Autumn–winter scenarios 2021–2022

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In this report we model potential dynamics of SARS-CoV-2 transmission in England from October 2021 until September 2022. We model COVID-19 booster doses, waning vaccine protection and vaccination of 12-15 year old children, as well as incorporating uncertainty via future behavioural changes.

Summary of changes since July 2021

- The analysis in this report builds on the work done in our previous report.
- We have updated our fitting methodology to achieve a closer fit to observed data. This is described in the 'Basic model assumptions' section.
- We utilise Department for Education school attendance data for England up to July 2021 to scale school-related contacts during times when schools are open.
- We consider four scenarios for future mobility: a no change scenario, and three scenarios where mobility returns to pre-pandemic levels (after 3 weeks, 3 months, and 6 months).
- We have updated our assumptions on vaccine protection (see Table 1, Table S1 and Table S2) and waning immunity (Table 3).
- We consider vaccination of 12-17 year olds, where we previously only considered vaccination of individuals aged 18 and above.
- We model booster vaccinations and vaccinated individuals without booster doses having reduced levels of protection (see Tables 2A and 2B).

Results

We frame our results in terms of the sensitivity of model trajectories to two key uncertainties: mobility and behaviour, and vaccine waning and boosters.

1. Mobility and behaviour

As before, this iteration of the LSHTM model uses Google Community Mobility indices to derive contact rates for each NHS England region modelled, based upon a measured relationship between Google Mobility indices and age-specific contact rates as measured by the CoMix study (**Fig. 1**). A new feature of the model for this report is that we now fit an additional time-varying "transmission adjustment" component in order to capture additional variability in transmission that is not explained by mobility data. The fitted transmission adjustment can be seen in the middle row of **Fig. 1**; there is a notable sharp peak around Christmas 2020.

For projecting forwards from October 2021 into the autumn and winter period, we use two different strategies for mobility and for the transmission adjustment. For mobility, as before, we smoothly ramp mobility indices from their current values to indicative values in the future representing different mobility scenarios. Here, we consider four scenarios: three scenarios in which mobility returns to pre-pandemic "baseline" levels but after different lengths of time (3 weeks, 3 months, or 6 months), and one scenario in which mobility stays at its current level for the remainder of the simulation (**Fig. 1**, top row). For the transmission adjustment, to project forwards, we fit an autoregressive integrated moving average (ARIMA) model to the transmission adjustment (i.e. from June 2020 to the end of September 2021) in order to capture the features of the random-walk–like curve, then simulate new ARIMA trajectories using the fitted parameters. **Fig. 1**, middle row, shows an example of a randomly-generated trajectory (purple) as well as the mean and interquartile range (IQR) over all randomly-generated trajectories (orange). We simulate 100 such trajectories—which are fitted and simulated separately for each NHS England region—for each modelled scenario. The combined impact of mobility and the transmission adjustment on the overall transmission potential can be seen in the bottom row of **Fig. 1**, which assumes that mobility indices return to pre-pandemic baseline levels after 6 months.

The rate at which mobility returns to the pre-pandemic baseline affects both the timing and the magnitude of projected epidemics over the next year (**Fig. 2**). When looking over a short timescale (October to December 2021), a slower return to baseline mobility decreases the total number of infections, hospital admissions, and deaths; however, over longer timescales, there is less of a difference between different rates of returning to baseline. This owes to an interaction between waning, seasonality, and mobility rates.

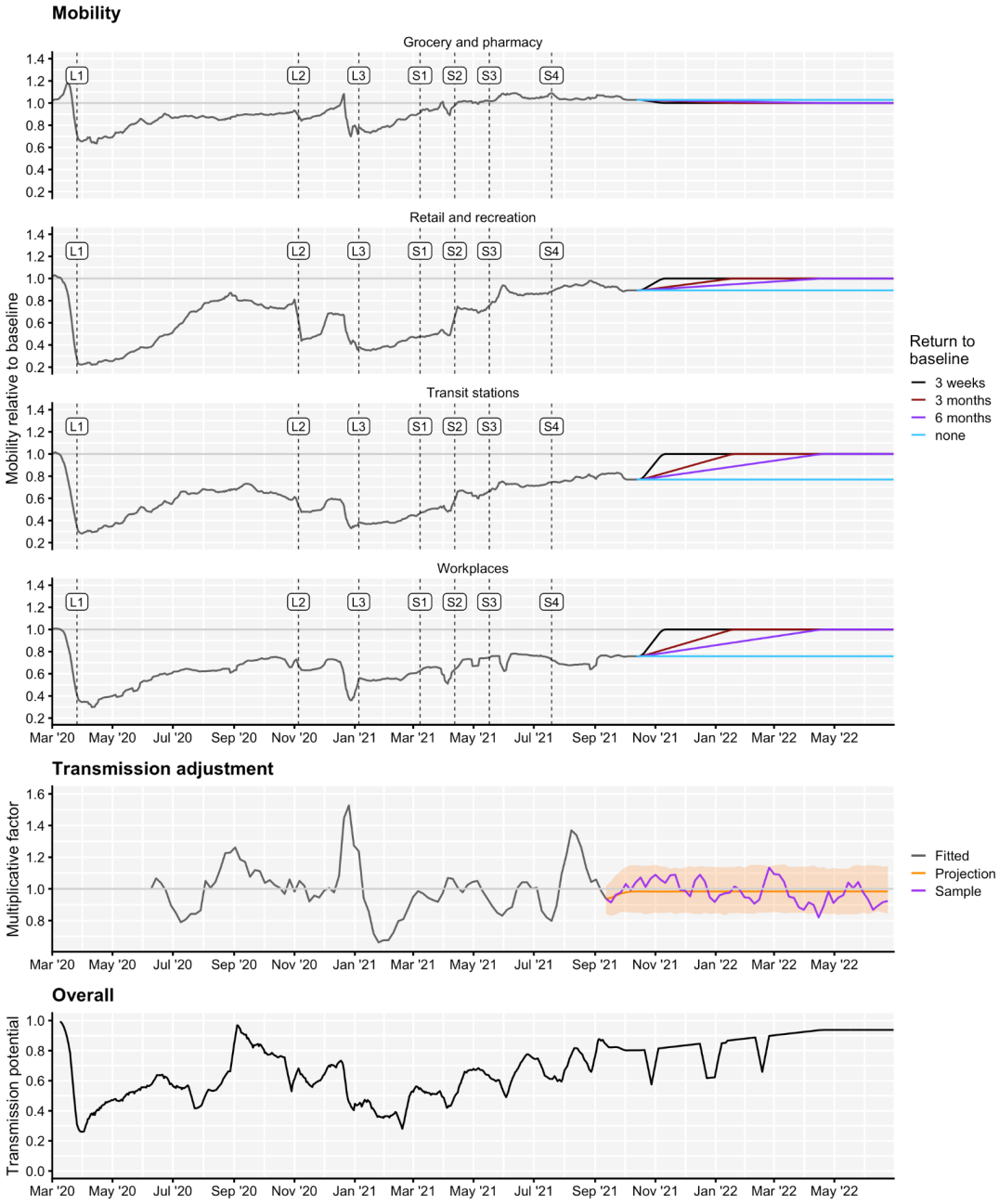
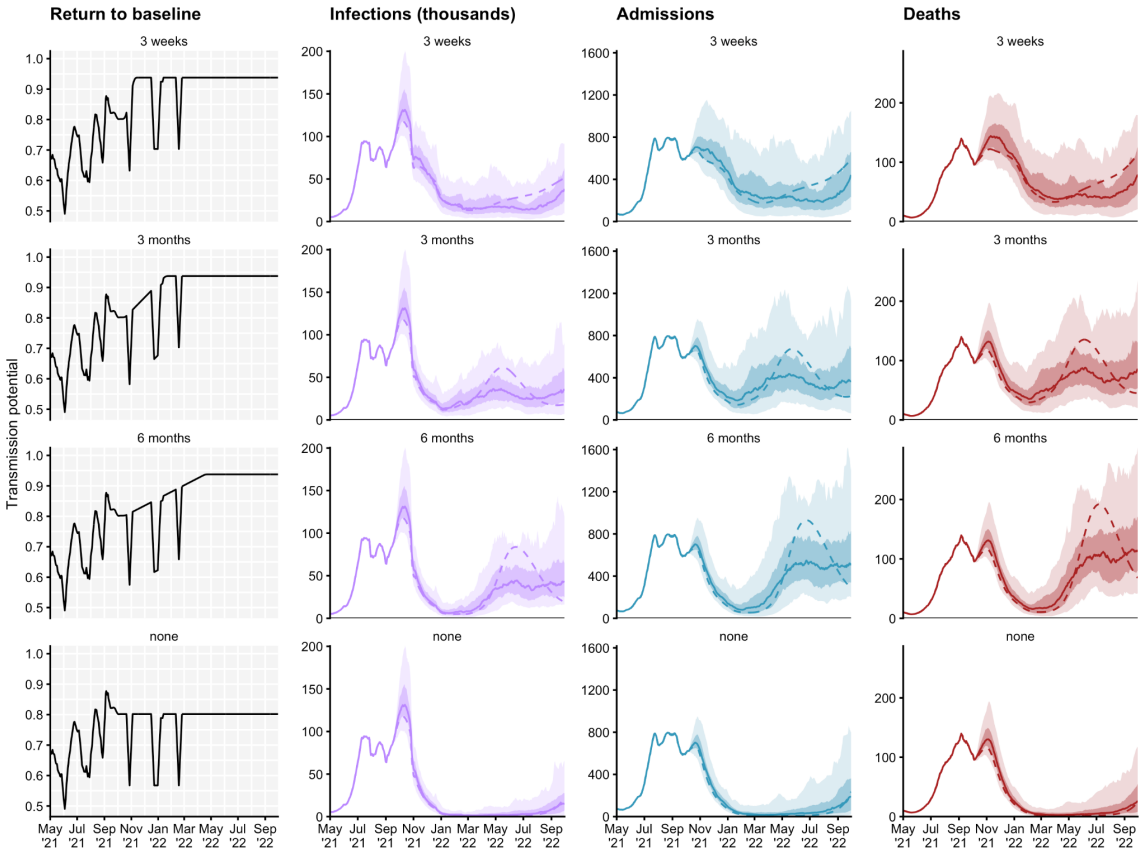


Fig. 1. Mobility scenarios, transmission adjustment, and overall transmission potential for the fitted model, shown from March 2020 to June 2022. **Top:** Historic Google Community Mobility data (grey) and assumed future mobility in England for no change (blue), a 6 month return to baseline levels (purple), a 3 month return to baseline levels (red) and a 3-week return to baseline levels (black) 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. **Middle:** Fitted transmission adjustment (grey), example projection (purple) and mean + interquartile range (orange) for projected transmission adjustments. **Bottom:** The "transmission potential" captures the overall impact of mobility (here, returning to baseline in 6 months) and transmission adjustments on the time-varying potential for effective transmission, ignoring the impact of immunity and novel variants.



Short-term outcomes from 1 Oct 2021 to 31 Dec 2021

Return to baseline	Infections	Admissions	Deaths
3 weeks	7,400,000 (5,800,000 - 9,200,000)	58,000 (47,000 - 83,000)	12,000 (9,100 - 16,000)
3 months	5,800,000 (4,600,000 - 7,200,000)	43,000 (36,000 - 59,000)	9,000 (7,200 - 12,000)
6 months	5,400,000 (4,300,000 - 7,000,000)	41,000 (34,000 - 56,000)	8,700 (7,000 - 11,000)
none	5,100,000 (4,100,000 - 6,700,000)	39,000 (32,000 - 53,000)	8,400 (6,800 - 11,000)

Longer-term outcomes from 1 Oct 2021 to 30 Sept 2022

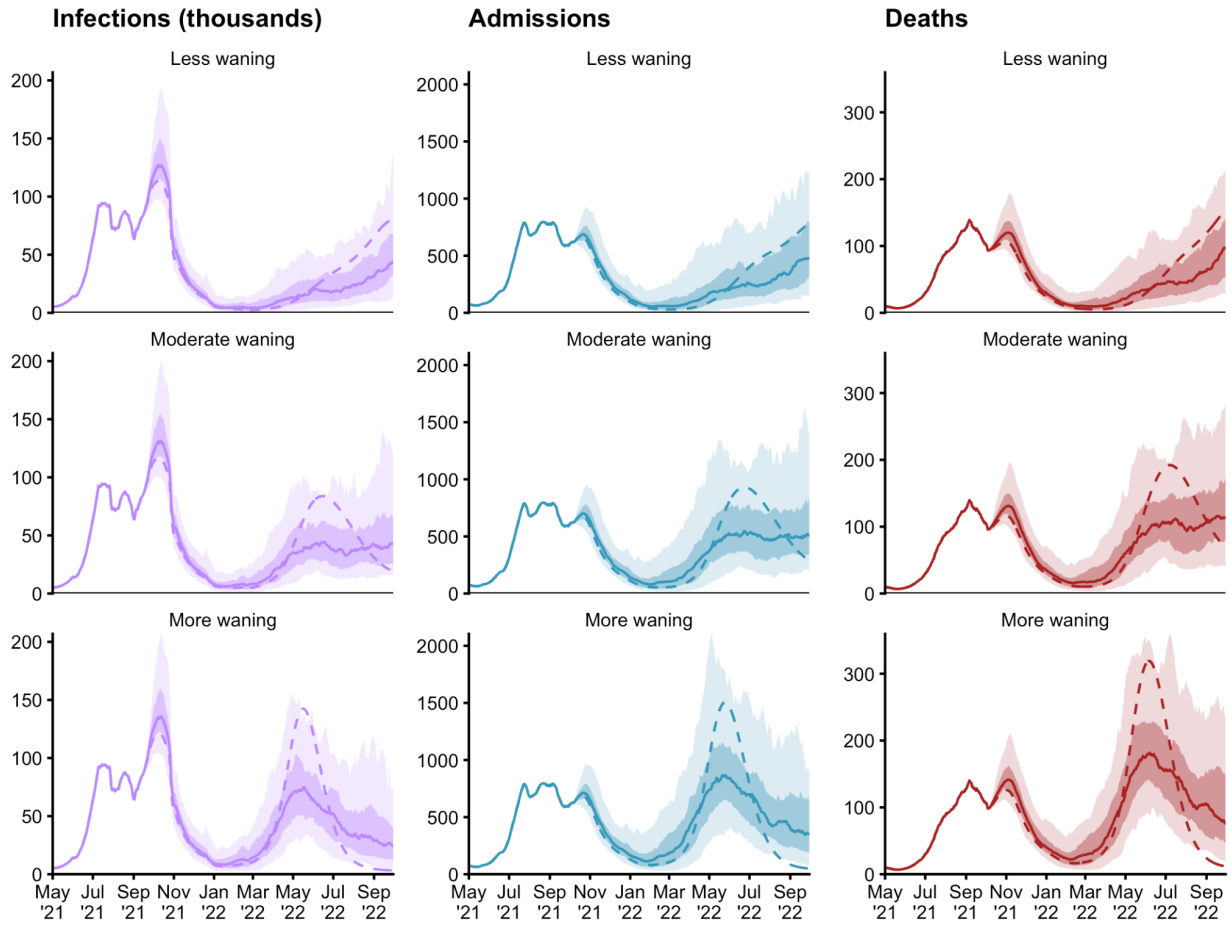
Return to baseline	Infections	Admissions	Deaths
3 weeks	14,000,000 (12,000,000 - 15,000,000)	150,000 (100,000 - 180,000)	29,000 (22,000 - 32,000)
3 months	14,000,000 (12,000,000 - 16,000,000)	150,000 (110,000 - 190,000)	30,000 (24,000 - 34,000)
6 months	14,000,000 (12,000,000 - 16,000,000)	150,000 (100,000 - 200,000)	30,000 (23,000 - 35,000)
none	6,700,000 (5,500,000 - 8,200,000)	61,000 (43,000 - 86,000)	11,000 (9,500 - 15,000)

Fig. 2. Impact of mobility changes on dynamics over the autumn and winter. **Plot:** Possible trajectories for infections, admissions, and deaths are simulated for different rates of return to pre-pandemic baseline. The shaded areas and solid lines show the 90% interquantile range, the 50% interquantile range, and the median for each time point, while the dashed line shows a sample trajectory. All scenarios assume moderate waning (see Table 2B) and 90% of individuals aged 50 and above receiving booster vaccines. **Tables:** the total number of infections, admissions, and deaths, over the shorter term (October to December 2021) and the longer term (October 2021 to September 2022). Note that delays to the return to baseline primarily delay, rather than reduce, the peak in these scenarios.

2. Vaccine waning and boosters

The extent to which vaccine protection wanes is a key uncertainty, and has not been measured over sufficiently long timescales to strongly constrain model parameters. We explore three different scenarios here, based on the measured reduction in vaccine protection after 15-19 weeks (for vaccine protection against death) or 20+ weeks (for vaccine protection against symptomatic disease and hospitalisation; Andrews et al.) following an individual's second dose. In the "less waning" scenario, we assume that these measured changes in protection after 15-20+ weeks represent the reduction in protection for an individual whose vaccine protection has fully waned (within the timescales of the simulation). In the "moderate waning" scenario, we assume that vaccine protection wanes a further 25% lower than these measured values, and in the "more waning" scenario, we assume that vaccine protection wanes to half of these measured values (**Table 2B**). Waning has a notably strong impact upon model trajectories (**Fig. 3**), with lower levels of waning substantially delaying and reducing the peak.

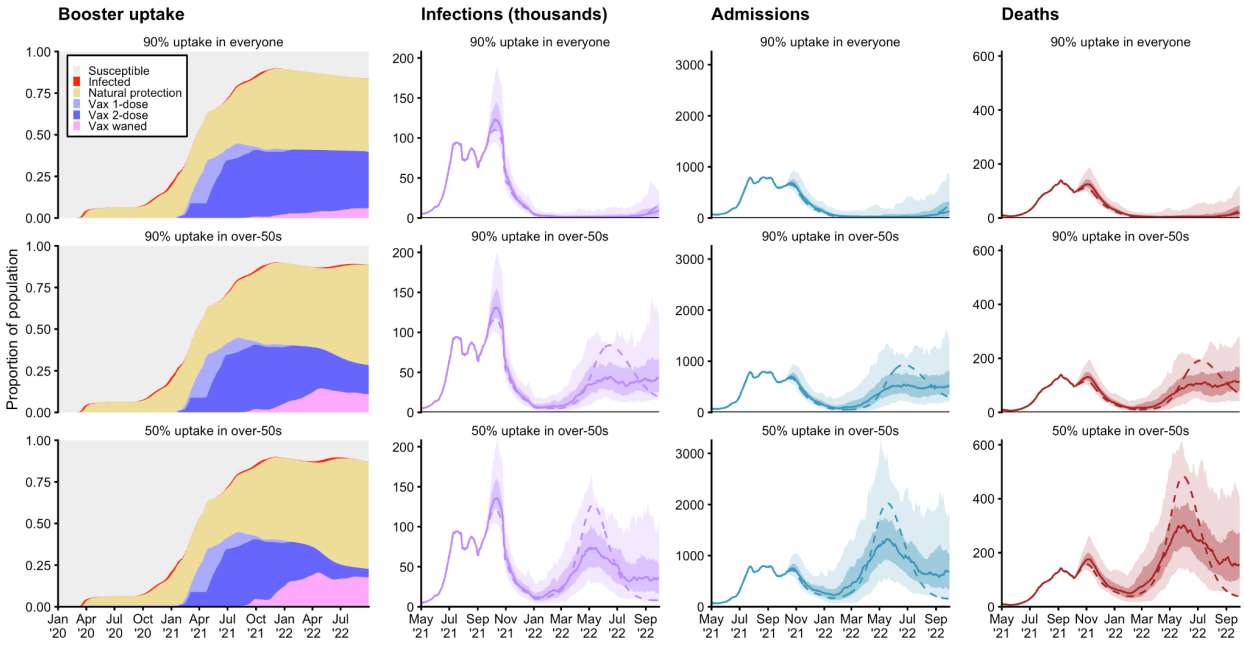
The uptake of booster doses among recipients of two doses also has a substantial impact upon dynamics. We contrast three illustrative scenarios: one in which half of eligible individuals aged 50 and above receive a booster; one in which 90% of eligible individuals aged 50 and above receive a booster; and one in which 90% of all individuals, regardless of age, receive a booster (**Fig. 4**). Greater booster coverage substantially reduces infections, deaths, and hospitalisations, because of its impact in reducing transmission.



Outcomes from 1 Oct 2021 to 30 Sept 2022

	Infections	Admissions	Deaths
Less waning	11,000,000 (8,600,000 - 13,000,000)	110,000 (70,000 - 150,000)	19,000 (14,000 - 24,000)
Moderate waning	14,000,000 (12,000,000 - 16,000,000)	150,000 (100,000 - 200,000)	30,000 (23,000 - 35,000)
More waning	17,000,000 (15,000,000 - 19,000,000)	190,000 (140,000 - 230,000)	39,000 (31,000 - 44,000)

Fig. 3. Impact of vaccine waning on dynamics over the autumn and winter. **Plot:** Possible trajectories for infections, admissions, and deaths are simulated for different rates of vaccine waning. The shaded areas and solid lines show the 90% interquantile range, the 50% interquantile range, and the median for each time point, while the dashed line shows a sample trajectory. All scenarios assume that mobility returns to pre-pandemic baseline levels in 6 months and that 90% of individuals aged 50 and above receive booster vaccinations. Assumptions for the various vaccine waning scenarios are listed in Table 2B. **Table:** the total number of infections, admissions, and deaths, from October 2021 to September 2022.



Outcomes from 1 Oct 2021 to 30 Sept 2022

Booster uptake among recipients of 2 doses	Infections	Admissions	Deaths
90% uptake in everyone	6,100,000 (5,000,000 - 7,400,000)	62,000 (44,000 - 92,000)	12,000 (9,000 - 15,000)
90% uptake in individuals aged 50 and above	14,000,000 (12,000,000 - 16,000,000)	150,000 (100,000 - 200,000)	30,000 (23,000 - 35,000)
50% uptake in individuals aged 50 and above	19,000,000 (16,000,000 - 21,000,000)	280,000 (200,000 - 350,000)	64,000 (49,000 - 75,000)

Fig. 4. Impact of booster uptake on dynamics over the autumn and winter. **Plot, left hand side:** The proportion of the population who are, from top to bottom: susceptible, infected, recovered and protected from natural infection, vaccinated with one dose levels of protection, vaccinated with two dose levels of protection and vaccinated and waned, with reduced levels of protection. **Plot, right hand side:** Possible trajectories for infections, admissions, and deaths are simulated for different rates of booster dose uptake. The shaded areas and solid lines show the 90% interquantile range, the 50% interquantile range, and the median for each time point, while the dashed line shows a sample trajectory. All scenarios assume that mobility returns to pre-pandemic baseline levels in 6 months and moderate waning of vaccine protection (see Table 2B). **Table:** the total number of infections, admissions, and deaths, from October 2021 to September 2022.

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. Since the previous report to SPI-M, we have made a number of changes to the fitting methods: the model fits more closely the dynamics of COVID-19 deaths, hospital admissions, hospital bed occupancy and intensive care unit (ICU) bed occupancy by allowing for time-varying adjustments to the infection fatality rate as well as hospitalisation rates to achieve fits to the data as observed. In addition, we employ a two-stage fitting process: initially, the model fits a number of scaling factors to contact rates for consecutive 6-week periods throughout the epidemic. After this initial round of fitting, we use a particle filter to improve the fit to PCR prevalence over time (the “transmission adjustment” of Fig. 1).

School openings and closings are accounted for in contacts among school-aged children, university-aged young adults and school/university staff. We assume that schools in England follow their traditional schedules (i.e. are closed during half-term periods and over summer holiday periods), and we combine these assumptions with Department for Education data on school attendance in England up to July 2021. 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 between the reopening of schools on 8th March 2021 and school closures in July 2021. This reduction in transmission is reflected in the model with a 30% reduction in school-related contacts. 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 three co-circulating SARS-CoV-2 variants: the Delta B.1.617.2, Alpha B.1.1.7 and pre-existing variants. The model structure has been extended from a similar two-variant model structure (Davies et al. 2021, Science) to consider three variants explicitly. 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 Public Health England (PHE) / the UK Health Security Agency (UKHSA) and the NHS (Davies et al. 2020 Lancet Inf Dis); the frequency of S gene target failure up to 15th February 2021 to capture the spread of Alpha B.1.1.7 (Davies et al. 2021, Science); and the

frequency of lineage B.1.617.2 in sequenced Pillar 2 cases up to September 2021 to capture the spread of Delta B.1.617.2.

We use PHE/UKHSA data recording the number of first COVID-19 vaccine doses delivered by age, geography and vaccine product from the 8th of December 2020 to the 3rd of October 2021 to inform the fraction of first-dose vaccinated individuals in each age group, NHS England region and by vaccine type over time. First-dose vaccine schedules are generated by combining vaccines already delivered with future schedules generated based on a number of assumptions (see 'Vaccine assumptions'). We specify a distribution for the duration of vaccinated individuals remaining at first-dose levels of protection before transitioning into second-dose protection. This distribution is chosen according to measured delays between first and second doses in the PHE/UKHSA vaccination data, separated into two periods (before and after the Joint Committee on Vaccination and Immunisation (JCVI) issued guidance on widening the dosing gap from 3 weeks to a maximum of 12 weeks).

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), then adjusted to better match observed hospitalisations and deaths in England. 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 Alpha B.1.1.7. For the third variant Delta B.1.617.2, we assume that the probability of severe outcomes is twice that of Alpha B.1.1.7. Throughout this report, we assume seasonality of 20% peak to trough, introduced from the 1st of April 2021.

Mobility assumptions

We base our assumptions on how social contact rates might be expected to change by referring to historical Google Community Mobility data and making assumptions about future mobility changes until September 2022 (Fig. 1). We consider four scenarios: we project current levels of mobility forwards (i.e. no change), and we consider a return to pre-pandemic baseline levels of mobility within a period of 3 weeks, 3 months and 6 months.

Vaccine assumptions

Vaccine schedules

First-dose vaccine schedules are generated by combining PHE/UKHSA data on vaccines delivered up to the 3rd of October 2021 in England with future schedules based on a number of assumptions related to vaccine product distribution, vaccine supply and vaccine uptake. The number of future first doses supplied for each day in the schedule are distributed into the seven NHS England regions according to the population size of each region. Existing first-dose

vaccination uptake for ages 20+ are used as uptake limits such that no future first doses are delivered to these age groups. We assume uptake is limited at 70% for individuals aged 12-19, delivering future first doses first to the 15-19 age group up to the uptake limit followed by 12-14 year olds. The allocated number of first 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). If doses are remaining after this process, leftover doses are carried over to either the next age group down up to the relevant uptake limit, the next NHS England region, the next day, or are not allocated in the schedule and are recorded as leftover doses.

First-dose vaccinated individuals transition into second dose protection according to a distribution controlling the duration of vaccinated individuals remaining at first-dose levels of protection. This distribution is chosen according to measured delays between first and second doses in the PHE/UKHSA vaccination data, separated into two periods (before and after the JCVI issued guidance on widening the dosing gap from 3 weeks to a maximum of 12 weeks). The duration that individuals have second-dose levels of protection is chosen to match the time between the start of the COVID-19 vaccination rollout (8th December 2020) and the start of the COVID-19 booster dose rollout (24th September 2021), less the time duration already assumed at first dose levels of protection. At the end of their second dose protection, individuals either receive booster doses and retain second-dose levels of protection, or move into a waned state with reduced levels of vaccine protection.

Vaccine effectiveness

We base our vaccine effectiveness assumptions on the latest available evidence. These may be subject to change in future work, 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 additionally consider individuals who have received two vaccine doses but no booster dose as having reduced levels of protection, with various scenarios considered in relation to vaccine protection (see Tables 2A and 2B).

We model vaccine protection against five separate outcomes: infection, disease (i.e. symptomatic infection), hospitalisation, mortality and onward transmission following a breakthrough infection (i.e. when an individual who has vaccine protection becomes infected). We assume the same vaccine effectiveness for the first two SARS-CoV-2 variants considered in the model (pre-Alpha B.1.1.7 and Alpha B.1.1.7), and separate specific vaccine effectiveness estimates for the Delta B.1.617.2 variant, shown in Table 1. Table S1 in the Supplementary Material section shows a summary of the relevant evidence we have used to guide our assumptions on vaccine effectiveness against Alpha B.1.1.7 and pre-existing variants of SARS-CoV-2. Table S2 in the Supplementary Material section shows a summary of the relevant evidence we have used to guide our assumptions on vaccine effectiveness against the Delta B.1.617.2 variant.

Our assumptions about the levels of vaccine protection for individuals who have received two vaccine doses but no booster dose, and their protection has waned, are shown in Tables 2A and 2B, along with comparable estimates used by the Warwick modelling team (Table 2A). To parametrise these reductions in vaccine protection, we have referred to Andrews et al., using the measured percentage change in protection for ages 16+ against symptomatic disease and hospitalisation between week 1 and 20+ weeks and against death between week 1 and 15-19 weeks. We have used the vaccine product specific percentage changes in protection against symptomatic disease to scale our estimates against infection and disease, and the percentage changes in protection against hospitalisation and death to scale our estimates against hospitalisation and death, respectively. We have calculated the mean percentage change across these three values for each vaccine product and used this change to scale our estimates for vaccine protection against onward transmission. Since we model an individual's average duration in second dose protection as 29.3 weeks, before they are either boosted and remain at two-dose levels of protection or are not boosted and wane, we consider these baseline assumptions for the levels of protection in the waned state as being optimistic, and we refer to this as the 'less waning' scenario. Therefore, we also consider an additional two scenarios for two-dose vaccinated and waned individuals, where we assume 25% (moderate waning) and 50% (more waning) reductions to the waned estimates shown in Table 2A. The full list of the assumed values for waning scenarios is shown in Table 2B.

Vaccine rollout

Future vaccine rollouts follow a Cabinet Office Scenario with an average of 200,000 first doses offered per week for those aged between 12 and 15.

Vaccine mix

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

- 75% Pfizer and 25% Moderna for <40 year olds
- 60% AstraZeneca, 30% Pfizer and 10% Moderna for 40+ year olds

Waning immunity

We model waning protection from SARS-CoV-2 infection developed from natural infection and vaccination. For waning protection from natural infection, we assume identical rates of waning for all three virus variants and for all age groups (Table 3). Once individuals who have recovered from natural infection wane, they return to a susceptible disease state; thus we model waning of natural immunity against different endpoints (infection, disease, hospitalisation, deaths and onward transmission) at the same rate. In contrast to previous reports, we no longer model individuals waning from second vaccination protection directly back to being susceptible. To account for booster vaccinations, upon leaving the second dose state, individuals either receive a booster vaccine and return to second dose levels of protection, or move into a third state with

reduced levels of vaccine protection across different outcomes (see Tables 2A and 2B). This third state corresponds to individuals who have received two vaccine doses followed by waning of their vaccine protection. Once individuals have moved into this waned state with reduced levels of vaccine protection, they are also allowed to wane back to being susceptible, with different rates considered for each vaccine product (Table 3). The assumed percentage loss in reduction here is based on measured percentage changes in vaccine protection against hospitalisation for each vaccine product in Andrews et al.

Variant of concern Delta B.1.617.2

Our analysis considers a third SARS-CoV-2 variant which has been parametrised in relation to the Delta / B.1.617.2 variant of concern, also referred to as VOC-21APR-02. We use sequenced Pillar 2 cases to inform the proportion of the Delta B.1.617.2 variant circulating versus the proportion of pre-Alpha B.1.1.7 and Alpha B.1.1.7 variants. We make assumptions about the level of vaccine protection against the Delta B.1.617.2 variant (Table 1). For each NHS England region the model fits an introduction time and relative transmissibility of the Delta B.1.617.2 variant (compared to the Alpha B.1.1.7 variant) to best match the sequencing data. We assume that the Delta B.1.617.2 variant has a two-fold higher probability of severe outcomes compared to assumed levels for the Alpha B.1.1.7 variant.

Table 1 - Assumptions for vaccine effectiveness against all SARS-CoV-2 outcomes

Outcome	Variant name	Vaccine effectiveness			
		*Pfizer-BioNTech**		*Oxford-AstraZeneca*	
		1 dose	2 doses	1 dose	2 doses
Infection	pre-Alpha & Alpha	70%	85%	70%	75%
	Delta^	62%	80%	43%	63%
Disease	pre-Alpha & Alpha	70%	90%	70%	80%
	Delta^	62%	81%	52%	65%
Hospitalisation	pre-Alpha & Alpha	85%	95%	85%	90%
	Delta^	92%	96%	84%	93%
Mortality	pre-Alpha & Alpha	85%	95%	85%	95%
	Delta^	92%	96%	95%	95%
Onward transmission	pre-Alpha & Alpha	47%	47%	47%	47%
	Delta^	24%	37%	5%	27%
Delay to efficacy		28 days	14 days	28 days	14 days

*We assume that the Moderna mRNA-1273 vaccine confers the same levels of protection as the Pfizer-BioNTech vaccine.

^For vaccine effectiveness with the Delta B.1.617.2 variant, we either scale the equivalent vaccine effectiveness assumption for pre-Alpha and Alpha variants by the unweighted mean change in protection from Alpha to Delta as measured by the references in Table S2, or assume equivalent values from the previous equivalent dose or the previous level of protection.

Table 2A - Assumptions for 2-dose vaccine effectiveness against all SARS-CoV-2 outcomes and 2-dose + waned (i.e. no booster dose), with comparison to Warwick values. The waned values shown here correspond to the 'less waning' scenario. All scenarios for waning vaccine protection are listed in Table 2B.

Outcome	**Variant name**	**Vaccine effectiveness**			
		*Pfizer-BioNTech**		*Oxford-AstraZeneca*	
		2 doses	Waned	2 doses	Waned
Infection	pre-Alpha & Alpha	85%	64%	75%	57%
	Delta	80%	60%	63%	48%
	Warwick all	85%	(50, 30, 0%)	70%	(50, 30, 0%)
Disease	pre-Alpha & Alpha	90%	68%	80%	60%
	Delta	81%	61%	65%	49%
	Warwick all	90%	(55, 35, 10%)	70%	(55, 35, 10%)
Hospitalisation	pre-Alpha & Alpha	95%	88%	90%	74%
	Delta	96%	89%	93%	76%
	Warwick all	95%	(85, 79, 70%)	95%	(85, 79, 70%)
Mortality	pre-Alpha & Alpha	95%	87%	95%	79%
	Delta	96%	88%	95%	79%
	Warwick all	98%	(85, 79, 70%)	98%	(85, 79, 70%)
Onward transmission	pre-Alpha & Alpha	47%	40%	47%	38%
	Delta	37%	32%	27%	22%
	Warwick all	30%	(20, 20, 20%)	30%	(20, 20, 20%)

*We assume that the Moderna mRNA-1273 vaccine confers the same levels of protection as the Pfizer-BioNTech vaccine.

Table 2B - Assumptions for 2-dose vaccine effectiveness against all SARS-CoV-2 outcomes and 2-dose + waned (i.e. no booster dose) scenarios. Values shown are rounded to the nearest whole percentage. Less waning assumes the same values shown in Table 2A, moderate waning assumes a 25% reduction in those values, and more waning assumes a 50% reduction in those values.

Outcome	**Variant name**	**Vaccine effectiveness**			
		*Pfizer-BioNTech**		*Oxford-AstraZeneca*	
		2 doses	Waned: less, moderate, more	2 doses	Waned: less, moderate, more
Infection	pre-Alpha & Alpha	85%	64%, 48%, 32%	75%	57%, 43%, 29%
	Delta	80%	60%, 45%, 30%	63%	48%, 36%, 24%
Disease	pre-Alpha & Alpha	90%	68%, 51%, 34%	80%	60%, 45%, 30%
	Delta	81%	61%, 46%, 31%	65%	49%, 37%, 25%
Hospitalisation	pre-Alpha & Alpha	95%	88%, 66%, 44%	90%	74%, 56%, 37%
	Delta	96%	89%, 67%, 45%	93%	76%, 57%, 38%
Mortality	pre-Alpha & Alpha	95%	87%, 65%, 44%	95%	79%, 59%, 40%
	Delta	96%	88%, 66%, 44%	95%	79%, 59%, 40%
Onward transmission	pre-Alpha & Alpha	47%	40%, 30%, 20%	47%	38%, 29%, 19%
	Delta	37%	32%, 24%, 16%	27%	22%, 17%, 11%

*We assume that the Moderna mRNA-1273 vaccine confers the same levels of protection as the Pfizer-BioNTech vaccine.

Table 3 - Waning immunity scenarios

Description	Assumed values (**waning**)	Vaccine
Waning of natural immunity	log(0.85)/-365, corresponding to 85% protection after 365 days = 1 year	
Waning of vaccine induced immunity (second dose to susceptible / naive)	0	
Waning of vaccine induced immunity (first dose to susceptible / naive and second dose to first dose)	0	
Waning of vaccine induced immunity (second dose + waned to susceptible / naive)	log(0.93)/-140, corresponding to 7% loss in protection after 20 weeks	Pfizer / Moderna
	log(0.82)/-140, corresponding to 18% loss in protection after 20 weeks	AstraZeneca

Supplementary material

Table S1 - Vaccine effectiveness against pre-B.1.1.7 and Alpha B.1.1.7 variants - relevant evidence and baseline model assumptions (updated 5th October 2021)

Description	Relevant evidence, assumed value shown in bold
Overall protection against infection for AstraZeneca dose 1	Shrotri et al. Table 4 adjusted hazard ratio 0.33 (0.16, 0.68) at 28-34 days post vaccination for protection against infection in care home residents. Pritchard et al., supplementary information, Table 6, adjusted odds ratio >= 21 days after first dose of AZ, no second dose, 0.39 (0.32, 0.46) for all positives. Glampson et al. results, Table 2, hazard ratio 0.26 (0.19, 0.35) for AZ between 22 and 28 days following first dose when comparing AZ vaccinated individuals with unvaccinated individuals. Thus a 74% reduction in risk of testing positive for COVID-19. Amirthalingam et al. results, adults aged 80 and above, 43% vaccine protection (24-58%) on days 28-34 following the first dose of AZ. Amongst 65-79 year olds 55% vaccine protection (48-61%) 28 days after the first dose of AZ. Amongst 50-64 year olds 50% vaccine protection (45-55%) 28 days after the first dose of AZ. Evidence of reductions in vaccine protection by 70 days post vaccination: 40% (23-53%) and 26% (18-33%) for 65-79 and 50-64 year olds respectively. Point estimates showed a decline after 8 weeks for individuals aged 80 and above (but wide confidence intervals). Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Alpha variant of 63% (55-69%) at least 21 days following the first dose of AZ. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 37% (32-42%) 28 days after the first dose of AZ. **0.7 (+28 days)**
Overall protection against disease for AstraZeneca dose 1	Pritchard et al., supplementary information, Table 6, adjusted odds ratio >= 21 days after first dose of AZ, no second dose, 0.29 (0.22, 0.38) for positive individuals with symptoms reported. Lopez Bernal et al. (cohort aged 70+ years of age) Table 3, ChAdOx1 adjusted odds ratio d1:28-34 0.4 (0.27-0.59). PHE's week 20 vaccine surveillance reports reports estimates of 53% (49-57%) vaccine protection against symptomatic disease at least 28 days following the first dose of AZ (compared to unvaccinated individuals). Compared to individuals between 4 and 13 days after the first dose, they estimate 58% (54-62%) protection against symptomatic disease. Whitaker et al. Table 4, adjusted vaccine effectiveness against symptomatic COVID-19 28-90 days post first dose of AZ 50.2% (40.8-58.2%) for individuals aged 16-64 and 60.9% (49.0-70.0%) for individuals aged 65 and over.

	Lopez Bernal et al. C report adjusted vaccine effectiveness against symptomatic infection with S-gene target negatives (i.e. Alpha variant) of 48.7% (45.2% to 51.9%). Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Alpha variant of 73% (67-77%) at least 21 days following the first dose of AZ. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 39% (32-45%) 28 days after the first dose of AZ. PHE's week 36 vaccine surveillance report estimates protection against symptomatic disease of 49% (46-52%) for the Alpha variant at least 28 days after a first vaccine dose. Andrews et al. report protection against symptomatic disease for the first dose of AZ as 44.5% (42.9 to 46.1%), at least 28 days following the first dose and up to the second dose if given. **0.7 (+28 days) as for infection**
Overall protection against hospitalisation for AstraZeneca dose 1	Lopez Bernal et al. Table 4, hazard ratio for risk of hospital admission in vaccinated vs unvaccinated individuals (subsection of cohort that are 80+ years of age) 0.63 (0.41 to 0.97) at least 14 days following first dose of AZ. 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. Ismail et al. estimate vaccine effectiveness against hospitalisation of 73% (60-81%) for 80+ year olds and 84% (74-89%) for 70-79 year olds, 28 days following the first dose of AZ. When analysis is not split across vaccine products, the same study estimates efficacy against hospitalisation of 80% (74-85%) for 80+ year olds and 82% (75-87%) for 70-79 year olds. Hyams et al. Table 2, adjusted vaccine effectiveness against hospitalisation (in individuals aged over 80 years of age) for one dose of ChAdOx1 nCov-19 80.4% (36.4 - 94.5%). PHE's week 26 vaccine surveillance report finds protection against hospitalisation with the Alpha variant of 79% (74-82%) following the first dose of AZ. Stowe et al. report vaccine effectiveness against hospitalisation of 76% (61-85%) following the first dose of AZ. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 78% (64-87%) for the Alpha variant at least 28 days after a first vaccine dose. Andrews et al. report protection against hospitalisation for the first dose of AZ as 82.5% (78.7 to 85.7%), at least 28 days following the first dose and up to the second dose if given. **0.85 (+28 days)**

Overall protection against mortality for AstraZeneca dose 1	Lopez Bernal et al. B (study in a care home population) estimated a hazard ratio of 0.45 (0.34 - 0.59) for cases vaccinated with one dose of AZ compared to unvaccinated cases, indicating an additional 55% (41-66%) protection against death given becoming a case for individuals vaccinated with one dose of AZ. Using the aforementioned estimate of a 55% increase and assuming this in addition to protection against disease of 0.7**,** we get overall protection against mortality of 86.5%. PHE's week 26 vaccine surveillance report finds protection against mortality with the Alpha variant of 79% (73-83%) and 83% (78-86%) for 40-64 and 65+ year olds respectively, following the first dose of AZ. Andrews et al. report protection against death for the first dose of AZ as 79.1% (68.8 to 86%), at least 28 days following the first dose and up to the second dose if given. **0.85 (+28 days)**
Overall protection against onward transmission for AstraZeneca dose 1	Harris et al. calculate an adjusted odds ratio of being a secondary case within a household of index cases vaccinated with ChAdOx1 (AstraZeneca) at least 21 days before testing positive as 0.52 (0.43-0.62) and index cases vaccinated with BNT162b2 (Pfizer-BioNTech) at least 21 days before testing positive as 0.54 (0.47-0.62). Shah et al. find that relative to the period before a healthcare worker was vaccinated, the hazard ratio for a household member of the vaccinated healthcare worker to become infected was 0.7 (0.63-0.78) for the period beginning 14 days following first vaccine dose and 0.46 (0.30-0.70) for the period beginning 14 days after the second vaccine dose (healthcare workers were vaccinated with either AstraZeneca or Pfizer). Braeye et al. (Belgium, mostly Alpha variant) estimated VE against onward transmission "at 62% (95% CI 57–67) for BNT162b2 and 52% (95% CI 33–69) for mRNA1273 for full vaccination. No significant effect against onward transmission was found for the 'viral-vector'-vaccines, but credibility intervals were large." Eyre et al. report an adjusted odds ratio of 0.82 (0.76, 0.88) for the effect of a case being partially vaccinated with AZ (dose 1 day 1 to dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive. **0.47 (+28 days)**
Overall protection against infection for AstraZeneca dose 2	Shrotri et al. Table 4 adjusted hazard ratio 0.32 (0.15, 0.66) at 35-48 days post vaccination in care home residents. Pritchard et al., supplementary information, Table 6, adjusted odds ratio post second dose of AZ 0.21 (0.12, 0.35) for all positives.

	Lopez Bernal et al. (cohort aged 70+ years of age) Table 3, ChAdOx1 adjusted odds ratio d1:>=35 days 0.27 (0.10 to 0.73). Amirthalingam et al. results, individuals aged 80+ years old had 96% (68-99%) and 82% (68-89%) vaccine effect at least 14 days following the second dose of AZ with 45-64 and 65-84 day intervals between first and second doses. “Those receiving their second dose outside of these recommended intervals also had high VE after two doses; for an ≥85 day interval, the estimated VE was 88% (95%CI: 48-97).” Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Alpha variant of 79% (56-90%) at least 14 days following the second dose of AZ. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 73% (66-78%) 14 days after the second dose of AZ. **0.75 (+14 days)**
Overall protection against disease for AstraZeneca dose 2	Pritchard et al., supplementary information, Table 6, adjusted odds ratio post second dose of AZ 0.08 (0.03, 0.22) for positive individuals with symptoms reported. 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. PHE’s week 20 vaccine surveillance report reports estimates of 89% (78-94%) vaccine protection against symptomatic disease at least 14 days following the second dose of AZ (compared to unvaccinated individuals). Compared to individuals between 4 and 13 days post first dose, they estimate 90% (80-95%) protection. Whitaker et al. Table 4, adjusted vaccine effectiveness against symptomatic COVID-19 at least 14 days following second dose of AZ 78% (69.7-84%) for individuals aged 16-64 and 76.4% (58.8-86.5%) for individuals aged 65 and over. Lopez Bernal et al. C report adjusted vaccine effectiveness against symptomatic infection with S-gene target negatives (Alpha variant) of 74.5% (68.4% to 79.4%) at least 14 days after the second dose of AZ. Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Alpha variant of 97% (93-98%) at least 14 days following the second dose of AZ. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 81% (72-87%) 14 days after the second dose of AZ. PHE’s week 36 vaccine surveillance report estimates protection against symptomatic disease of 89% (87-90%) for the Alpha variant at least 14 days after a second vaccine dose. Andrews et al. report protection against symptomatic disease for the second dose of AZ as 81.7% (79.0 to 84.0%), at least 14 days following the second dose.

	0.8 (+14 days)
Overall protection against hospitalisation for AstraZeneca dose 2	Ismail et al. estimate vaccine effectiveness against hospitalisation of 92% (87-95%) 14 days after a second dose across both AZ and Pfizer vaccines. PHE's week 26 vaccine surveillance report finds protection against hospitalisation with the Alpha variant of 94% (81-98) following the second dose of AZ. Stowe et al. report vaccine effectiveness against hospitalisation of 86% (53-96%) following the second dose of AZ. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 93% (80-97%) for the Alpha variant at least 14 days after a second vaccine dose. Andrews et al. report protection against hospitalisation for the second dose of AZ as 93.9% (84.9 to 97.5%), at least 14 days following the second dose. **0.9 (+14 days)**
Overall protection against mortality for AstraZeneca dose 2	PHE's week 26 vaccine surveillance report finds protection against mortality with the Alpha variant of 92% (76-98%) and 94% (80-98%) for 40-64 and 65+ year olds respectively, following the second dose of AZ. Andrews et al. report protection against death for the second dose of AZ as 100% at least 14 days following the second dose. **0.95 (+14 days)**
Overall protection against onward transmission for AstraZeneca dose 2	Shah et al. find that relative to the period before a healthcare worker was vaccinated, the hazard ratio for a household member of the vaccinated healthcare worker to become infected was 0.7 (0.63-0.78) for the period beginning 14 days following first vaccine dose and 0.46 (0.30-0.70) for the period beginning 14 days after the second vaccine dose (healthcare workers were vaccinated with either AstraZeneca or Pfizer). Braeye et al. (Belgium, mostly Alpha variant) estimated VE against onward transmission "at 62% (95% CI 57–67) for BNT162b2 and 52% (95% CI 33–69) for mRNA1273 for full vaccination. No significant effect against onward transmission was found for the 'viral-vector'-vaccines, but credibility intervals were large." Eyre et al. report an adjusted odds ratio of 0.37 (0.22, 0.63) for the effect of a case being fully vaccinated with AZ (dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive. **0.47 (+14 days)**
Overall protection against	Hall et al. Table 2, full cohort adjusted hazard ratio d1>=21

infection for Pfizer dose 1	days 0.30 (0.15-0.45). Pritchard et al. supplementary information, Table 6, adjusted odds ratio >= 21 days after first dose of Pfizer, no second dose, 0.34 (0.29, 0.40) for all positives. Shrotri et al. Table 4 adjusted hazard ratio 0.47 (0.20, 1.06) at 28-34 days post vaccination for protection against infection in care home residents. Glampson et al. results, Table 2, hazard ratio 0.22 (0.18, 0.27) for Pfizer between 22 and 28 days following first dose when comparing Pfizer vaccinated individuals with unvaccinated individuals. Thus a 78% reduction in risk of testing positive for COVID-19. Mason et al. Table 2, vaccine effect of 55.2% (40.8 - 66.8%) 21-27 days post first dose, of 53.7% (35.4 - 66.6%) 28-34 days post first dose and of 70.1% (55.1 - 80.1%) 35-41 days post first dose in individuals aged 80-83 years of age. Azamgarhi et al. Table 2, 14 days after first vaccination dose in healthcare workers find an adjusted hazard ratio of 0.3 (0.09,0.94) for protection against documented infection. Amirthalingam et al. results, 80+ year olds had 61% (49-71%) vaccine protection with a 3-week dosing schedule at 28-34 days post first dose of Pfizer. 80+ year olds with the longer dosing interval had 52% (39-63%) vaccine protection 28-34 days following the first dose of Pfizer. “Amongst 65-79 year-olds, VE began to increase from 10-13 days after vaccination, reaching 53% (95%CI: 45-60) on days 28-34, and remained at a similar level between 35-69 days (5-10 weeks). A similar trend was observed in the BNT162b2 recipients aged 50- 64 years with a VE of 58% at days 28-34. Whilst there was some evidence of a 10-20% decrease in VE by 10 weeks after the first dose, there was an apparent rise again in VE at the final interval, although with wide confidence intervals”. Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Alpha variant of 59% (52-65%) at least 21 days following the first dose of Pfizer. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 38% (29-45%) 28 days after the first dose of Pfizer. **0.7 (+28 days)**
Overall protection against disease for Pfizer dose 1	Lopez Bernal et al. (cohort aged 70+ years of age) Table 2, odds ratio vs day 4-9, d1:28-34 0.30 (0.22-0.41). Pritchard et al., supplementary information, Table 6, adjusted odds ratio >= 21 days after first dose of Pfizer, no second dose, 0.22 (0.17, 0.28) for positive individuals with symptoms reported. PHE’s week 20 vaccine surveillance report estimates protection against symptomatic disease at least 28 days following the first dose of Pfizer as 54% (50-58%) compared to unvaccinated individuals. Compared to individuals between 4 and 13 days post first dose, they estimate 57% (53-61%) protection. Whitaker et al. Table 4, adjusted vaccine

	effectiveness against symptomatic COVID-19 28-90 days post first dose of Pfizer 48.6% (27.9-63.3%) for individuals aged 16-64 and 56.6% (47.6-64.1%) for individuals aged 65 and over. Lopez Bernal et al. C report adjusted vaccine effectiveness against symptomatic infection with S-gene target negatives (i.e. Alpha variant) of 47.5% (41.6% to 52.8%). Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Alpha variant of 73% (68-76%) at least 21 days following the first dose of Pfizer. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 27% (13-39%) 28 days after the first dose of Pfizer. PHE's week 36 vaccine surveillance report estimates protection against symptomatic disease of 49% (46-52%) for the Alpha variant at least 28 days after a first vaccine dose. Andrews et al. report protection against symptomatic disease for the first dose of Pfizer as 45.7% (44 to 47.3%), at least 28 days following the first dose and up to the second dose if given. **0.7 (+28 days)**
Overall protection against hospitalisation for Pfizer dose 1	Lopez Bernal et al. Table 4, hazard ratio for risk of hospital admission in vaccinated vs unvaccinated individuals (subsection of cohort that are 80+ years of age) 0.57 (0.48 to 0.67) at least 14 days following first dose of Pfizer. Hyams et al. Table 2, adjusted vaccine effectiveness (in individuals aged 80 years and above) 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%. Table 3 split vaccine effect into age groups. Ismail et al. estimate vaccine effectiveness against hospitalisation of 81% (76-85%) for 80+ year olds and 81% (73-87%) for 70-79 year olds, 28 days following the first dose of Pfizer. When the analysis is not split across vaccine products, the same study estimates protection against hospitalisation of 80% (74-85%) for 80+ year olds and 82% (75-87%) for 70-79 year olds, 28 days following the first vaccine dose. Mason et al. Table 2, vaccine effect against hospital admission of 50.1% (19.9 - 69.5%) 21-27 days post first dose, of 63.7% (37.1 - 79.2%) 28-34 days post first dose and of 75.6% (52.8 - 87.6%) 35-41 days post first dose in individuals aged 80-83 years of age.

	Vaccine effect against A&E (accident & emergency) hospital attendance of 57.8% (30.8 - 74.5%) 21-27 days post first dose, of 68.1% (45.2 - 80.9%) 28-34 days post first dose and of 78.9% (60.0 - 89.9%) 35-41 days post first dose in individuals aged 80-83 years of age. PHE's week 26 vaccine surveillance report finds protection against hospitalisation with the Alpha variant of 82% (78-85%) following the first dose of Pfizer. Stowe et al. report vaccine effectiveness against hospitalisation of 83% (62-93%) following the first dose of Pfizer. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 78% (64-87%) for the Alpha variant at least 28 days after a first vaccine dose. Andrews et al. report protection against hospitalisation for the first dose of Pfizer as 85.2% (81.6 to 88.1%), at least 28 days following the first dose and up to the second dose if given. **0.85 (+28 days)**
Overall protection against mortality for Pfizer dose 1	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. Lopez Bernal et al. B (study in a care home population) estimated a hazard ratio of 0.56 (0.47 - 0.68) for cases vaccinated with one dose of Pfizer compared to unvaccinated cases, indicating an additional 44% (32-53%) protection against death given becoming a case for individuals vaccinated with one dose of Pfizer. Using the aforementioned estimate of a 44% increase and assuming this in addition to protection against disease of 0.7**,** we get overall protection against mortality of 0.832. PHE's week 26 vaccine surveillance report finds protection against mortality with the Alpha variant of 73% (67-77%) and 77% (72-81%) for 40-64 and 65+ year olds respectively, following the first dose of Pfizer. Andrews et al. report protection against death for the first dose of Pfizer as 73.1% (65 to 79.3%), at least 28 days following the first dose and up to the second dose if given. **0.85 (+28 days)**
Overall protection against onward transmission for Pfizer dose 1	Harris et al. calculate an adjusted odds ratio of being a secondary case within a household of index cases vaccinated with ChAdOx1 (AstraZeneca) at least 21 days before testing positive as 0.52 (0.43-0.62) and index cases vaccinated with BNT162b2 (Pfizer-BioNTech) at least 21 days before testing positive as 0.54 (0.47-0.62). Shah et al. find that relative to the period before a healthcare worker was vaccinated, the hazard ratio for a household member of the vaccinated healthcare worker to become infected was 0.7 (0.63-0.78) for the period beginning 14 days following first vaccine dose and 0.46 (0.30-0.70) for the period beginning 14 days after the second vaccine dose (healthcare workers were vaccinated with either

	AstraZeneca or Pfizer). Braeye et al. (Belgium, mostly Alpha variant) estimated VE against onward transmission "at 62% (95% CI 57–67) for BNT162b2 and 52% (95% CI 33–69) for mRNA1273 for full vaccination. No significant effect against onward transmission was found for the 'viral-vector'-vaccines, but credibility intervals were large." Eyre et al. report an adjusted odds ratio of 0.74 (0.70, 0.80) for the effect of a case being partially vaccinated with Pfizer (dose 1 day 1 to dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive. **0.47 (+28 days)**
Overall protection against infection for Pfizer dose 2	Hall et al. Table 2, full cohort adjusted hazard ratio d2>=7 days 0.15 (0.04-0.26). Pritchard et al., supplementary information, Table 6, adjusted odds ratio post second dose of Pfizer 0.20 (0.15, 0.26) for all positives. Haas et al. estimate vaccine protection against SARS-CoV-2 infection (both asymptomatic and symptomatic and symptoms unknown) of 95.3% (94.9-95.7%). Shrotri et al. Table 4 adjusted hazard ratio 0.35 (0.17, 0.71) at 35-48 days post vaccination (first dose) for protection against infection in care home residents, but no estimates related to second vaccine dose. Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Alpha variant of 78% (68-84%) at least 14 days following the second dose of Pfizer. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 92% (90-93%) 14 days after the second dose of Pfizer. **0.85 (+14 days)**
Overall protection against disease for Pfizer dose 2	Lopez Bernal et al. (cohort aged 70+ years of age) Table 2, odds ratio vs day 4-9, d2:14+ 0.11 (0.07-0.15). Haas et al. estimate vaccine protection against symptomatic COVID-19 >7 days after second dose of 97% (96.7-97.2%). Pritchard et al., supplementary information, Table 6, adjusted odds ratio post second dose of Pfizer 0.05 (0.02, 0.09) for positive individuals with symptoms reported. PHE's week 20 vaccine surveillance report estimates protection against symptomatic disease at least 14 days following the second dose of Pfizer as 90% (82-95%) compared to unvaccinated individuals. Compared to individuals between 4 and 13 days post first dose, they estimate 91% (83-95%) protection. Whitaker et al. Table 4, adjusted vaccine effectiveness against symptomatic COVID-19 at least 14 days following the second dose of Pfizer 93.3% (85.8-96.8%) for individuals aged 16-64 and 86.7% (80.1-91.1%) for individuals aged 65 and over. Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Alpha variant of 97%

	(96-98%) at least 14 days following the second dose of Pfizer. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 92% (88-94%) 14 days after the second dose of Pfizer. PHE's week 36 vaccine surveillance report estimates protection against symptomatic disease of 89% (87-90%) for the Alpha variant at least 14 days after a second vaccine dose. Andrews et al. report protection against symptomatic disease for the second dose of Pfizer as 95.0% (93.8 to 95.9%) at least 14 days following the second dose. **0.9 (+14 days)**
Overall protection against hospitalisation for Pfizer dose 2	Dagan et al. estimate vaccine effectiveness against hospitalisation of 87% (55–100%) >7 days after second dose. Haas et al. estimate vaccine protection against COVID-19 related hospitalisation >7 days after second dose of 97.2% (96.8-97.5%). Ismail et al. estimates vaccine protection against hospitalisation of 93% (89-95%) for individuals aged 80+ years 14 days after receiving their second dose of Pfizer. When the analysis is not split by vaccine type, the same study estimates protection against hospitalisation of 92% (87-95%) for 80+ year olds 14 days after second dose. PHE's week 26 vaccine surveillance report finds protection against hospitalisation with the Alpha variant of 98% (96-99%) following the second dose of Pfizer. Stowe et al. report vaccine effectiveness against hospitalisation of 95% (78-99%) following the second dose of Pfizer. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 93% (80-97%) for the Alpha variant at least 14 days after a second vaccine dose. Andrews et al. report protection against hospitalisation for the second dose of Pfizer as 97.9% (91.4 to 99.5%) at least 14 days following the second dose. **0.95 (+14 days)**
Overall protection 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 (no estimates for second dose protection). The same study estimates protection against severe disease of 92% (75-100%) >7 days following the second dose of Pfizer. Haas et al. estimate vaccine protection against death >7 days after second dose of 96.7% (96.0-97.3%). Lopez Bernal et al. B (study in a care home population) estimated a hazard ratio of 0.31 (0.14 - 0.69) for cases vaccinated with two doses of Pfizer compared to unvaccinated cases, indicating an additional 69% (31-86%) protection against death given becoming a case for individuals vaccinated with two doses of Pfizer. Using the aforementioned estimate of a 69% increase and assuming this in addition to protection against disease of 0.9, we get overall protection

	against mortality of 96.9%. PHE's week 26 vaccine surveillance report finds protection against mortality with the Alpha variant of 98% (94-99%) for both 40-64 and 65+ year olds following the second dose of Pfizer. Andrews et al. report protection against death for the second dose of Pfizer as 96.3% (89.9 to 98.6%) at least 14 days following the second dose. **0.95 (+14 days)**
Overall protection against onward transmission for Pfizer dose 2	Shah et al. find that relative to the period before a healthcare worker was vaccinated, the hazard ratio for a household member of the vaccinated healthcare worker to become infected was 0.7 (0.63-0.78) for the period beginning 14 days following first vaccine dose and 0.46 (0.30-0.70) for the period beginning 14 days after the second vaccine dose (healthcare workers were vaccinated with either AstraZeneca or Pfizer). Braeye et al. (Belgium, mostly Alpha variant) estimated VE against onward transmission "at 62% (95% CI 57–67) for BNT162b2 and 52% (95% CI 33–69) for mRNA1273 for full vaccination. No significant effect against onward transmission was found for the 'viral-vector'-vaccines, but credibility intervals were large." Eyre et al. report an adjusted odds ratio of 0.18 (0.12, 0.29) for the effect of a case being fully vaccinated with Pfizer (dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive. **0.47 (+14 days)**

Table S2 - Vaccine effectiveness against B.1.617.2 Delta variant - relevant evidence and baseline model assumptions (updated 5th October 2021)

Description	**Relevant evidence, assumed value shown in bold**
Overall protection against infection for AstraZeneca dose 1	Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Delta variant of 46% (35-55%) at least 21 days following the first dose of AZ. This is a **26.98% reduction** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 18% (9-25%) 28 days after the first dose of AZ. This is a **51.35% reduction** on their equivalent estimate for the Alpha variant. **Alpha assumption 0.7**

	0.43 = 0.7 * (1 - 0.39) (+28 days)
Overall protection against disease for AstraZeneca dose 1	Lopez Bernal et al. C report adjusted vaccine effectiveness against symptomatic infection with S-gene target positives (Delta variant) of 30.0% (24.3-35.3%) at least 21 days after the first dose of AZ. A **38.4% reduction** on their estimate of equivalent vaccine protection against the Alpha variant. Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Delta variant of 40% (28-50%) at least 21 days following the first dose of AZ. This is a **45.21% reduction** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 33% (23-41%) 28 days after the first dose of AZ. This is a **15.38% reduction** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against symptomatic disease of 35% (32-38%) for the Delta variant at least 28 days after a first vaccine dose. This is a **28.57% reduction** compared to their equivalent estimate for Alpha. Andrews et al. report protection against symptomatic disease for the first dose of AZ as 43.3% (42.3 to 44.2%), at least 28 days following the first dose and up to the second dose if given. This is a **2.7% reduction** compared to their equivalent estimate for Alpha. **Alpha assumption 0.7** **0.52 = 0.7 * (1-0.26) (+28 days)**
Overall protection against hospitalisation for AstraZeneca dose 1	Stowe et al. report vaccine effectiveness against hospitalisation of 71% (51-83%) following the first dose of AZ. This is a **6.58% reduction** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 80% (69-88%) for the Delta variant at least 28 days after a first vaccine dose. This is a **2.56% increase** compared to their equivalent estimate for Alpha. Andrews et al. report protection against hospitalisation for the first dose of AZ as 81.4% (78.7 to 83.7%), at least 28 days following the first dose and up to the second dose if given. This is a **1.3% reduction** compared to their equivalent estimate for Alpha. **Alpha assumption 0.85** **0.84 = 0.85 * (1-0.017) (+28 days)**
Overall protection against	Andrews et al. report protection against death for the first dose

mortality for AstraZeneca dose 1	of AZ as 88.4% (78.2 to 93.8%), at least 28 days following the first dose and up to the second dose if given. This is a **11.8% increase** compared to their equivalent estimate for Alpha. **Alpha assumption 0.85** **0.95 = 0.85 * (1 + 0.118) (+28 days)**
Overall protection against onward transmission for AstraZeneca dose 1	Eyre et al. report an adjusted odds ratio of 0.98 (0.90, 1.06) for the effect of a case being partially vaccinated with AZ (dose 1 day 1 to dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive (N.B. this estimate has a non-significant p-value), equivalent to vaccine protection of 2%. Their equivalent estimate for Alpha is 0.82 (0.76, 0.88), therefore vaccine protection of 18%. This is a **88.9% overall reduction** in vaccine effect from Alpha to Delta. **Alpha assumption 0.47** **0.05 = 0.47 * (1 - 0.889) (+28 days)**
Overall protection against infection for AstraZeneca dose 2	Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Delta variant of 67% (62-71%) at least 14 days following the second dose of AZ. This is a **15.19% reduction** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 60% (53-66%) 14 days after the second dose of AZ. This is a **17.81% reduction** on their equivalent estimate for the Alpha variant. **Alpha assumption 0.75** **0.63 = 0.75 * (1-0.165) (+14 days)**

Overall protection against disease for AstraZeneca dose 2	Lopez Bernal et al. C report adjusted vaccine effectiveness against symptomatic infection with S-gene target positives (Delta variant) of 67.0% (61.3% to 71.8%) at least 14 days after the second dose of AZ. A **10.07% reduction** on their estimate of equivalent vaccine protection against the Alpha variant. Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Delta variant of 71% (66-74%) at least 14 days following the second dose of AZ. This is a **26.8% reduction** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 61% (51-70%) 14 days after the second dose of AZ. This is a **24.69% reduction** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against symptomatic disease of 79% (78-80%) for the Delta variant at least 14 days after a second vaccine dose. This is an **11.24% reduction** compared to their equivalent estimate for Alpha. Andrews et al. report protection against symptomatic disease for the second dose of AZ as 65.2% (64.9 to 65.6%), at least 14 days following the second dose. This is a **20.2% reduction** compared to their equivalent estimate for Alpha. **Alpha assumption 0.8** **0.65 = 0.8 * (1 - 0.186) (+14 days)**
Overall protection against hospitalisation for AstraZeneca dose 2	Stowe et al. report vaccine effectiveness against hospitalisation of 92% (75-97%) following the second dose of AZ. This is a **6.98% increase** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 96% (91-98%) for the Delta variant at least 14 days after a second vaccine dose. This is a **3.23% increase** compared to their equivalent estimate for Alpha. Andrews et al. report protection against hospitalisation for the second dose of AZ as 93.0% (92.4 to 93.5%), at least 14 days following the second dose. This is a **1% reduction** compared to their equivalent estimate for Alpha. **Alpha assumption 0.9** **0.93 = 0.9 * (1 + 0.0307) (+14 days)**
Overall protection against mortality for AstraZeneca dose 2	Andrews et al. report protection against death for the second dose of AZ as 92.7% (90.7 to 94.3%), at least 14 days following the second dose. This is a **7.3% reduction**

	compared to their equivalent estimate for Alpha. **Alpha assumption 0.95** **0.95 (+14 days), as for dose 1 protection against mortality**
Overall protection against onward transmission for AstraZeneca dose 2	Eyre et al. report an adjusted odds ratio of 0.64 (0.57, 0.72) for the effect of a case being fully vaccinated with AZ (dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive, equivalent to vaccine protection of 36%. Their equivalent estimate for Alpha is 0.37 (0.22, 0.63), therefore vaccine protection of 63%. This is a **42.9% overall reduction** in vaccine effect from Alpha to Delta. **Alpha assumption 0.47** **0.27 = 0.47 * (1 - 0.429) (+14 days)**
Overall protection against infection for Pfizer dose 1	Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Delta variant of 57% (50-63%) at least 21 days following the first dose of Pfizer. This is a **3.39% reduction** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 30% (17-41%) 28 days after the first dose of Pfizer. This is a **21.05% reduction** on their equivalent estimate for the Alpha variant. **Alpha assumption 0.7** **0.62 = 0.7 * (1-0.12) (+28 days)**

Overall protection against disease for Pfizer dose 1	Lopez Bernal et al. C report adjusted vaccine effectiveness against symptomatic infection with S-gene target positives (Delta variant) of 35.6% (22.7% to 46.4%) at least 21 days after the first dose of Pfizer. A **25.05% reduction** on their estimate of equivalent vaccine protection against the Alpha variant. Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Delta variant of 58% (51-64%) at least 21 days following the first dose of Pfizer. This is a **20.55% reduction** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 33% (15-47%) 28 days after the first dose of Pfizer. This is a **22.22% reduction** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against symptomatic disease of 35% (32-38%) for the Delta variant at least 28 days after a first vaccine dose. This is a **28.57% reduction** compared to their equivalent estimate for Alpha. Andrews et al. report protection against symptomatic disease for the first dose of Pfizer as 51.9% (51.4 to 52.4%), at least 28 days following the first dose and up to the second dose if given. This is a **13.6% increase** compared to their equivalent estimate for Alpha. **Alpha assumption 0.7** **0.62 (+28 days) as for infection, otherwise would be 0.58**
Overall protection against hospitalisation for Pfizer dose 1	Stowe et al. report vaccine effectiveness against hospitalisation of 94% (46-99%) following the first dose of Pfizer. This is a **13.25% increase** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 80% (69-88%) for the Delta variant at least 28 days after a first vaccine dose. This is a **2.56% increase** compared to their equivalent estimate for Alpha. Andrews et al. report protection against hospitalisation for the first dose of Pfizer as 91.8% (90.4 to 93%), at least 28 days following the first dose and up to the second dose if given. This is a **7.7% increase** compared to their equivalent estimate for Alpha. **Alpha assumption 0.85** **0.92 = 0.85 * (1+0.078) (+28 days)**
Overall protection against mortality for Pfizer dose 1	Andrews et al. report protection against death for the first dose of Pfizer as 88.6% (77.3 to 94.3%), at least 28 days following the first dose and up to the second dose if given. This is a

	21.2% increase compared to their equivalent estimate for Alpha. **Alpha assumption 0.85** **0.92 (+28 days) as for hospitalisation**
Overall protection against onward transmission for Pfizer dose 1	Eyre et al. report an adjusted odds ratio of 0.87 (0.81, 0.94) for the effect of a case being partially vaccinated with Pfizer (dose 1 day 1 to dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive, equivalent to vaccine protection of 13%. Their equivalent estimate for Alpha is 0.74 (0.70, 0.80), therefore vaccine protection of 26%. This is a **50% overall reduction** in vaccine effect from Alpha to Delta. **Alpha assumption 0.47** **0.24 = 0.47 * (1 - 0.5) (+28 days)**
Overall protection against infection for Pfizer dose 2	Pouwels et al. report vaccine effectiveness against all PCR-confirmed infections with the Delta variant of 80% (77-83%) at least 14 days following the second dose of Pfizer. This is a **2.56% increase** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against PCR-confirmed infection (regardless of symptom status) of 79% (75-82%) 14 days after the second dose of Pfizer. This is a **14.13% reduction** on their equivalent estimate for the Alpha variant. **Alpha assumption 0.85** **0.8 = 0.85 * (1-0.057) (+14 days)**

Overall protection against disease for Pfizer dose 2	Lopez Bernal et al. C report adjusted vaccine effectiveness against symptomatic infection with S-gene target positives (Delta variant) of 88.0% (85.3% to 90.1%) at least 14 days after the second dose of Pfizer. A **6.08% reduction** on their estimate of equivalent vaccine protection against the Alpha variant. Pouwels et al. report vaccine effectiveness against symptomatic PCR-confirmed infections with the Delta variant of 84% (82-86%) at least 14 days following the second dose of Pfizer. This is a **13.4% reduction** on their equivalent estimate for the Alpha variant. Sheikh et al. report vaccine effectiveness against symptomatic PCR-confirmed infection of 83% (78-87%) 14 days after the second dose of Pfizer. This is a **9.78% reduction** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against symptomatic disease of 79% (78-80%) for the Delta variant at least 14 days after a second vaccine dose. This is an **11.24% reduction** compared to their equivalent estimate for Alpha. Andrews et al. report protection against symptomatic disease for the second dose of Pfizer as 83.5% (83.3 to 83.6%), at least 14 days following the second dose. This is a **12.1% reduction** compared to their equivalent estimate for Alpha. **Alpha assumption 0.9** **0.81 = 0.9 * (1 - 0.105) (+14 days)**
Overall protection against hospitalisation for Pfizer dose 2	Stowe et al. report vaccine effectiveness against hospitalisation of 96% (86-99%) following the second dose of Pfizer. This is a **1.05% increase** on their equivalent estimate for the Alpha variant. PHE's week 36 vaccine surveillance report estimates protection against hospitalisation of 96% (91-98%) for the Delta variant at least 14 days after a second vaccine dose. This is a **3.23% increase** compared to their equivalent estimate for Alpha. Andrews et al. report protection against hospitalisation for the second dose of Pfizer as 96.7% (96.3 to 97%), at least 14 days following the second dose. This is a **1.2% reduction** compared to their equivalent estimate for Alpha. **Alpha assumption 0.95** **0.96 = 0.95 * (1 + 0.0103) (+14 days)**

Overall protection against mortality for Pfizer dose 2	Andrews et al. report protection against death for the second dose of Pfizer as 95.2% (93.7 to 96.4%), at least 14 days following the second dose. This is a **1.1% reduction** compared to their equivalent estimate for Alpha. **Alpha assumption 0.95** **0.96 (+14 days) as for hospitalisation**
Overall protection against onward transmission for Pfizer dose 2	Eyre et al. report an adjusted odds ratio of 0.35 (0.26, 0.48) for the effect of a case being fully vaccinated with Pfizer (dose 2 +14 days) compared to an unvaccinated case in relation to the likelihood of a contact testing PCR-positive, equivalent to vaccine protection of 65%. Their equivalent estimate for Alpha is 0.18 (0.12, 0.29), therefore vaccine protection of 82%. This is a **20.7% overall reduction** in vaccine effect from Alpha to Delta. **Alpha assumption 0.47** **0.37 = 0.47 * (1 - 0.207) (+14 days)**