Interim roadmap assessment: prior to steps 3 and 4

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We model Steps 3 and 4 of the UK Government's Spring 2021 "Roadmap" out of lockdown in England. To capture behavioural changes in response to the easing of restrictions, we project future increases in population mobility that may be expected to result at each roadmap stage. If a new SARS-CoV-2 variant does not spread in England, our projections suggest that Steps 3 and 4 are likely to lead to a resurgence in cases, hospital admissions, and deaths, but of a smaller magnitude than the January 2021 wave. The spread of a SARS-CoV-2 variant exhibiting partial immune escape or substantially increased transmissibility may result in a large resurgence of cases, with potentially as many or more deaths than seen during the January 2021 wave if no reactive measures are imposed in response. This work makes assumptions about the nature and impact of roadmap Steps 3 and 4 which cannot be verified until policy decisions are finalised and behavioural responses can be measured.

Summary of findings

- Our baseline results (i.e. without the introduction of further new SARS-CoV-2 variants of concern) suggest that Step 3 of the roadmap is likely to result in an increase in the reproduction number to above one from mid-May 2021. This is expected to lead to a wave of hospitalisations and deaths in the summer months. Enacting Step 4 of the roadmap in June 2021 is likely to lead to a longer period when the reproduction number is at or above one, and therefore more hospitalisations and deaths over the summer months.
- The size of any summer wave in 2021, in terms of severe outcomes is very difficult to predict. The key uncertainties include:
    - The effectiveness of vaccines in protecting vaccinated individuals against SARS-CoV-2 infection, disease and other severe outcomes
    - The effect that easing restrictions will have on contact patterns and behaviour
    - The rate that natural and vaccine induced immunity wanes
    - Any additional effect of seasonality, not already included, on changes in contacts
- We modelled two additional scenarios designed to capture the spread of new variants of concern (VOC): a vaccine escape VOC (with lower transmissibility than B.1.1.7 but only 50% cross immunity) and a more infectious VOC (with 100% cross immunity between it and previous variants). Both scenarios are expected to lead to large increases in hospitalisations and deaths, if no further action is taken in response. However, the escape mutant may result in a more prolonged epidemic.

- When the reproduction number is close to one, small changes can have a large impact on the resulting epidemiology. For this reason, the pattern of schools opening or other seasonal factors are likely to have a relatively large effect in the coming months.
- Results are very dependent on as yet unverifiable assumptions regarding the impact of easing restrictions on individuals' behaviour.

Summary of changes since March 2021

- We have updated our vaccine effectiveness assumptions since the previous round of roadmap modelling, assuming higher overall protection from both AstraZeneca and Pfizer vaccines (Table 1).
- We include additional vaccine protection against severe outcomes (i.e. hospitalisation and death), where previously we only modelled protection against SARS-CoV-2 infection and disease.
- We have made more optimistic assumptions related to future mobility changes than those considered previously; we do not assume a complete return to pre-pandemic baseline levels across all mobility measures.
- We assume that the introduction of mass testing and mask wearing in schools from March 2021 results in an additional 30% reduction in transmission resulting from school related contacts.
- We now assume in our baseline scenario that vaccine- and naturally-induced immunity wanes, but we include an additional scenario without waning immunity.

Methods & assumptions

Basic model assumptions

We use an age- and geographically-structured deterministic compartmental model of SARS-CoV-2 transmission. Geographic structure is by NHS England region and age groups are divided into 5-year age bands from 0–4 to 70–74 years with an additional age group comprising individuals aged 75 years and over. Further details of the model and how it has been fitted to data are given in Davies et al. 2020 (Lancet Inf Dis) and Davies et al. 2021 (Science). The model uses Google Community Mobility data to track mobility in various settings: workplaces, retail & recreation venues, transit stations, and grocery & pharmacy locations. School openings and closings are accounted for in contacts among school-aged children, university-aged young adults and school/university staff. The relationship between mobility data and social contact rates is derived from the historical relationship between Google Community Mobility indices and social contact rates as measured by the CoMix study in 2020 (Davies et al. 2020, Lancet Inf Dis).

The model tracks two SARS-CoV-2 variants: B.1.1.7 versus pre-existing variants (Davies et al. 2021, Science), and has been extended to consider a third variant for additional illustrative modelling of the potential future impact of immune escape variants of concern.

The model is fitted to PCR prevalence as measured by the Office for National Statistics (ONS); seroprevalence as measured by REACT-2, UK Biobank, and the ONS; daily incidence of COVID-19 deaths, hospital admissions, hospital bed occupancy, and ICU admissions as provided by PHE and the NHS (Davies et al. 2020 Lancet Inf Dis); and the frequency of *S* gene target failure up to 15th February 2021 to capture the spread of B.1.1.7 (Davies et al. 2021, Science).

We use Public Health England (PHE) data recording the number of first and second vaccine doses delivered by age, geography and vaccine product from the 8th of December 2020 to the 22nd of April 2021 to inform the fraction of vaccinated individuals in each age group, NHS England region and by vaccine type and dose over time. Vaccine schedules are generated by combining vaccines already delivered with future schedules generated based on a number of assumptions (see 'Vaccine assumptions') and ensuring that all first doses are followed up with equivalent second doses at most 12 weeks later (see also 'Vaccine schedules' for a full description).

The age-specific probability of clinical symptoms is adopted from Davies et al (Nature Medicine, 2020) using data from 6 countries. The age-specific probability of hospital admission, ICU admission, and death given infection are fitted to data from England, with the relative rates by age group based on data collected by a large meta-analysis of the COVID-19 infection fatality rate (Levin et al., Eur J Epi 2020) and based on data collected by ISARIC (the CO-CIN study) for England (Davies et al., Lancet Inf Dis 2020). Each of these age-specific probabilities of severe outcomes is allowed to vary over the course of the epidemic in England and vary between pre-existing variants and B.1.1.7. In scenarios with a vaccine escape variant (such as B.1.351), the probability of severe outcomes is assumed to be the same as for B.1.1.7. We do not yet have good data on the probability of severe outcomes for infection with B.1.351.

Roadmap assumptions

We base our assumptions on how social contact rates might be expected to change at each stage of the roadmap by referring to historical Google Community Mobility data and making assumptions about future mobility changes (Figure 1). For each stage of the roadmap we consider "low", "medium", and "high" scenarios for future changes in mobility, with various assumptions made across four mobility indices (Grocery and pharmacy, Retail and recreation, Transit stations and Workplaces). The values of the basic reproduction number resulting from the "low", "medium" and "high" mobility scenarios, with and without schools open, are shown in Table 5.

Grocery and pharmacy mobility is currently at or above baseline levels, so we assume no future changes in this metric for all three mobility scenarios considered. For retail and recreation, our "low" scenario assumes mobility will return to the highest level recorded since the pandemic began (August 2020) following roadmap Step 4. The "medium" mobility scenario makes the same assumption but for roadmap Step 3. The "high" scenario for retail and recreation assumes mobility levels increase further over the summer of 2021 and exceed pre-pandemic baseline levels following roadmap Step 4 due to good weather and high spirits.

We do not expect either Transit or Workplace mobility to return to pre-pandemic baseline levels. Our "medium" scenario assumes that transit-related mobility reaches similar levels to late September 2020 following roadmap Step 3, whilst the "low" scenario assumes the same level is reached following roadmap Step 4. Workplace mobility levels are already nearly as high as those observed during September and October of 2020. Our "low" scenario assumes workplace mobility reaches 75% of baseline levels following roadmap Step 3, similar levels to those recorded in October 2020. Our "medium" scenario assumes workplace mobility reaches 80% of baseline levels, as this was a similar mobility change to the one observed previously between roadmap Steps 2 and 3.

We assume no change in workplace mobility following roadmap Step 4 for both "low" and "medium" scenarios, to compensate for more adults staying at home rather than travelling to work during school holidays. The "high" scenario for workplace mobility assumes an increase in mobility for both roadmap Steps 3 and 4. Although we assume future mobility changes for "low", "medium" and "high" scenarios, we assume that an additional level of control is maintained via contact tracing and social distancing (i.e. through physical distancing, mask wearing and hand hygiene), equivalent to a reduction in R of 30-40% in total, as fitted for each NHS England region during the summer of 2020. We also include additional sensitivity analyses where we assume that this additional control is reduced by 10 percentage points (see Figure 3).

Transmission in schools

We assume that schools in England follow their traditional schedules (i.e. are closed during half-term periods and over summer holiday periods). However, to reflect the introduction of mass testing within educational facilities in the Spring of 2021, we have assumed an additional 30% reduction in transmission related to educational settings following the reopening of schools on 8th March 2021. This reduction in transmission is reflected in the model with a 30% reduction in school-related contacts.

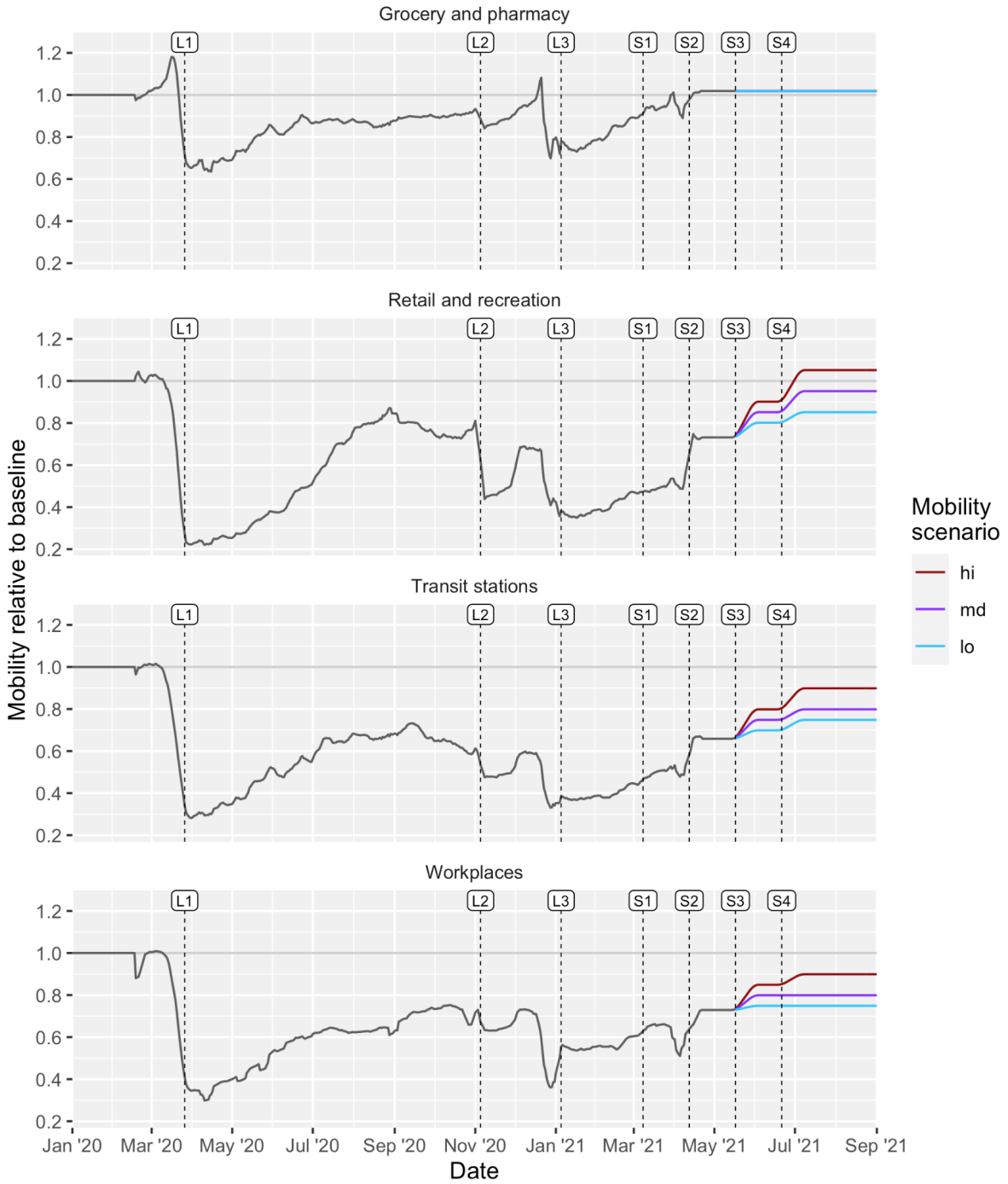

Figure 1 - Historic Google Community Mobility data (grey) and assumed future mobility in England for low (blue), medium (purple) and high (red) scenarios used for model projections. Mobility indices are measured relative to baseline mobility levels recorded during early 2020, prior to the COVID-19 pandemic. The beginning of each lockdown and each roadmap Step is marked with a vertical dashed line.

Vaccine schedules

Vaccine schedules are generated by combining PHE data on vaccines delivered up to 22nd April 2021 in England with future schedules based on a number of assumptions related to vaccine effectiveness, vaccine supply and vaccine uptake (see 'Vaccine assumptions' section). The number of future doses supplied for each day in the schedule are distributed into the seven NHS England regions according to the population size of each region. The number of vaccine doses per region per day are initially allocated to age groups in the model according to the existing age distribution of all doses delivered. Beginning with the oldest age group, the allocated number of doses per day, per region and per age group are divided into specified proportions of vaccine products relevant to each age group (see 'Vaccine mix' section). Second doses are delivered at most 12 weeks after their equivalent first dose. Once all required second doses have been allocated, leftover doses for that day, region and age group are delivered as first doses up to the specified uptake limit (Table 2). If doses are remaining after second and first doses have been delivered, these leftover doses are carried over to either the next age group down, the next NHS England region, the next day, or are not allocated in the schedule and are recorded as leftover doses.

Vaccine assumptions

Vaccine effectiveness

We base our vaccine effectiveness assumptions on the latest available evidence. These may be subject to change in future reports, as new evidence emerges. We currently treat individuals who have been and will be vaccinated with Moderna vaccines the same as individuals receiving Pfizer vaccines. We model individuals who have received different vaccine products (e.g. AstraZeneca and Pfizer/Moderna) and one or two vaccine doses separately, assuming separate efficacy estimates for each category. We model vaccine protection against four outcomes: infection, disease (i.e. symptomatic infection), hospitalisation and mortality. An overview of all assumed vaccine efficacies for vaccines against pre-B.1.1.7 and B.1.1.7 variants is shown in Table 1. For full details including relevant evidence related to assumed values, please refer to Table S1 in the Supplementary Material section.

Vaccine supply

The vaccine rollout in England is assumed to follow a schedule of an average of 2.7 million doses per week from 26th April until 19th July 2021, and then 2 million doses per week thereafter.

Vaccine uptake

We base our assumptions related to vaccine uptake on evidence related to vaccine sentiment (ONS, ONS, Ansell et al.). A summary of the central uptake assumptions is shown in Table 2. For full details including relevant evidence related to vaccine uptake assumptions, please refer to Table S2 in the Supplementary Material section.

Vaccine mix

The following proportions of each vaccine product are used in the vaccine schedules projected forwards:

- 75% Pfizer and 25% Moderna for <30 year olds
- 60% AstraZeneca, 30% Pfizer and 10% Moderna for 30-49 year olds
- Actual mix of AstraZeneca, Pfizer and Moderna first doses already delivered to 50+ year olds

Table 1 - Vaccine effectiveness against all outcomes (pre B.1.1.7 and B.1.1.7 variants)

	ChAdOx1 Oxford AstraZeneca		BNT162b2 Pfizer BioNTech^	
	First dose	Second dose	First dose	Second dose
Protection against infection*	**0.67** (0.5)	**0.68** (0.5)	**0.7** (0.55)	**0.85** (0.7)
Protection against disease*	**0.67** (0.6)	**0.78** (0.67)	**0.7** (0.55)	**0.89** (0.74)
Protection against hospitalisation*	**0.845** (0.8)	**0.9** (0.85)	**0.845** (0.8)	**0.9** (0.85)
Protection against death*	**0.845** (0.8)	**0.9** (0.85)	**0.845** (0.8)	**0.9** (0.85)
Dose to efficacy delay	28 days	14 days	28 days	14 days

*Central scenario estimates are in bold, with pessimistic scenario estimates shown below in brackets. Values are assumed to be equal for the pre-B.1.1.7 and B.1.1.7 variants, which are considered separately in the model. Equivalent assumptions for the third variant escape mutant scenario are shown in Table 4.

^The BNT162b2 Pfizer BioNTech efficacies listed are also used for individuals in the model receiving the Moderna mRNA-1273 vaccine

Table 2 - Vaccine uptake assumptions

Ages	Uptake limit (**central)**
0-14	**0%**
15-19	**33.72%** = 84.3%*(⅖)
20-24	**84.3%**
25-29	**84.3%**
30-34	**89.2%**
35-39	**89.2%**
40-44	**88.9%**
45-49	**88.9%**
50-54	**95.4%**
55-59	**95.7%**
60-64	**96%**
65-69	**96.7%**
70-74	**98.9%**
75+	**98.9%**

Waning immunity

We consider scenarios with and without waning protection from SARS-CoV-2 infection developed from natural infection and vaccination. For all scenarios, we assume that rates of waning are identical for all three virus variants considered in the model. For scenarios with waning immunity, we assume that both natural and vaccine induced immunity wane at identical rates (Table 3). We further assume that waning of immunity against different endpoints (infection, disease, hospitalisation and deaths) occurs at the same rate. We also assume that rates of waning are identical across all age groups in the model. Many of these assumptions are likely to not hold in practice, but there is currently an absence of data on differential rates of immunity against different outcomes, from different routes (vaccines and naturally occuring) and for different population groups. For details including relevant evidence related to waning immunity, please refer to Table S4 in the Supplementary Material section.

Table 3 - Waning immunity scenarios

Description	Assumed values (**waning**)	Assumed values (**no waning**)
Waning of natural immunity	log(0.85)/-182.5, corresponding to 85% protection after 365 / 2 days = 6 months	0
Waning of vaccine induced immunity (second dose to susceptible / naive)	log(0.85)/-182.5, corresponding to 85% protection after 365 / 2 days = 6 months	0
Waning of vaccine induced immunity (first dose to susceptible / naive)	0	0
Waning of vaccine induced immunity (second dose to first dose)	0	0

New variants of concern (VOCs)

We also consider scenarios introducing variants of concern. We consider two scenarios related to the characteristics of a VOC: an escape mutant with 80% transmissibility relative to B.1.1.7 and 50% cross protection from prior infection with other SARS-CoV-2 variants, and an increased transmissibility variant with 150% transmissibility relative to B.1.1.7 and 100% cross protection from prior infection with other SARS-CoV-2 variants. Each of these variants is introduced into the model by seeding 5 daily infections with the third virus variant (which is modelled explicitly) from 1st January 2021 onwards. We base our assumptions around vaccine effectiveness for the escape mutant variant of concern scenario on limited evidence available related to vaccine effectiveness against the B.1.351 variant (Table 4). For the increased transmissibility scenario, we assume vaccine effectiveness values shown in Table 1.

Table 4 - Vaccine efficacy assumptions for third immune escape variant (e.g. B.1.351)

	Description	Assumed values*
AstraZeneca dose 1	Overall protection against infection	0.104, +28 days
	Overall protection against disease	0.104, +28 days
	Overall protection against hospitalisation	0.40, +28 days
	Overall protection against mortality	0.40, +28 days
AstraZeneca dose 2	Overall protection against infection	0.104, +14 days
	Overall protection against disease	0.104, +14 days
	Overall protection against hospitalisation	0.40, +14 days
	Overall protection against mortality	0.40, +14 days
Pfizer dose 1	Overall protection against infection	0.12, +28 days
	Overall protection against disease	0.12, +28 days
	Overall protection against hospitalisation	0.50, +28 days
	Overall protection against mortality	0.50, +28 days
Pfizer dose 2	Overall protection against infection	0.25, +14 days
	Overall protection against disease	0.25, +14 days
	Overall protection against hospitalisation	0.70, +14 days
	Overall protection against mortality	0.70, +14 days

*There is limited information on vaccine effectiveness against SARS-CoV-2 variant B.1.351. We made the simplifying assumption that overall vaccine protection against B.1.351 infection is the same as overall vaccine protection against B.1.351 disease, given that these values are very similar in the case of the wild-type variant (see **Table 1**). AZ effectiveness against B.1.351 infection was taken from Madhi et al. (their Table 2, vaccine efficacy of 10.4% (-76.8 to 54.8) against mild to moderate illness associated with B.1.351 variant >14 days after second injection), while Pfizer effectiveness against B.1.351 infection was estimated using Fig. 2C of Khoury et al., assuming a 10-fold reduction in neutralising titre associated with B.1.351 (https://www.nejm.org/doi/full/10.1056/NEJMc2103740). For both AZ and Pfizer, we used Fig. 3A of Khoury et al. to estimate protection against severe infection corresponding to the calculated protection against infection, treating protection against severe infection as equivalent to protection against hospitalisation and mortality.

Table 5 - R_0 values related to assumed low, medium and high mobility scenarios for roadmap Steps 3 and 4, with schools open and closed.

	Step 3		Step 4	
	Schools closed	Schools open	Schools closed	Schools open
Low mobility	2.31	2.56	2.47	2.71
Medium mobility	2.56	2.80	2.81	3.05
High mobility	2.82	3.05	3.38	3.60

Results & discussion

The projected effect of roadmap Step 3 alone is shown in Figure 2. The easing of restrictions is expected to lead to a rise in the reproduction number which is expected to be above one. The half term school holiday in May/June 2021 results in a temporary reduction in the reproduction number. The gradual decline thereafter is due to accumulation of immunity in the population, largely through vaccination but also through natural infection. The reproduction number is expected to be below 1 before the summer school holidays beginning in July 2021 suppresses it further. Nevertheless, the increase in transmission would be expected to lead to an increase in hospital admissions and deaths over the summer period. These increases are expected to be relatively small in comparison to the winter 2020/2021 wave, assuming that the vaccine effectiveness is high.

If there is no waning of immunity induced by natural infection and vaccination and/or additional seasonal effects then the increases in hospitalisations and deaths over the summer resulting from Step 3 alone are expected to be modest (Table 6). It should be noted that there remains considerable uncertainty in these projections resulting from the unknown effect of the easing of restrictions on behaviour - i.e. within a scenario, the differences between the “low”, “mid” and “high” projections are relatively large.

Figure 3 and Table 6 show the projected effects of taking Steps 3 and 4 of the roadmap. The further easing of restrictions at Step 4 is expected to maintain the reproduction number above 1 for longer - indeed, for most of the “mid” and “high” scenarios the reproduction number is expected to stay above one until the school summer holidays begin in July 2021. This leads to a larger summer epidemic wave, resulting in more hospitalisations and deaths (Table 6). Under the “mid” or “low” mobility scenarios then this summer wave is expected to be relatively modest. However, under the “high” mobility scenario this summer wave could lead to an appreciable burden of illness and deaths and some pressure on the health service. For instance, under the baseline assumptions and “high” contacts, peak hospital demand could exceed 10,000 beds

and daily deaths could exceed 300 (Figure 3 and Table 6). It is worth stressing that even under the “high” contact assumptions, mobility does not return to normal levels (see Figure 1).

The “additional relaxation” scenario shows that if social distancing measures (e.g. mask wearing) are also reduced, the summer wave is likely to be more severe. If, on the other hand, there are additional seasonal factors that reduce transmission over the summer months (not already captured by changes in mobility and school attendance), then the effect of the summer wave can be attenuated. Note that as the reproduction number is expected to be around one, small changes resulting from seasonal effects can have a relatively large effect. Also note that we have not modelled any results beyond the end of September 2021. Seasonal factors that reduce transmission in the summer months, would be expected to lead to an increase in transmission during the winter months.

Figure 3 also shows the impact of waning immunity. In the absence of evidence on vaccine-induced waning immunity, we have chosen to model the decline in vaccine induced immunity in an analogous way to the waning of natural infection (with protection falling by about 15% in 6 months). If immunity remains high, then much of the serious impact of the summer wave can be averted (Figure 3). Ensuring that high second dose coverage is maintained would therefore appear to be very important. A summary of the results shown in Figures 2 and 3 is given in Table 6.

Figure 4 shows the potential impact of new variants of concern on the burden of COVID-related disease. The vaccine escape scenario assumes that the new variant is 20% less transmissible than B.1.1.7, but has only 50% cross protection between it and pre-existing variants. The “high transmissibility” scenario assumes that the new variant is 50% more infectious than B.1.1.7 but there is complete cross protection between it and previous variants. The escape mutant scenario assumes vaccine effectiveness against the VOC shown in Table 4. The high transmissibility VOC assumes vaccine effectiveness estimate shown in Table 1. Either scenario could result in very significant summer waves of infection, with a significant increase in hospitalisations and deaths, assuming no further measures are introduced (such as reimposition of non-pharmaceutical interventions or vaccine boosters targeted at the new VOC). However, these two scenarios also show qualitatively different patterns; the escape mutant VOC leads to a more protracted epidemic as it is also able to infect individuals that have been previously vaccinated or infected by existing SARS-CoV-2 variants.

Table 6 - Summary of projections for total COVID-19 deaths, total COVID-19 hospitalisations, and peak hospital bed occupancy for England, over the time period 12th May – 30th September 2021. Medium mobility assumptions are shown, with low and high mobility assumptions shown below in brackets.

Step 3 of roadmap only

Indicator	Main scenario	No waning of immunity	Lower vaccine effectiveness	With seasonality
Total deaths	8,200 (5,000-13,500)	2,600 (1,600-4,900)	17,400 (10,600-25,800)	3,200 (1,800-5,500)
Total hospitalisations	36,200 (25,700-56,700)	12,700 (8,500-23,000)	68,200 (41,100-102,100)	14,400 (8,900-27,100)
Peak hospital beds occupied	4,100 (2,300-7,400)	1,300 (700-2,700)	8,200 (4,900-11,900)	1,500 (800-2,800)

Steps 3 and 4 of roadmap

Indicator	Main scenario	No waning of immunity	Lower vaccine effectiveness	With seasonality	Additional relaxation
Total deaths	11,200 (6,100-23,900)	4,000 (1,800-9,400)	21,900 (12,900-43,800)	4,400 (2,300-11,900)	19,600 (10,300-36,600)
Total hospitalisations	51,900 (28,700-99,200)	17,300 (8,500-42,400)	93,300 (55,300-160,200)	23,200 (9,500-56,600)	82,500 (45,600-150,600)
Peak hospital beds occupied	5,700 (2,900-12,100)	1,900 (900-5,600)	10,600 (6,000-20,600)	2,200 (900-6,400)	9,800 (5,700-19,400)

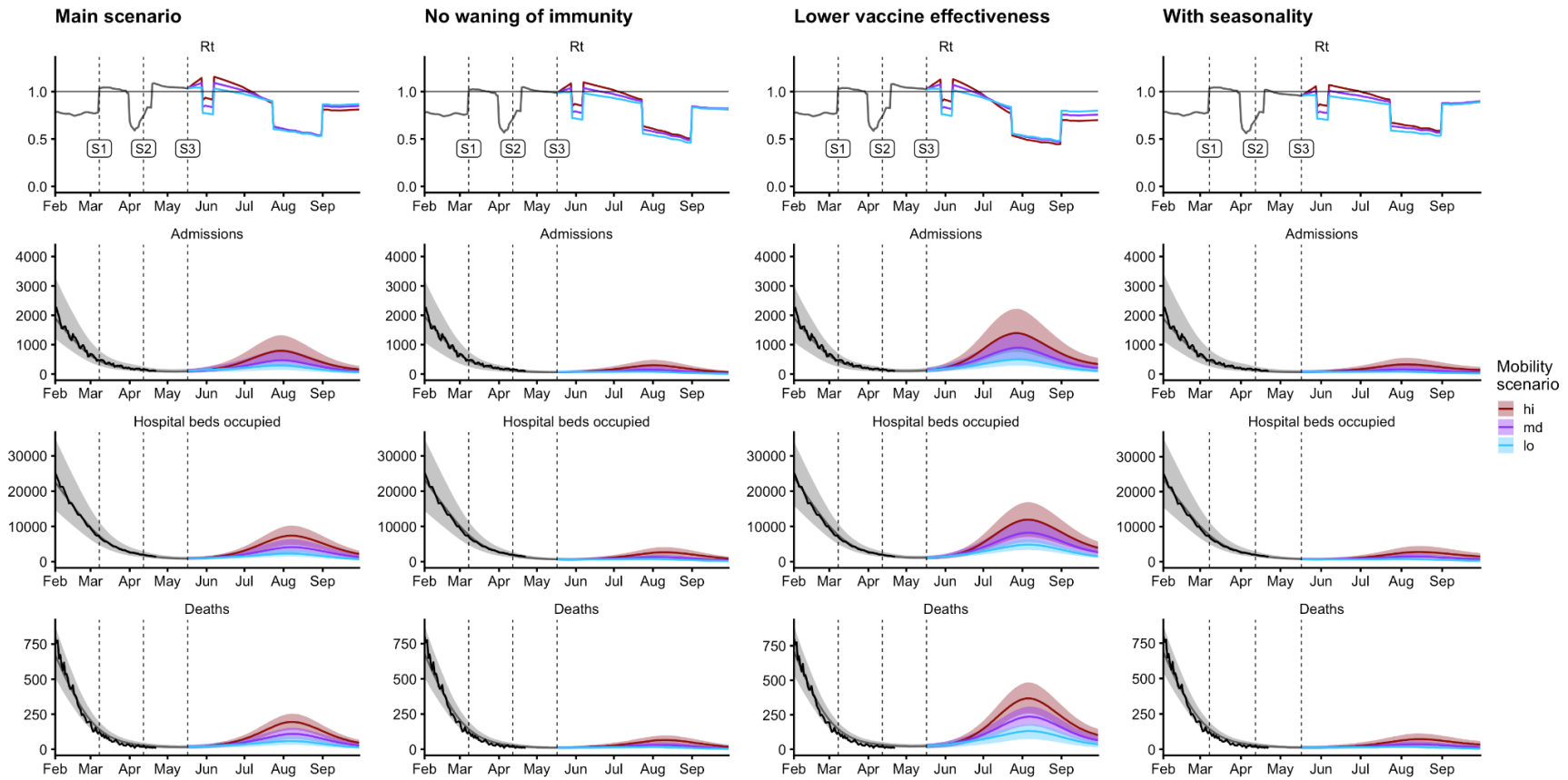

Figure 2 - Overview of central scenarios with assumed mobility changes at roadmap Step 3 only. The beginning of each roadmap Step is marked with a vertical dashed line. For each scenario considered, we show the effective reproduction number (Rt), hospital admissions, the number of hospital beds occupied and the daily number of deaths for England overall. Data (black) and model fits (grey) are shown up to 23rd April 2021 and roadmap Step 3 respectively. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from May to September 2021. From left to right, the main scenario considers waning of natural and vaccine induced immunity of 15% over 6 months (Table 3) with central assumptions used for vaccine effectiveness (Table 1) and uptake (Table 2). The second scenario assumes no waning of natural or vaccine induced immunity. The third scenario assumes lower vaccine effectiveness (Table 1). The fourth scenario assumes 10% higher transmission occurs in winter compared to summer to capture the effects of seasonality.

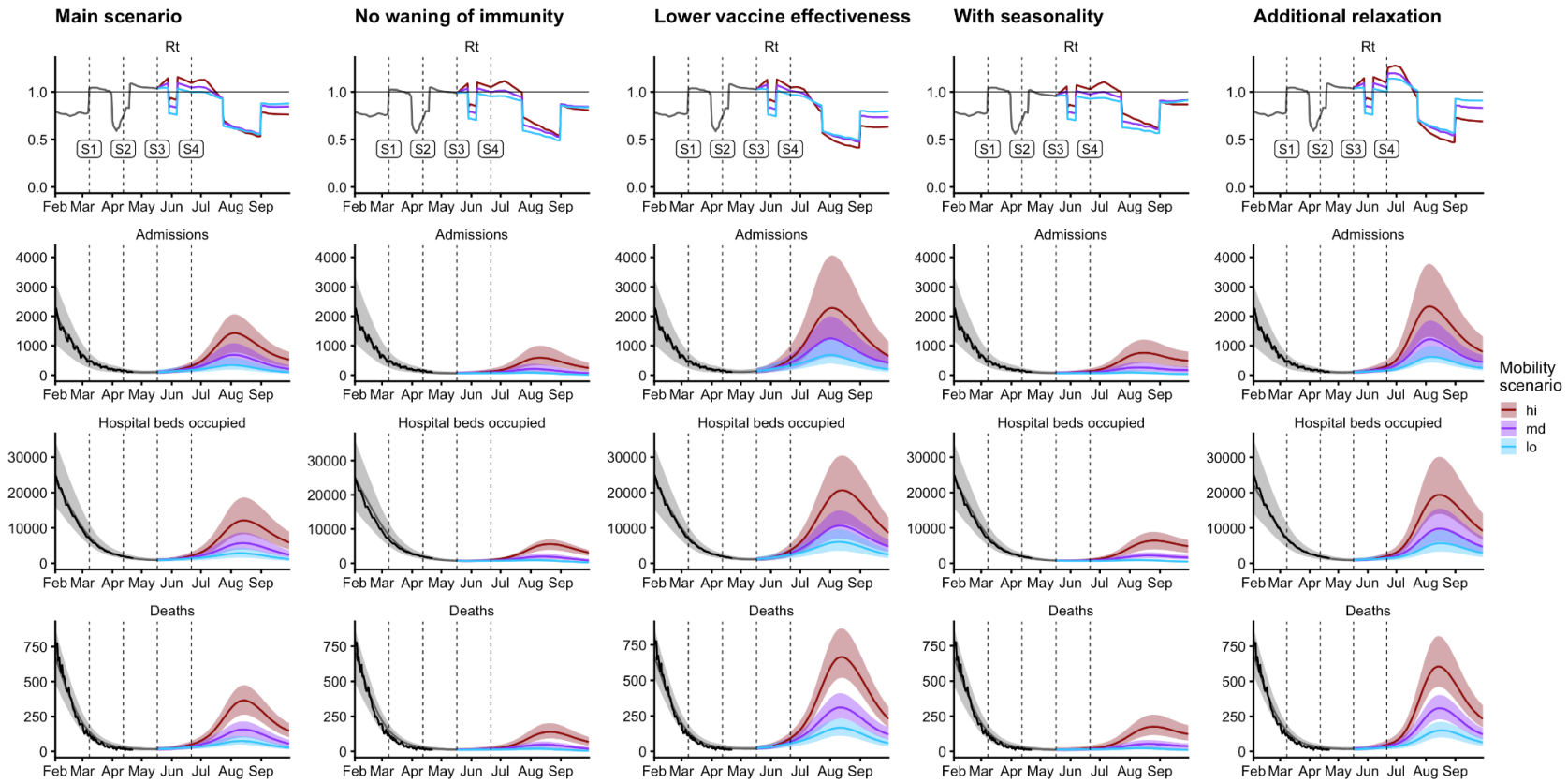

Figure 3 - Overview of central scenarios with assumed mobility changes at roadmap Steps 3 and 4. The beginning of each roadmap Step is marked with a vertical dashed line. For each scenario considered, we show the effective reproduction number (Rt), hospital admissions, the number of hospital beds occupied and the daily number of deaths for England overall. Data (black) and model fits (grey) are shown up to 23rd April 2021 and roadmap Step 3 respectively. Low (blue), medium (purple) and high (red) mobility scenarios are used to project forwards from May to September 2021. From left to right, the main scenario considers waning of natural and vaccine induced immunity of 15% over 6 months (Table 3) with central assumptions used for vaccine effectiveness (Table 1) and uptake (Table 2). The second scenario assumes no waning of natural or vaccine induced immunity. The third scenario assumes lower vaccine effectiveness (Table 1). The fourth scenario assumes 10% higher transmission occurs in winter compared to summer to capture the effects of seasonality. The fifth scenario assumes an additional 10% relaxation of individuals' social distancing measures in addition to future mobility changes.

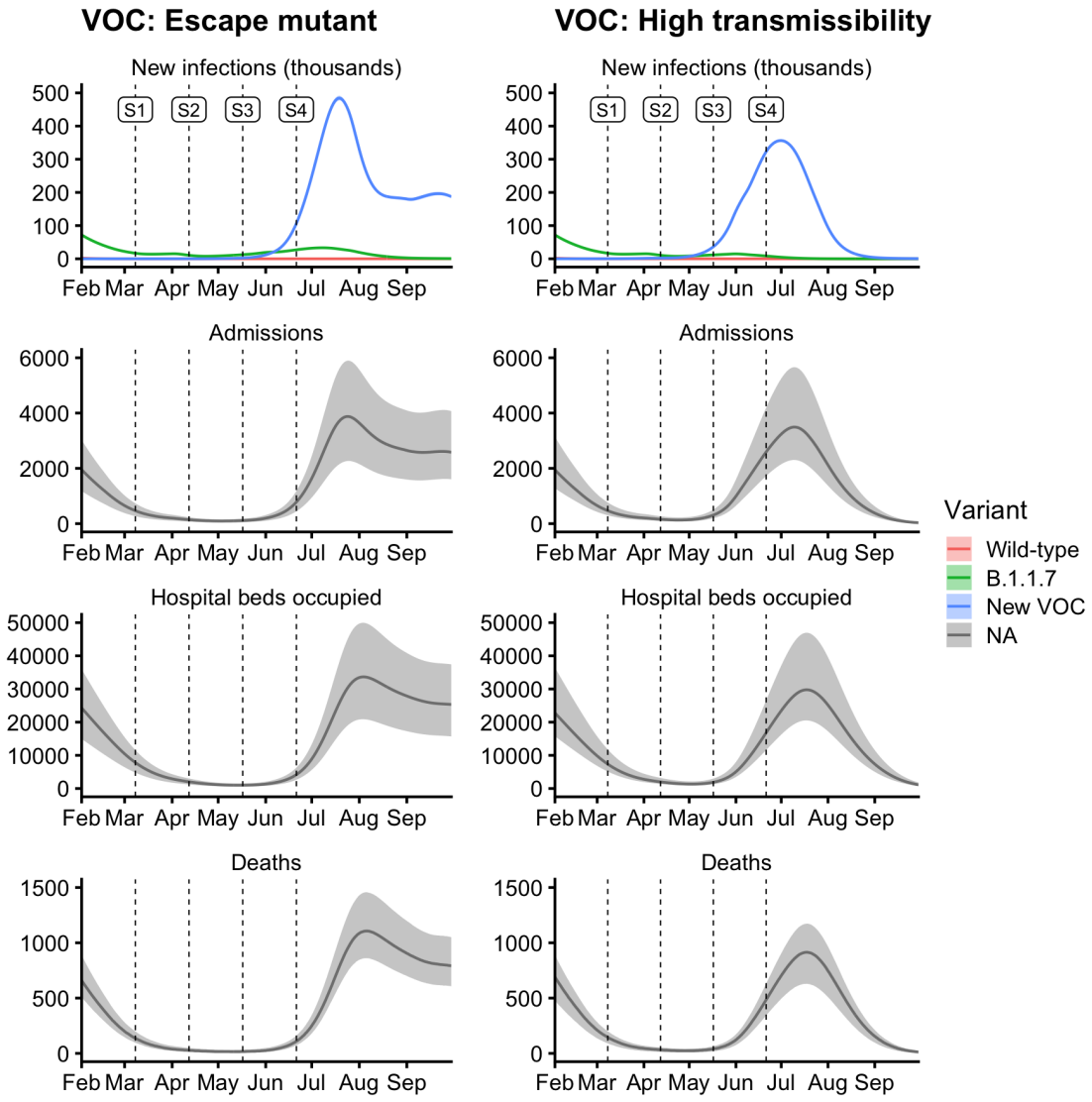

Figure 4 - Overview of scenarios considering variants of concern with immune escape properties and roadmap Steps 3 and 4, using the medium mobility scenario only, and projecting forwards to September 2021. The beginning of each roadmap Step is marked with a vertical dashed line. For each scenario considered we show the number of new infections by variant and the number of hospital admissions, hospital beds occupied and deaths across all variants in England. For the escape mutant scenario we assume vaccine efficacies against the VOC shown in Table 4. For the high transmissibility VOC we assume vaccine efficacies shown in Table 1. The escape mutant scenario assumes 80% transmissibility relative to B.1.1.7, and 50% cross protection from prior infection with other SARS-CoV-2 variants. The high transmissibility scenario assumes 150% transmissibility relative to B.1.1.7 and 100% cross protection from prior infection with other SARS-CoV-2 variants. Each VOC is introduced into the model with 5 new infections every day from 1 January 2021.

Supplementary material

Table S1 - Vaccine effectiveness assumed values and relevant evidence

Description	Assumed value (**central**) & relevant evidence	Assumed value (**pessimistic**) & relevant evidence
Overall protection against infection for AstraZeneca dose 1	0.67, +28 days Shrotri et al. results, secondary analyses, paragraph 1, p.8 adjusted hazard ratio 0.33 (0.16, 0.68) at 28-34 days post vaccination. Pritchard et al. supplementary Table 7, adjusted odds ratio >=21 days after first dose of AZ 0.36 (0.3, 0.45).	0.5, +28 days Voysey et al. B Table 1, efficacy of ChAdOx1 nCoV-19 after two doses, cases > 14 days after second dose, SD/SD efficacy 49.5% (37.7%, 59.0%)
Overall protection against disease for AstraZeneca dose 1	0.67, +28 days Lopez Bernal et al. Table 3, ChAdOx1 adjusted odds ratio d1:28-34 0.4 (0.27-0.59), adjusting 0.6 up to equivalent estimate for protection against infection (see cell above)	0.6, +28 days Lopez Bernal et al. Table 3, ChAdOx1 adjusted odds ratio d1:28-34 0.4 (0.27-0.59)
Overall protection against hospitalisation for AstraZeneca dose 1	0.845, +28 days Vasileiou et al. Table 2, vaccine programme effect for ChAdOx1 21-27 days post first vaccine is 81% (72 to 87%), 28-34 days post first vaccine is 88% (75-94%), 35-41 days post first vaccine is 97% (63-100%). Smaller numbers. Table 3 splits analysis into age groups for ChAdOx1: 65-79 years 21-27 days post first dose 68% (31 to 85%), 80+ years 21-27 days post first dose 77% (63 to 86%) and 28-34 days post first dose 81% (60 to 91%). Small numbers for 65-79 years old and for 18-64 years old so difficult to directly compare but overall the vaccine effect appears stronger in the younger (65-79 years) cohort than the older (80+) cohort, for the first three time points which enable comparison. Effect reversed for fourth time point.	0.8, +28 days Hyams et al. Table 2, adjusted vaccine effectiveness for one dose of ChAdOx1 80.4% (36.4 - 94.5%). Study cohort is adults aged >=80 years admitted to hospital with COVID-19 disease or other acute respiratory disease.
Overall protection against mortality	0.845, +28 days	0.8, +28 days

for AstraZeneca dose 1		
Overall protection against infection for AstraZeneca dose 2	0.68, +14 days Shrotri et al. results, secondary analyses, paragraph 1, p.8 adjusted hazard ratio 0.32 (0.15, 0.66) at 35-48 days post vaccination	0.5, +14 days Voysey et al. B Table 1, efficacy of ChAdOx1 nCoV-19 after two doses, cases > 14 days after second dose, SD/SD efficacy 49.5% (37.7%, 59.0%)
Overall protection against disease for AstraZeneca dose 2	0.78, +14 days Voysey et al. A randomised controlled trial for ChAdOx1 nCoV-19 vaccine AZD1222, Table 3, average of efficacies more than 14 days after a second dose for LD/SD and SD/SD in 'COV002 (UK), age 18–55 years with >8 weeks' interval between vaccine doses*' row -> 0.778 = (0.9+0.656)/2	0.67, +14 days from Voysey et al. A, Table 2, vaccine efficacy against any symptomatic COVID-19 disease more than 14 days after a second dose of ChAdOx1: 67.1% (52.3 - 77.3%)
Overall protection against hospitalisation for AstraZeneca dose 2	0.9, +14 days Assume same levels of protection against hospitalisation as PZ vaccine after second dose	0.85, +14 days
Overall protection against mortality for AstraZeneca dose 2	0.9, +14 days	0.85, +14 days
Overall protection against infection for Pfizer dose 1	0.7, +28 days Hall et al. Table 2, full cohort adjusted hazard ratio d1>=21 days 0.30 (0.15-0.45). Pritchard et al. supplementary Table 7, adjusted odds ratio >=21 days after first dose of Pfizer 0.33 (0.28, 0.39).	0.55, +28 days
Overall protection against disease for Pfizer dose 1	0.7, +28 days Lopez Bernal et al. Table 2, odds ratio vs day 4-9, d1:28-34 0.30 (0.22-0.41)	0.55, +28 days
Overall protection against hospitalisation for	0.845, +28 days Hyams et al. Table 2, adjusted	0.8, +28 days

Pfizer dose 1	vaccine effectiveness for one dose of BNT162b2 71.4% (43.1 - 86.2%). When the analysis of the effectiveness of one dose of BNT162b2 was restricted to the period covered by the ChAdOx1nCoV-19 analysis after the end of 2020, the observed adjusted estimate was 79.3% (95% CI 47.0-92.5) (P=0.0014). Dagan et al. estimate vaccine effectiveness against hospitalisation of 74% (56–86%) 14-20 days after first dose and 78% (61–91%) 21 to 27 days after first dose. Vasileiou et al. Table 2, vaccine effect for BNT162b2 21-27 days post first vaccine is 78% (71 to 83) and 28-34 days post first vaccine is 91% (85 to 94). Estimated vaccine effect against hospitalisation is reduced for later time points to 78% and 77%.	
Overall protection against mortality for Pfizer dose 1	0.845, +28 days Dagan et al. estimate vaccine effectiveness against mortality of 72% (19–100%) 14-20 days after first dose and 84% (44–100%) 21 to 27 days after first dose.	0.8, +28 days
Overall protection against infection for Pfizer dose 2	0.85, +14 days Hall et al. Table 2, full cohort adjusted hazard ratio d2>=7 days 0.15 (0.04-0.26). Pritchard et al. supplementary Table 7, adjusted odds ratio post second dose of Pfizer 0.28 (0.21, 0.36).	0.7, +14 days
Overall protection against disease for Pfizer dose 2	0.89, +14 days Lopez Bernal et al. Table 2, odds ratio vs day 4-9, d2:14+ 0.11 (0.07-0.15)	0.74, +14 days
Overall protection against hospitalisation for Pfizer dose 2	0.9, +14 days Dagan et al. estimate vaccine effectiveness against hospitalisation of 87% (55–100%) >7 days after second dose	0.85, +14 days
Overall protection	0.9, +14 days	0.85, +14 days

against mortality for Pfizer dose 2	Dagan et al. estimate vaccine effectiveness against mortality of 72% (19–100%) 14-20 days after first dose and 84% (44–100%) 21 to 27 days after first dose.	

Table S2 - Vaccine uptake assumed values and relevant evidence

Ages	Uptake limit (**central**) & relevant evidence
0-14	**0%**
15-19	**33.72%** = 84.3%*(%) 84.3% = mean of 82% (ages 18-29) (Ansell et al.[A]), 83% (ages 16-29) (ONS[B]) and 88% (ages 16-29) (ONS[C])
20-24	**84.3%** As cell above
25-29	**84.3%** As cell above
30-34	**89.2%** Mean of 84.6% (ages 30-39) (Ansell et al.[A]), 92% (ages 30-49) (ONS[B]) and 91% (ages 30-49) (ONS[C])
35-39	**89.2%** As cell above
40-44	**88.9%** Mean of 83.8% (ages 40-49) (Ansell et al.[A]), 92% (ages 30-49) (ONS[B]) and 91% (ages 30-49) (ONS[C])
45-49	**88.9%** As cell above
50-54	**95.4%** Mean of 92.1% (ages 50-59) (Ansell et al.[A]), 98% (ages 50-69) (ONS[B]) and 96% (ages 50-54) (ONS[C])

55-59	**95.7%** Mean of 92.1% (ages 50-59) (Ansell et al.[A]), 98% (ages 50-69) (ONS[B]) and 97% (ages 55-59) (ONS[C])
60-64	**96%** Mean of 93% (ages 60-69) (Ansell et al.[A]), 98% (ages 50-69) (ONS[B]) and 97% (ages 60-64) (ONS[C])
65-69	**96.7%** Mean of 93% (ages 60-69) (Ansell et al.[A]), 98% (ages 50-69) (ONS[B]) and 99% (ages 65-69) (ONS[C])
70-74	**98.9%** Mean of 98.7% (ages 70+) (Ansell et al.[A]), 99% (ages 70+) (ONS[B]) and 99% (ages 70-74) (ONS[C])
75+	**98.9%** Mean of 98.7% (ages 70+) (Ansell et al.[A]), 99% (ages 70+) (ONS[B]) and 99% (ages 75-79 and 80+) (ONS[C])

[A]Estimates from Ansell et al., second round of survey (February 2021) including questions on vaccine acceptance on a representative sample of UK (excluding NI) residents, reporting age distributed probabilities of respondents being 'likely or very likely to take vaccine'.
[B]Estimates from ONS Coronavirus and the social impacts on Great Britain dataset published 23rd April 2021. Survey between 14th April and 18th April 2021 reports percentages of respondents with positive vaccine sentiment by age group.
[C]Estimates from ONS Coronavirus and vaccine hesitancy dataset published 1st April 2021. Survey between 17th February and 14th March 2021 reports percentages of respondents with positive vaccine sentiment by age group.

Table S3 - Vaccine efficacy parameters in full (variants 1 and 2, pre-B.1.1.7 and B.1.1.7)

	ChAdOx1 Oxford AstraZeneca		BNT162b2 Pfizer BioNTech	
	First dose	Second dose	First dose	Second dose
Overall protection against infection* ei	**0.67** (0.5)	**0.68** (0.5)	**0.7** (0.55)	**0.85** (0.7)
Overall protection against disease* ed	**0.67** (0.6)	**0.78** (0.67)	**0.7** (0.55)	**0.89** (0.74)
Protection against disease given infection ed_i	**0** (0.2)	**0.3125** (0.34)	**0** (0)	**0.2667** (0.1333)
Overall protection against hospitalisation* eh	**0.845** (0.8)	**0.9** (0.85)	**0.845** (0.8)	**0.9** (0.85)
Protection against hospitalisation given infection and disease eh_{id}	**0.53** (0.5)	**0.55** (0.55)	**0.48** (0.56)	**0.09** (0.42)
Overall protection against mortality* em	**0.845** (0.8)	**0.9** (0.85)	**0.845** (0.8)	**0.9** (0.85)
Protection against mortality given infection and disease em_{id}	**0.53** (0.5)	**0.55** (0.55)	**0.48** (0.56)	**0.09** (0.42)

*Central scenario estimates are in bold, with pessimistic scenario estimates below in brackets. Efficacies are assumed to be equal for the pre-B.1.1.7 and B.1.1.7 variants, which are considered separately in the model.

Table S4 - Waning immunity relevant evidence

Study	Duration	Central estimate	Lower bound	Upper bound
Leidi et al.	Mean follow up 35.6 weeks (sero+) and 34.7 (sero-)	94% reduction in hazard of SARS-CoV-2 positive test given seropositive status	86%	98%
Hall et al.	28.9 weeks = 1339078 person days/6614 study size/7 days	Prior history of SARS-CoV-2 infection associated with 83% lower risk of infection, median protective effect observed 5 months after infection	76%	87%
Abu-Raddad et al.	Antibody positive cohort had a mean follow-up duration of 16.3 weeks	Efficacy of natural infection against reinfection was estimated at 95.2%	94.1%	96.0%
Lumley et al.	30 weeks follow up time	"Positive baseline anti-spike antibodies were associated with lower rates of PCR-positivity (with or without symptoms) (adjusted rate ratio 0.24 [95% CI 0.08-0.76, p=0.015]" Assume efficacy of natural infection against reinfection of 76%	24%	92%
Hansen et al.	28 weeks	"Protection against repeat infection was 80·5% (95% CI 75·4–84·5)."	75.4%	84.5%
Unweighted mean	27.76 weeks = 194.32 days	85.74%	71.1%	91.5%