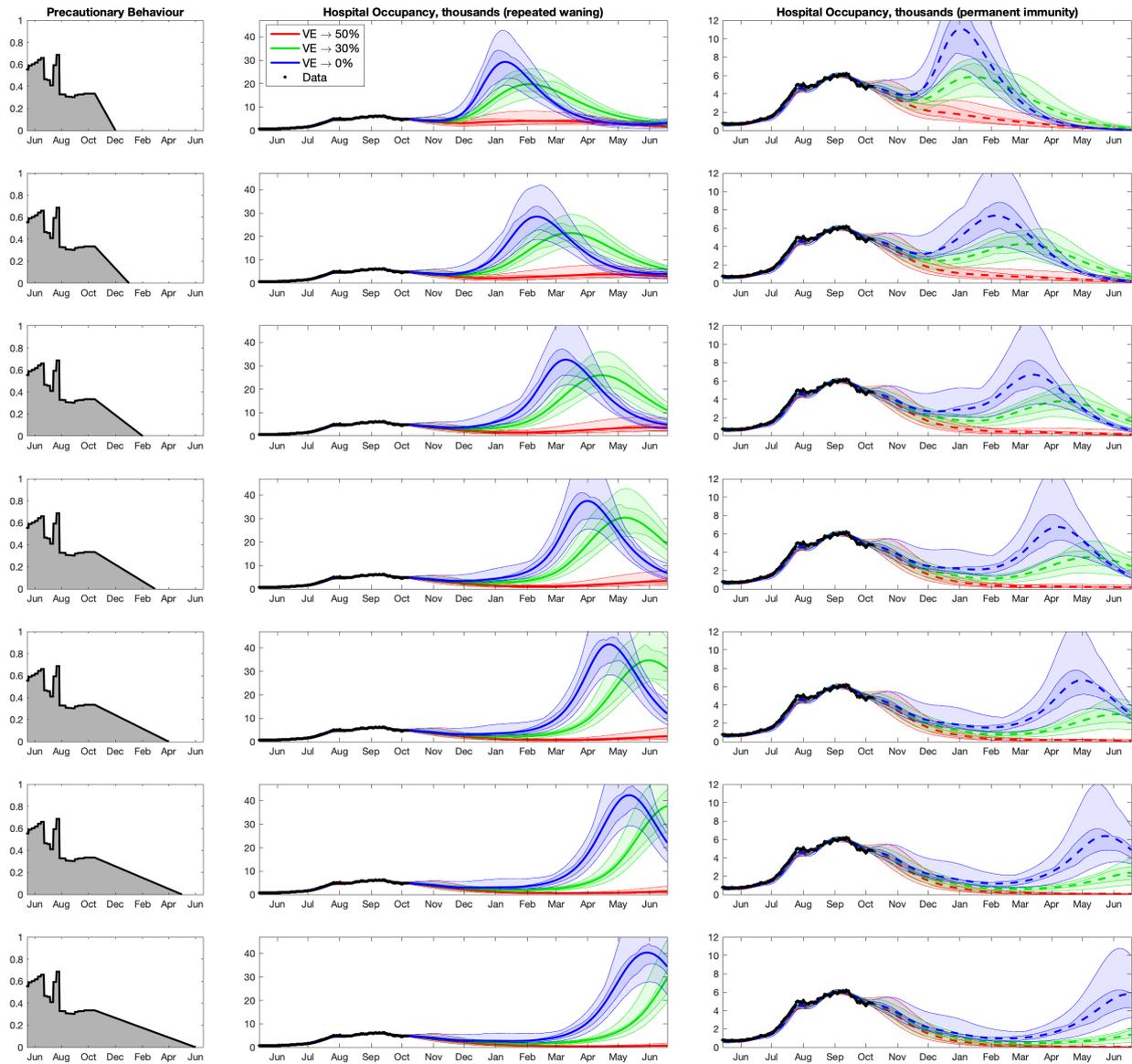


**Fig. 12:** Projected dynamics of hospital occupancy with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows). Simulations include waning vaccine efficacy, booster vaccination, vaccination of children (a single dose for those age 12-17) and seasonality at 10%. Results are for the whole of England from combining projections for the seven NHS regions, shaded areas give the 50% and 95% prediction interval while the lines correspond to the mean value; black dots show the data to 8th October 2021.

# Appendix 4: Deaths
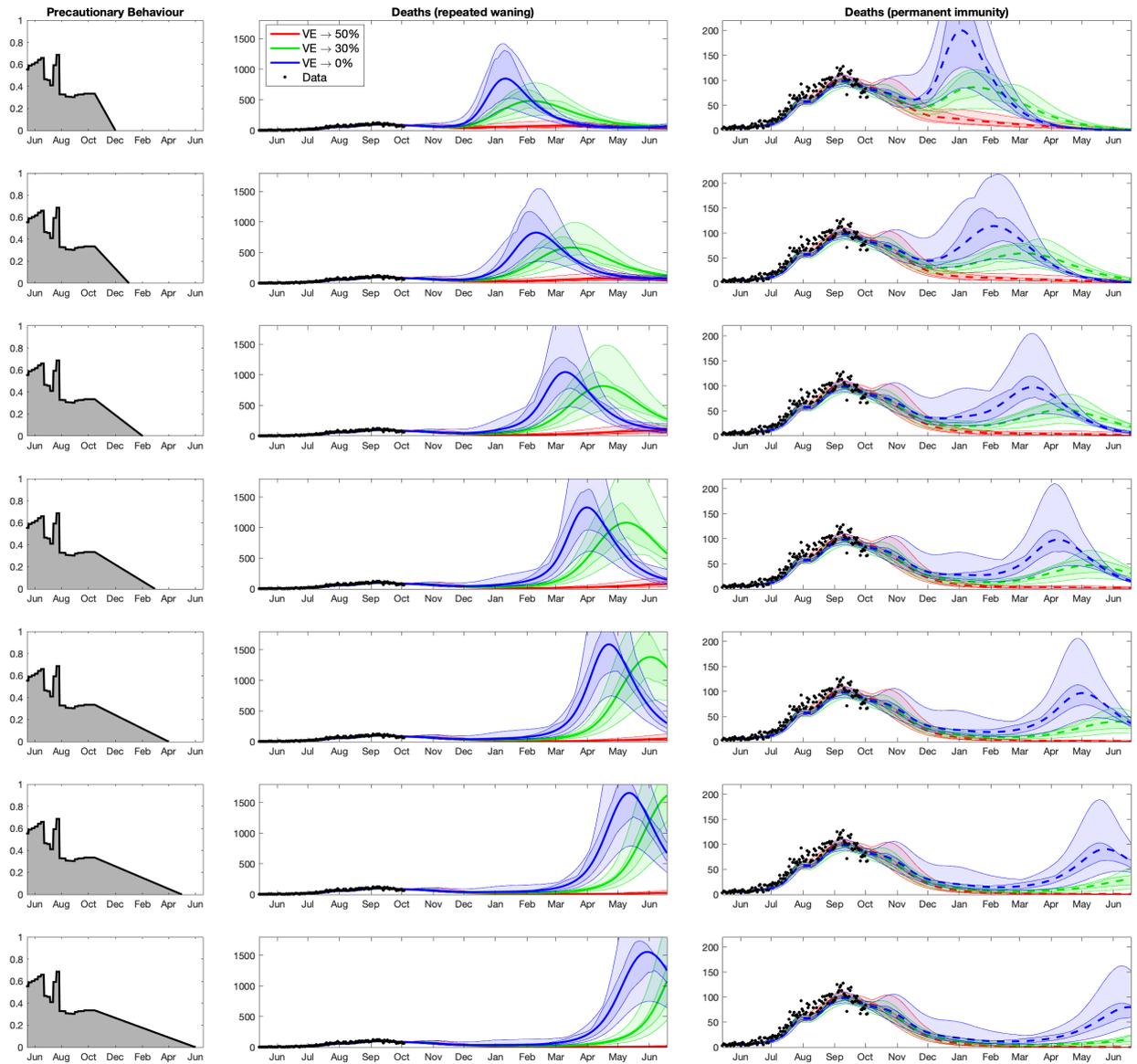


**Fig. 13:** Projected dynamics of daily deaths (within 28 days of a positive COVID test) with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows). Simulations include waning vaccine efficacy, booster vaccination, vaccination of children (a single dose for those age 12-17) and seasonality at 10%. Results are for the whole of England from combining projections for the seven NHS regions, shaded areas give the 50% and 95% prediction interval while the lines correspond to the mean value; black dots show the data to 8th October 2021.

# Appendix 5: New Infections
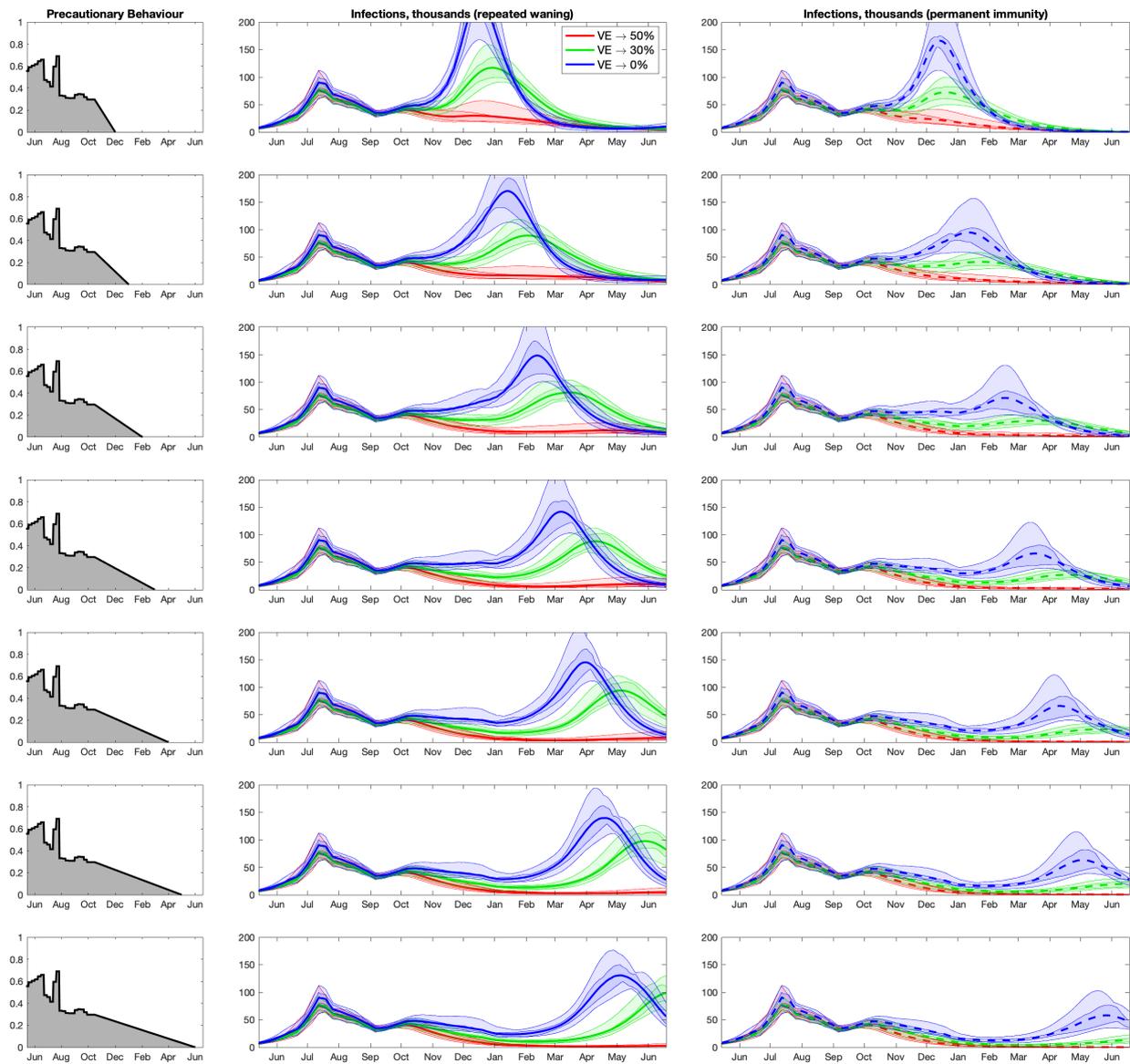


**Fig. 14:** Projected dynamics of new infections with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows). Simulations include waning vaccine efficacy, booster vaccination, vaccination of children (a single dose for those age 12-17) and seasonality at 10%. Results are for the whole of England from combining projections for the seven NHS regions, shaded areas give the 50% and 95% prediction interval while the lines correspond to the mean value; black dots show the data to 8th October 2021.

# Appendix 6: Summary of Sensitivity, cumulative deaths

This corresponds to Fig. 8 in the main text, but shows the cumulative number of deaths over the next eight months.
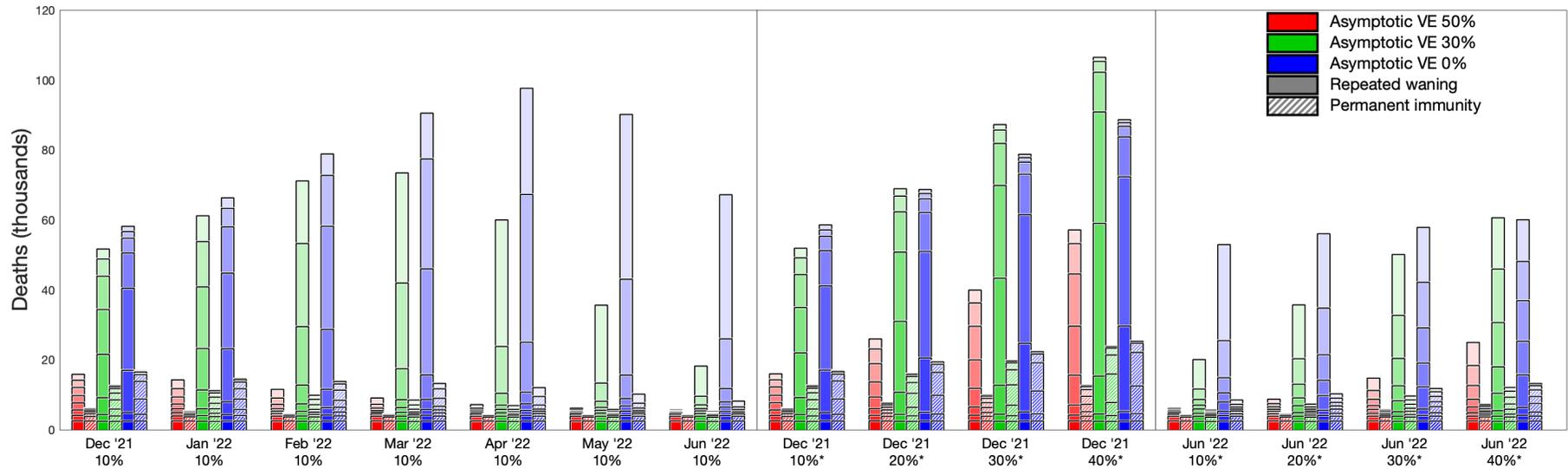
**Fig. 15:** Bars showing the mean total number of deaths over the next eight months (October - December 2021, January-May 2022; each block corresponds to one month, with earliest months at the bottom). Colours refer to the level of asymptotic waning; solid or hashed refers to the action of boosting; while the label on the x-axis gives the date when precautionary behaviour declines to zero and the strength of seasonal forcing, those with an asterisk include a return to pre-COVID mixing over a 2-week Christmas period. (See Fig 8 for a more complete description).

# Appendix 7: Wales

This provides the same plots as Fig. 5 and Fig. 8 but for the Welsh population. It should be noted that available data for Wales is less fine-scale than for England, so the projections are likely to be less robust.
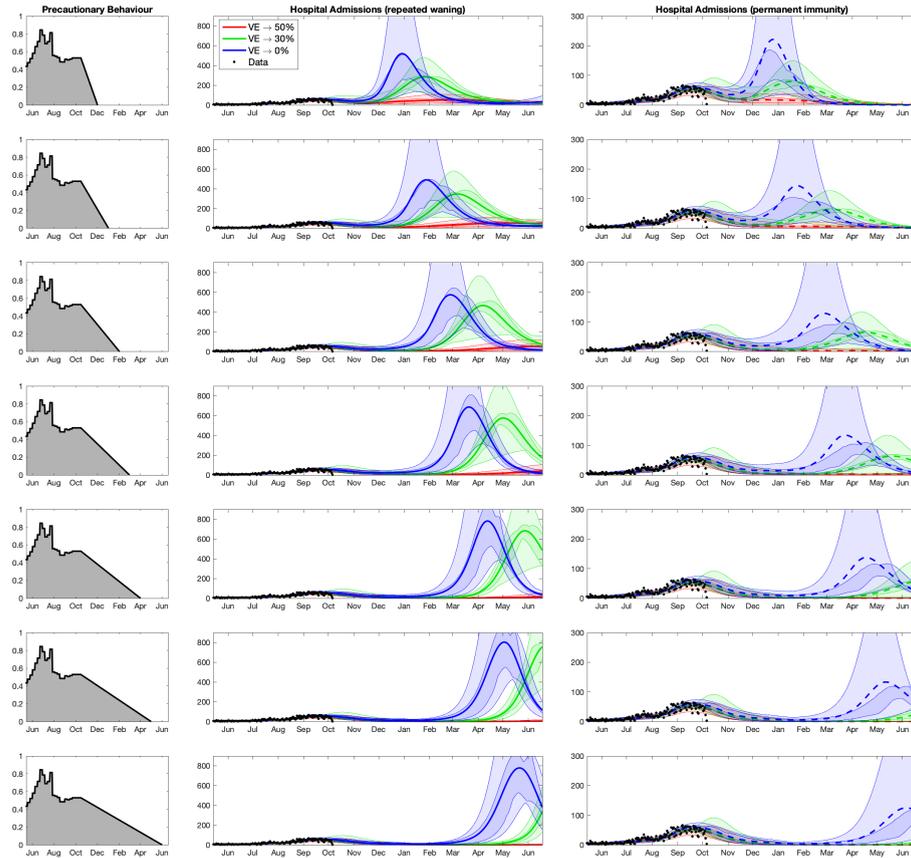


**Fig. 16:** Projected dynamics of daily hospital admissions with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows). Black dots show the data to 8th October 2021.
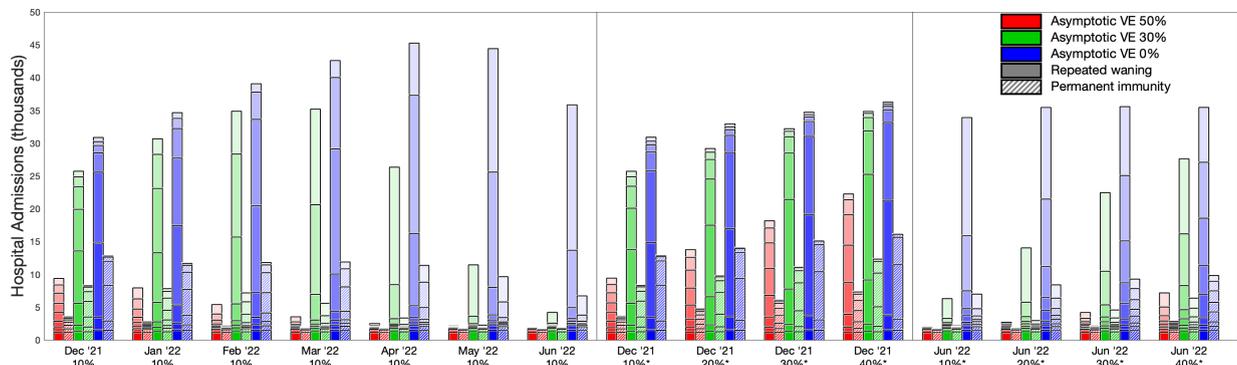


**Fig. 17:** Bars showing the mean number of hospital admissions over the next eight months (October - December 2021, January-May 2022). Colours refer to the level of asymptotic waning; solid or hashed refers to the action of boosting; while the label on the x-axis gives the date when precautionary behaviour declines to zero and the strength of seasonal forcing, those with an asterisk include a return to pre-COVID mixing over a 2-week Christmas period. (See Fig 8 for a more complete description).

# Appendix 8: Scotland

This provides the same plots as Fig. 5 and Fig. 8 but for the Scottish population. It should be noted that available data for Scotland is less fine-scale than for England, so the projections are likely to be less robust.
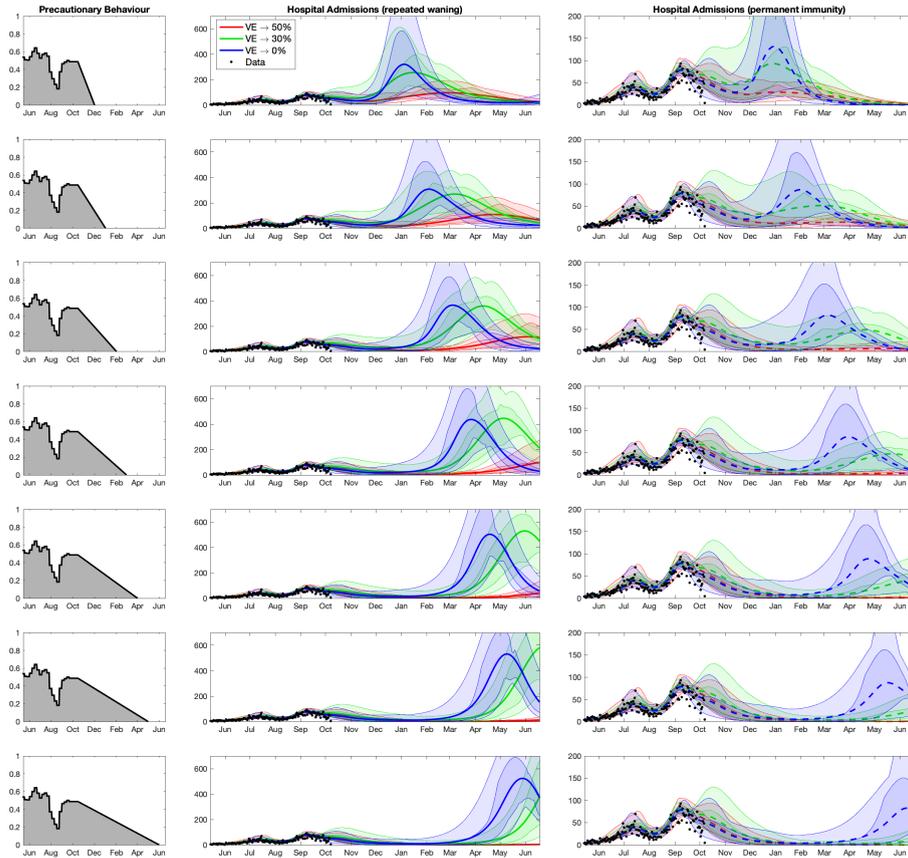


**Fig. 18:** Projected dynamics of daily hospital admissions with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows). Black dots show the data to 8th October 2021.
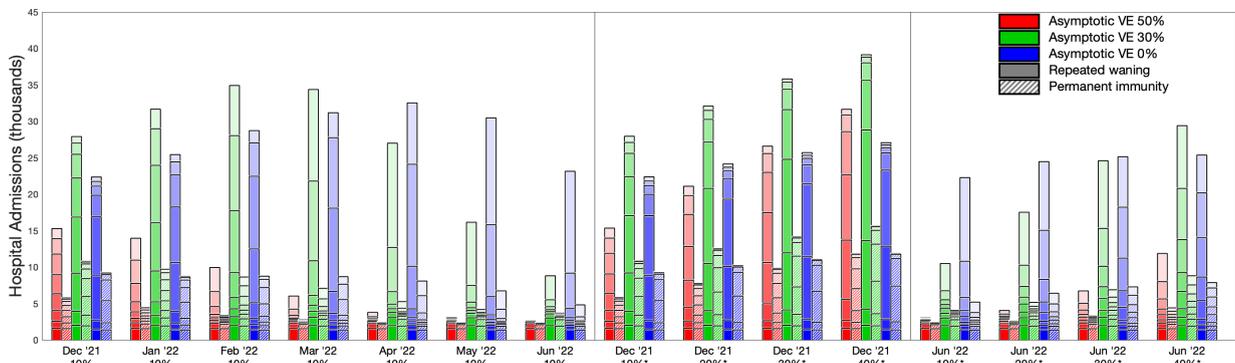


**Fig. 19:** Bars showing the mean number of hospital admissions over the next eight months (October - December 2021, January-May 2022). Colours refer to the level of asymptotic waning; solid or hashed refers to the action of boosting; while the label on the x-axis gives the date when precautionary behaviour declines to zero and the strength of seasonal forcing, those with an asterisk include a return to pre-COVID mixing over a 2-week Christmas period. (See Fig 8 for a more complete description).

# Appendix 9: Northern Ireland

This provides the same plots as Fig. 5 and Fig. 8 but for the population of Northern Ireland. It should be noted that available data for Northern Ireland is less fine-scale than for England, so the projections are likely to be less robust.
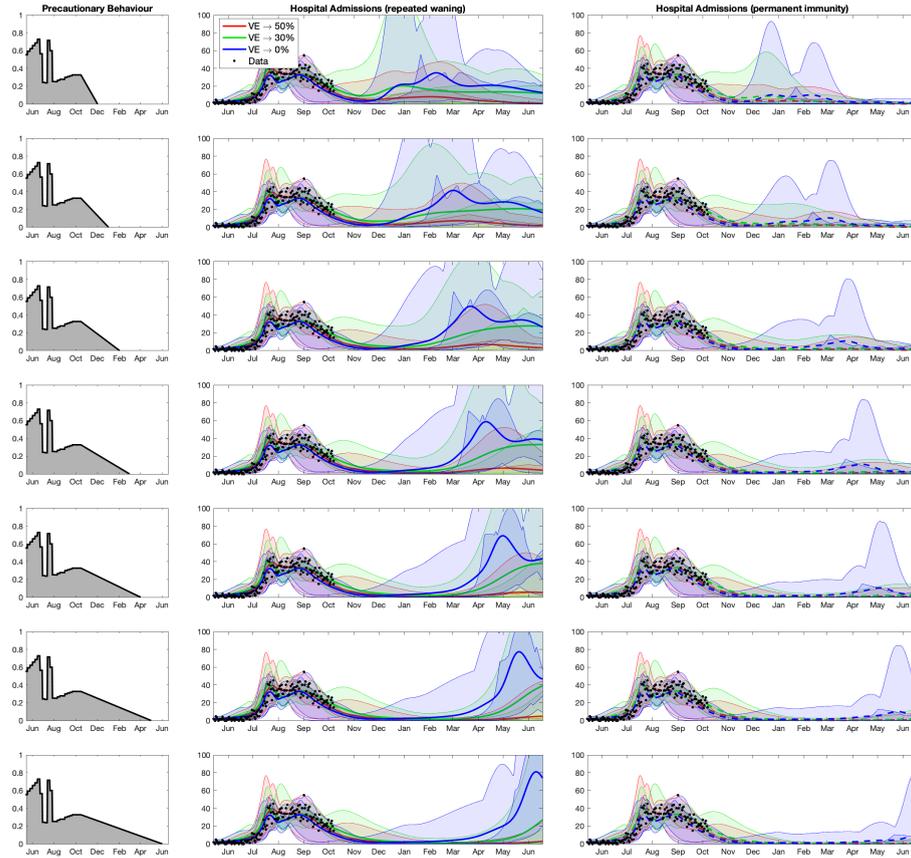


**Fig. 20:** Projected dynamics of daily hospital admissions with three waning efficacy assumptions (colours), two assumptions about boosting (central and right-hand columns) and different relaxation rates to pre-COVID behaviour (rows). Black dots show the data to 8th October 2021.
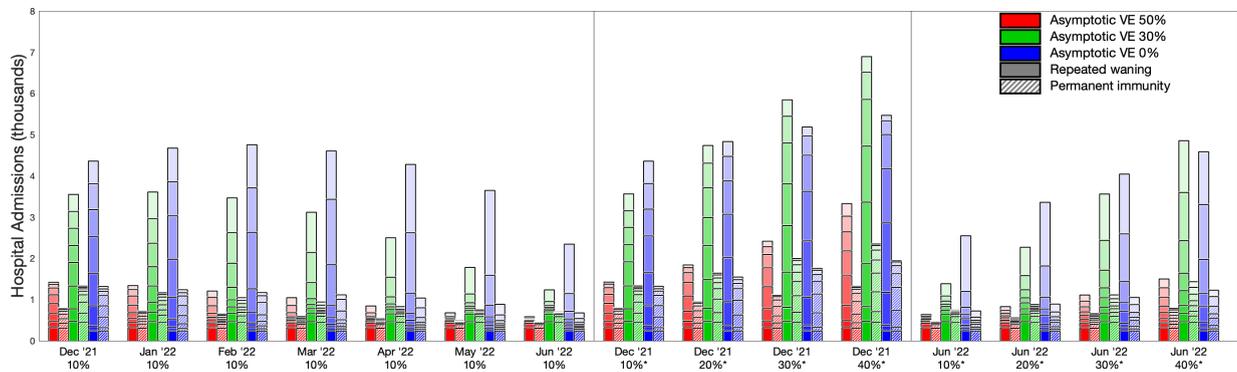


**Fig. 21:** Bars showing the mean number of hospital admissions over the next eight months (October - December 2021, January-May 2022). Colours refer to the level of asymptotic waning; solid or hashed refers to the action of boosting; while the label on the x-axis gives the date when precautionary behaviour declines to zero and the strength of seasonal forcing, those with an asterisk include a return to pre-COVID mixing over a 2-week Christmas period. (See Fig 8 for a more complete description).

# Appendix 10: Age-structured dynamics for permanent immunity after boosting
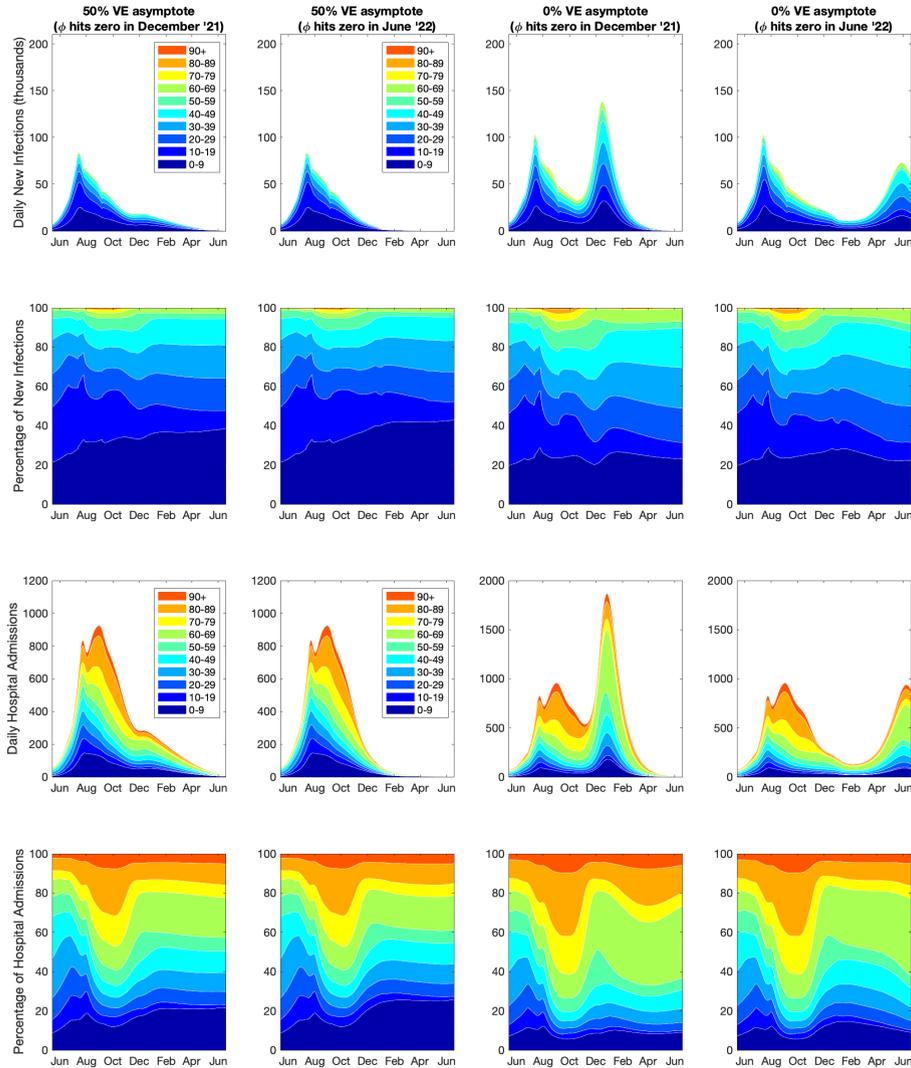


**Fig. 22:** Age structured dynamics of infection and hospital admissions under the assumption that vaccine efficacy is permanent after boosting. Columns 1 and 2 correspond to optimistic assumptions about waning efficacy with the asymptotic level of vaccine efficacy against infection set at 50%; columns 3 and 4 are more pessimistic assumptions in which vaccine efficacy eventually reaches 0%. In columns 1 and 3 we force the precautionary behaviour, $\phi$, to decline to zero by December 2021, whereas in columns 2 and 4 $\phi$ does not reach zero until June 2022. Row 1 is the number of new daily infections; row 2 is the percentage of new infections in each age group; row 3 is the number of daily hospital admissions (notice the different y-scales to capture the full dynamics); while row 4 is the percentage of admissions in each age group. Colours scale from blue (bottom) to red (top) in increasing 10-year age bands.

# References

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