# **Title:** Modelling COVID-19 vaccination in the UK – Impact of the Autumn 2022 and Spring 2023 booster campaigns

## Supplementary Material

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# Supplementary

**Model description**

The combined calibration and prediction period of the model is 03 January 2022 to 14 August 2023, when the Omicron variant was dominant. During this period, three different vaccination programmes were carried out: Spring 2022 (21/03/22–06/09/2022), Autumn 2022 (07/09/22–12/02/2022), and Spring 2023 (17/04/23–30/06/2023).[1] Aligning with this, the model used January 2022 to September 2022 (36 weeks) as the calibration period, and September 2022 to August 2023 as the prediction period (48 weeks) to assess the impact of Autumn 2022/Spring 2023 booster vaccinations.

At the start of the model calibration period (03/01/2022), individuals began in the Susceptible (S), Vaccinated with primary first dose ($V_{k=1}$), Vaccinated with primary second dose ($V_{k=2}$), Vaccinated with booster prior to Autumn 2022 ($V_{k=3}$), infectious, inpatient, hybrid immunity (HI), natural immunity, or recovered (R) compartments. Consistent with published SEIRD models, the susceptible (S) compartment represents those without any immunity, either from infection or vaccine induced protection. The exposed (E) compartment contains those who have contracted COVID-19 but are not yet infectious. After a period of exposure, a proportion of the exposed population may experience symptoms and progress to the infectious symptomatic ($I_S$) compartment. Those who are infectious with no symptoms progress to the infectious asymptomatic ($I_A$) compartment. Those in the infectious asymptomatic compartment resolve the infection naturally to move to recovered (R) and can become susceptible again. Some of the infectious cohort can resolve the infection naturally and move to the recovered (R) compartment while those who do not resolve the infection naturally may have to get admitted to the hospital (H) compartment or intensive care unit (IC) compartment. We explicitly model the admission to hospital, ICU, and death compartments. From the hospital or intensive care compartments, individuals can move to recovered/hybrid immunity (R/HI) or death (D). Those in the recovered (R) compartment have natural immunity from infection that wanes over time, resulting in them re-entering the susceptible compartment (S).

To capture social contact dynamics of the population, contact rates were scaled using a time-varying transmission rate, $\beta$, piecewise constant function (Supplementary Table 4). In the absence of Government-enforced non-pharmaceutical interventions (e.g. lockdown) during the study period, the choice of change points for $\beta$ corresponded to official school term dates in England, as these have been demonstrated to drive measurable changes in social mixing in the population (Supplementary Table 4).[2] It should be noted that change points for $\beta$ apply to term dates in England only, and although

Welsh, Scottish, and Northern Irish term dates may differ slightly, these differences were perceived to be small and the impact to be minimal.

Model compartments were extended to include different vaccination strata corresponding to the primary two doses and booster vaccinations (Figure 1). The booster compartment was split between the boosters pre- and post-Autumn 2022 ($V_{k=3}$ and $V_{k=5}$). Additional compartments for waned cohorts from boosted ($V_{k=4}$ and $V_{k=6}$) were also included. Correspondingly, there were two waned compartments; one for the booster that was introduced pre-Autumn 2022 and one for the waned cohorts from boosters that were introduced post-Autumn 2022. Those in the waned compartments lose their protection to infection, however, they retain the protection from hospitalization and death. Hence, once the cohort gets exposed from the waned boosted compartments, they join the exposed compartment from the booster compartment, as both of these cohorts will have similar protection from hospitalization and death. An all-or-nothing protection was modelled, whereby patients are either in the vaccinated compartments where fixed vaccine effectiveness (VE) estimates are applied or have moved via waning to the susceptible or waned compartments where there is no protection applied. Vaccinated cohorts from all different vaccinated strata have the same path as their non-vaccinated counterparts, with the difference that the probability of infection, symptomatic disease, hospitalization, ICU admission, and death is dependent on the vaccination strata. This probability depends on the vaccine effectiveness for the corresponding outcome. The vaccinated cohorts who resolve an infection naturally or with health care intervention move to the HI compartment with cumulative natural immunity and immunity from vaccine protection. The model assumes that asymptomatic patients (from unvaccinated or vaccinated strata) will not die due to the infection and death happens only when the infection becomes severe and after hospital admission or ICU admission.

The dynamics of COVID-19 infection were described by a set of ordinary differential equations (ODEs) and were solved using the function “ode” in R using the default integrator “lsoda.”[3] Model outputs included estimates of weekly number of COVID-19 infections, weekly incidence rates, overall hospitalization admission rates per 100,000 people, and weekly number of deaths due to COVID-19 from hospitalized patients. The model also estimated long COVID cases, number of bed days in general ward and ICU, and productivity losses.

**Parallel flow**

To calibrate the model using PCR positivity from the ONS infection survey and estimate transmission rates, the model adopts a parallel flow process describing how the compartments relate to the data.

This was described by Baguelin et al,[4] as an observation model for inferring influenza transmission from cases and survey data and has since been widely used in respiratory pathogen models, including SARS-CoV-2.[5,6] The model considers a biologic delay distribution from the moment an individual is exposed to testing positive by polymerase chain reaction (PCR). This delay distribution is smaller than the one from exposed to either recovery or death. Therefore, the parallel flow describes the process of newly exposed individuals becoming cases, as described below.

Upon infection, an exposed individual (E) enters the PCR flow in a pre-positive compartment ($T_{PCRpre}$) before moving into the PCR-positive compartment ($T_{PCRpos}$) and then ultimately into the PCR-negative compartment ($T_{PCRneg}$). The rate of outflow from these compartments follows an exponential distribution where the parameters correspond to the Omicron variant.[6] This correlates to a mean duration of approximately 2.6 days in the pre-PCR positive compartment and about 16.1 days in PCR-positive compartment.

**Model initialization**

The model calibration period corresponds to a 36-week period following January 2022, after the start of both the pandemic and the first booster roll-out. Therefore, careful initialization of compartments in the model was required. The starting exposed population was taken from GOV.UK case data for week 2 of the time horizon (by 11/01/2022) assuming that those individuals would have been exposed to the virus in week 1 to be infectious in week 2.[7] The starting infectious population was taken from GOV.UK case data for week 1 of the time horizon (03/01/2022).[7] Exploratory analysis investigating a starting population sourced from ONS data yielded similar estimates for the calibration parameters and predicted clinical outcomes averted. It was assumed that 70% of these infections were symptomatic and 30% were asymptomatic.[8,9] The starting inpatient population was taken from observed ONS hospitalisation rates.[10] Of these patients, 96.1% were general ward patients and 3.9% were ICU patients.[11] The susceptible compartment was initialised comprising the calibrated proportion of the population who had waned from primary vaccination (Supplementary Table 6), in addition to 3% of the UK population, which were assumed to be representative of those who were never infected or vaccinated, based on official UK estimates of seropositivity at the start of January 2022.[12] The remainder of the population was distributed between the recovered and hybrid immunity compartments, proportionate to dose 1, dose 2 and booster coverage, in line with the UKHSA age-stratified vaccination stratification data (Supplementary Table 10).[13,14]

UKHSA vaccination coverage data considers anyone who has received a vaccination as being protected, regardless of time since vaccination. Therefore, the age-stratified proportion of the vaccinated population who have waned immunity (both from primary series and from booster) were

included in the set of parameters to be estimated (calibration parameters). The calibrated proportion waned from primary dose protection (Supplementary Table 6), was taken from the primary series starting population ($V_{k=1,}$ $V_{k=2}$) and added to the susceptible starting population ($V_{k=0}$). The calibrated proportion of the population waned from booster dose protection (Supplementary Table 6) was taken from the boosted starting population ($V_{k=3}$) and added to the starting population of the booster waned compartment ($V_{k=4}$).

**Model calibration**

The model was fitted to age-stratified weekly infection prevalence calculated (multiplying percentage positivity with the age stratified population size) from the PCR-positivity reported by the ONS[15] (percentage testing positive for COVID-19 by nose and throat swabs) for hospital admissions per week per 100,000 from official UK Government figures,[16] and ONS estimates of mortality due to COVID-19,[17] each month over the 36 week period from January to August 2022.

For settings where case surveillance systems were unreliable,[18] due to the significant reduction in testing behavior observed in the UK over time and the disbanding of the infrastructure supporting the community-based testing program in February 2022, representative infection surveys can be used as a stronger evidence base to anchor transmission model inference.[6,19] The age-stratified PCR positivity data from the ONS is used as a target to estimate the transmission dynamics of infection. Monthly death data was converted to weekly data using a uniform distribution.

The values of calibrated parameters, including nine transmission rates, $\beta_{c1}, \ldots, \beta_{c9}$; age-stratified severity multipliers for probability of hospitalization or ICU given infection, and age-stratified severity multipliers for probability of death given hospitalization or ICU admission were inferred (Supplementary Table 6). This was done by using the values of the age-stratified severity of hospitalization and death for the original SARS-COV-2 variant[5] multiplied with age-stratified multipliers to estimate the change in severity between the first epidemic wave with the original SARS-CoV-2 variant to the study period, dominated by the Omicron clade of variant.

Estimated PCR positivity, hospitalizations, and mortality were calibrated against the corresponding target datasets by minimizing the log-likelihood function. We use a negative binomial distribution with an assumed level of dispersion.[6] The optimization was done using the “optim” function in R that uses L-BFGS-B algorithm. This algorithm is a limited-memory modification of the Broyden–Fletcher–Goldfarb–Shanno (BFGS) quasi-Newton method.[20] A single overall log-likelihood function was defined as the scaled and equally weighted sum of the output of each negative binomial function, ensuring no

bias to any of the target datasets. The parameters of the calibration function are outlined in Supplementary Table 6.

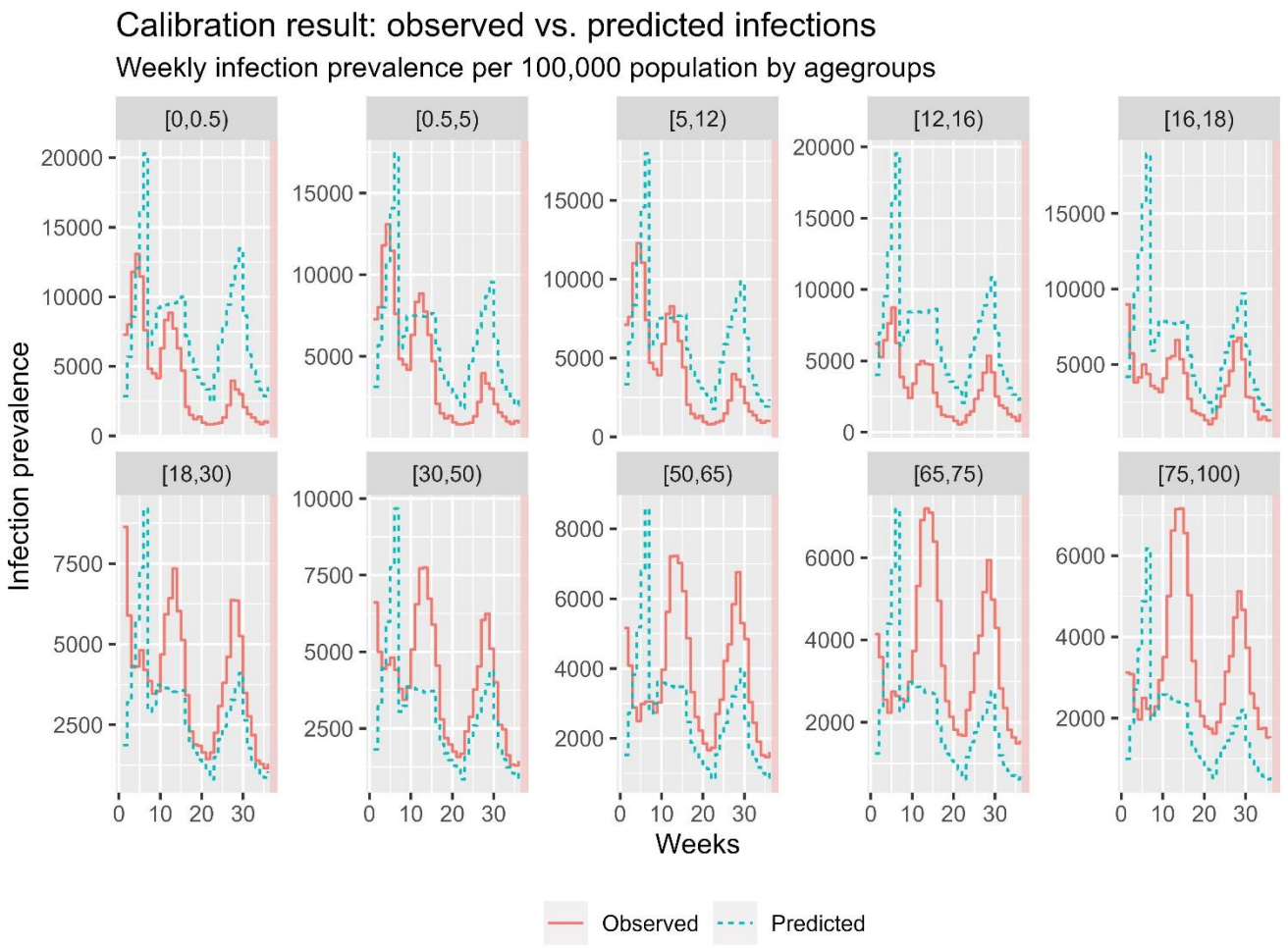
**Model limitations**

As COVID-19 transitions into its endemic phase and COVID-19 testing and infrastructure reduces, there is uncertainty surrounding the accuracy and appropriateness of the data to which the model is calibrated to. There have been some attempts to mitigate this limitation through calibrating to test positivity data from ONS surveys,[21] as opposed to absolute case rates, however, there still remains a likelihood that infections are underestimated by the ONS, due to missing data and also by the delay in processing. This under-reporting may account for the higher number of infections predicted for the Autumn/Spring booster compared to no booster. The drivers of these increased infections are due to hybrid immunity from the introduction of natural immunity with marginally greater protection from infection than booster protection alone, counteracting some of the impact of vaccination. Further, in this model, vaccine protection against symptomatic infection was applied to exposed individuals, thereby reducing the number and severity of symptomatic cases and increasing the number of asymptomatic cases in the Autumn/Spring scenario,[22] relative to symptomatic cases. Cases that would be symptomatic in no booster scenario were asymptomatic in the Autumn/Spring scenario due to vaccine efficacy reducing severity of infection. Also, the effect of booster vaccinations is diluted due to time independent VE and observed high protection from infection in hybrid immunity compartments.

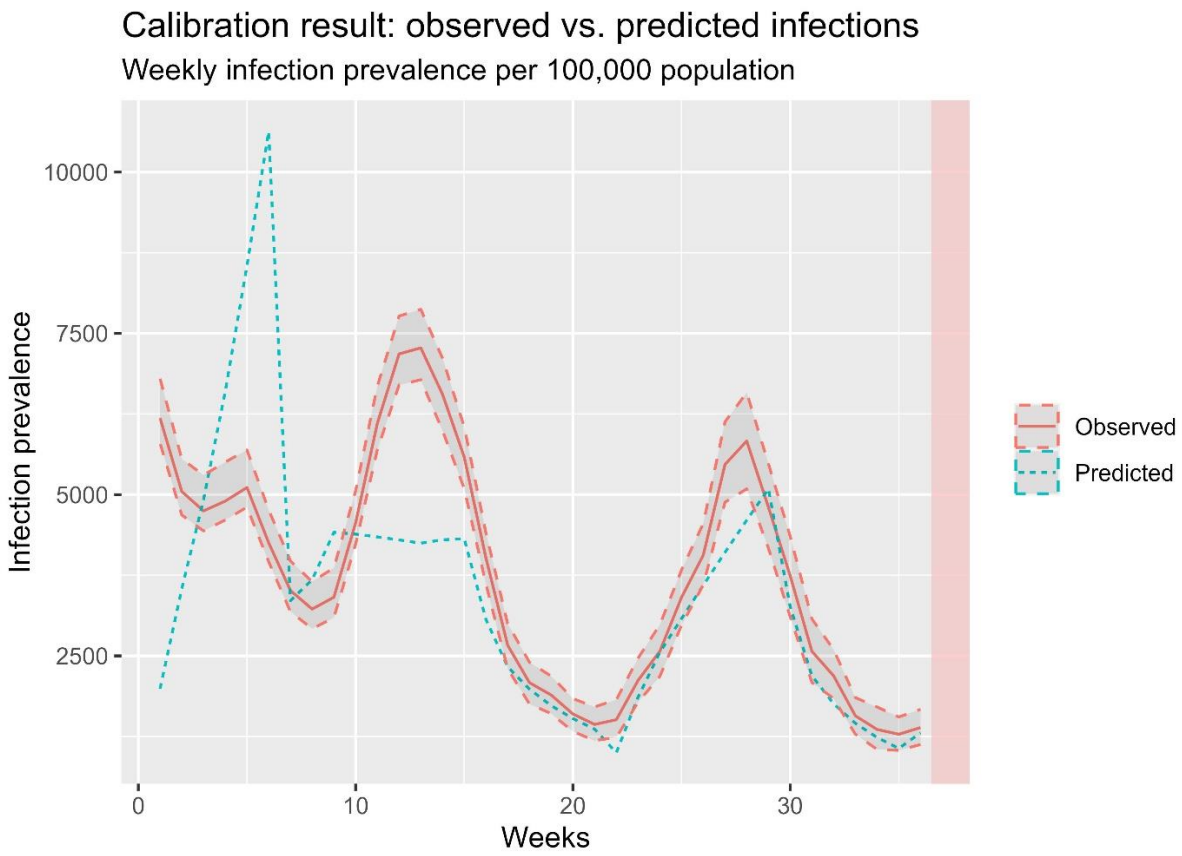
The model is sensitive to parametric assumptions, both distributional such as parameter limits and policy-based such as vaccine uptake. Uncertainties surrounding the definition, etiology, VE, and impact of vaccination on long COVID still exist. Additionally, there is no resource limit in the model, all individuals may be modelled to hospitalization or ICU where required, which does not reflect real world scenarios due to limited bed capacity. It should be noted that some limitations arise from the model assumptions that influence the calibration.

The model assumes that approximately 3% of the population in the UK were completely susceptible (i.e. had no previous immunity due to prior infection or vaccination, in all age groups) to COVID-19 infection in early 2022, at the start of the model.[12] The model is limited to the sensitivity around this assumption for age groups 75 and older, as the fraction of people in this age group with no infection or vaccination-induced immunity, or were not hospitalised, was approximately 4%. Moreover, as the model prediction depends on the population at the beginning of the prediction period/end of the calibration period, the influence of the initial population is not expected to be significant.

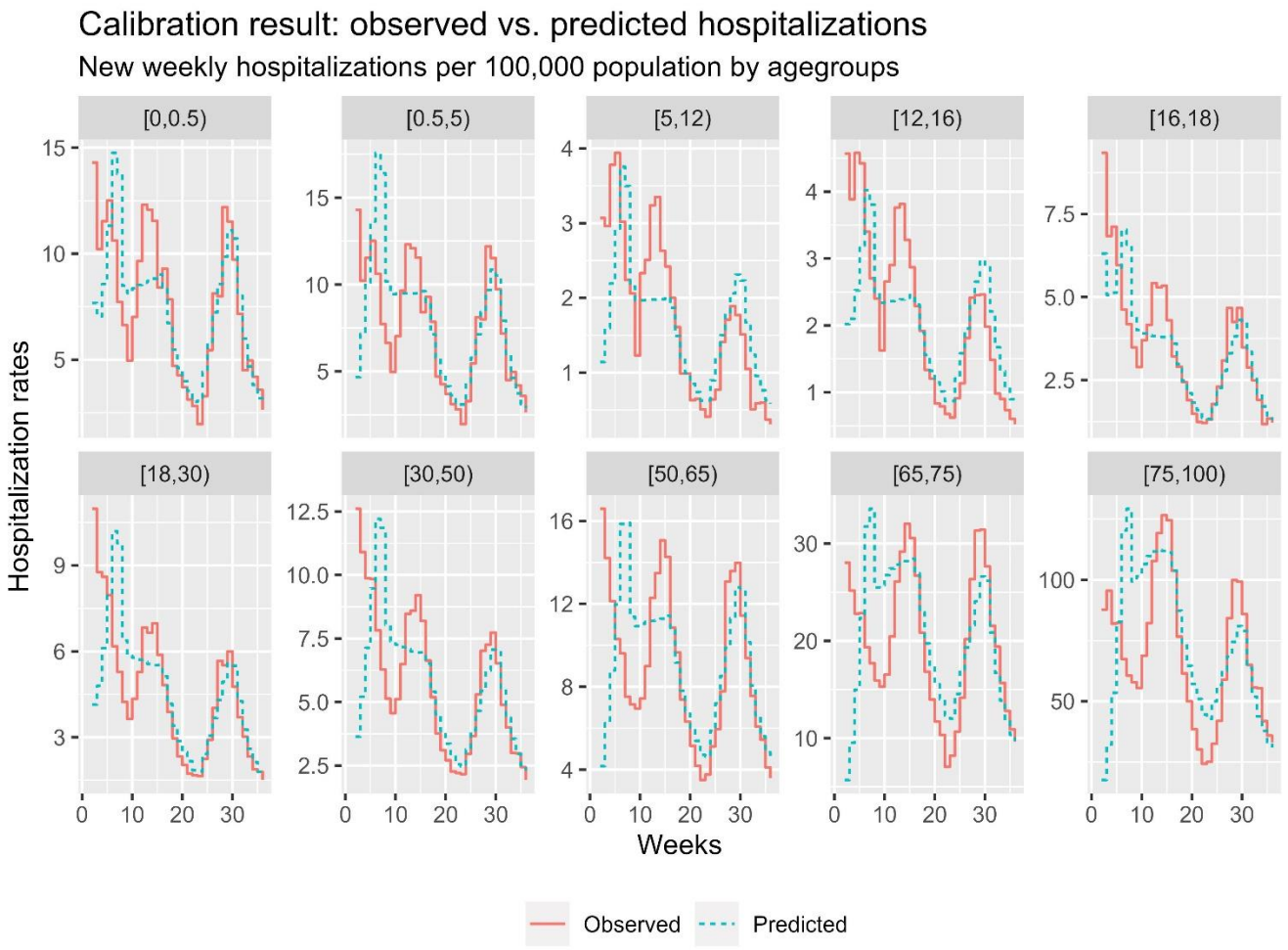
The VE was fixed for the model time horizon and only depends on the primary doses, monovalent, or bivalent vaccines. We have included a DSA for the clinical parameters; however, the model is restricted to use fixed calibrated parameters. The VE used in the model was not included in the sensitivity analysis as in the context of dynamic models it is known that many model parameters, particularly those related to mixing and transmission, are correlated with each other. Thus, following ISPOR best practise guidelines,[23] sensitivity analysis on calibrated parameters is not carried out. The model assumes that the individuals in the waned booster compartment have similar protection from hospitalization and death as those in the booster compartment which may result in underestimation of vaccine impact in the model. The model also does not differentiate between the length of hospital stay for the recovered population and for those dying during the hospital stay.



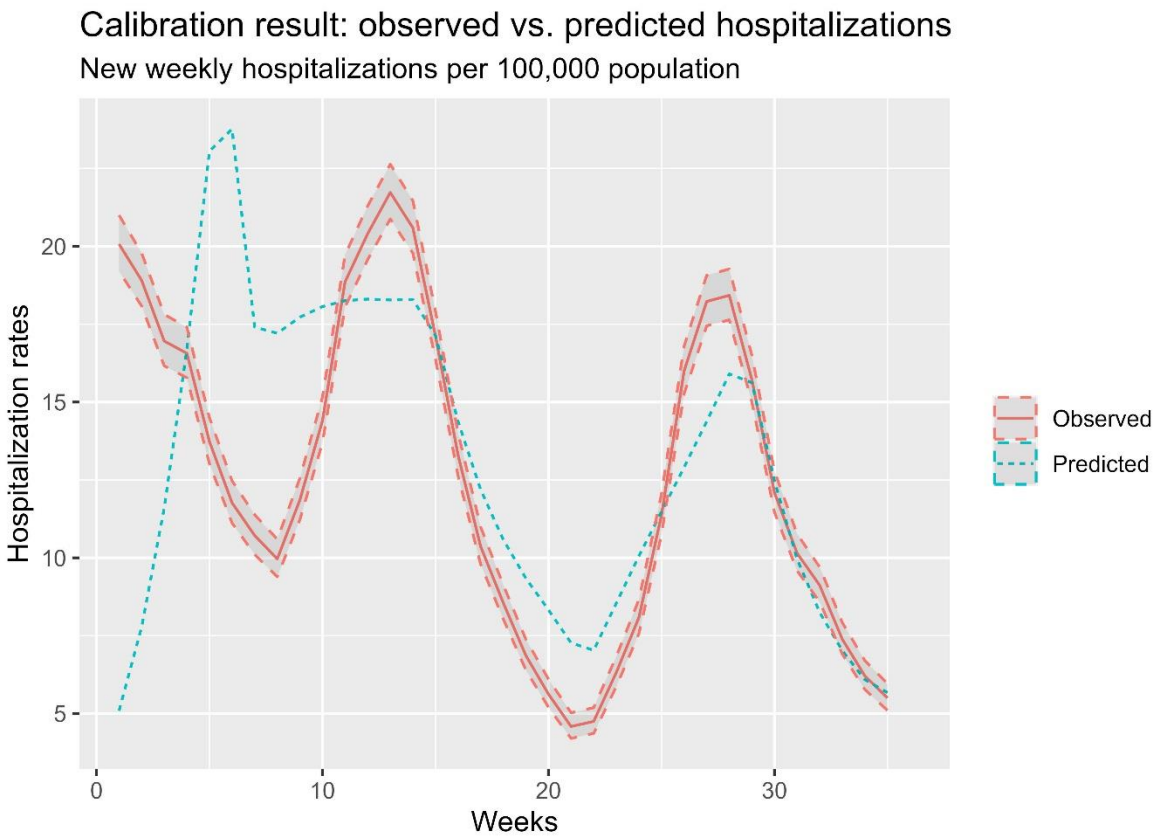

**Supplementary Figure 1: Modelled vs observed weekly prevalence of positive PCR tests per 100,000 population over the calibration period, stratified by age group.**



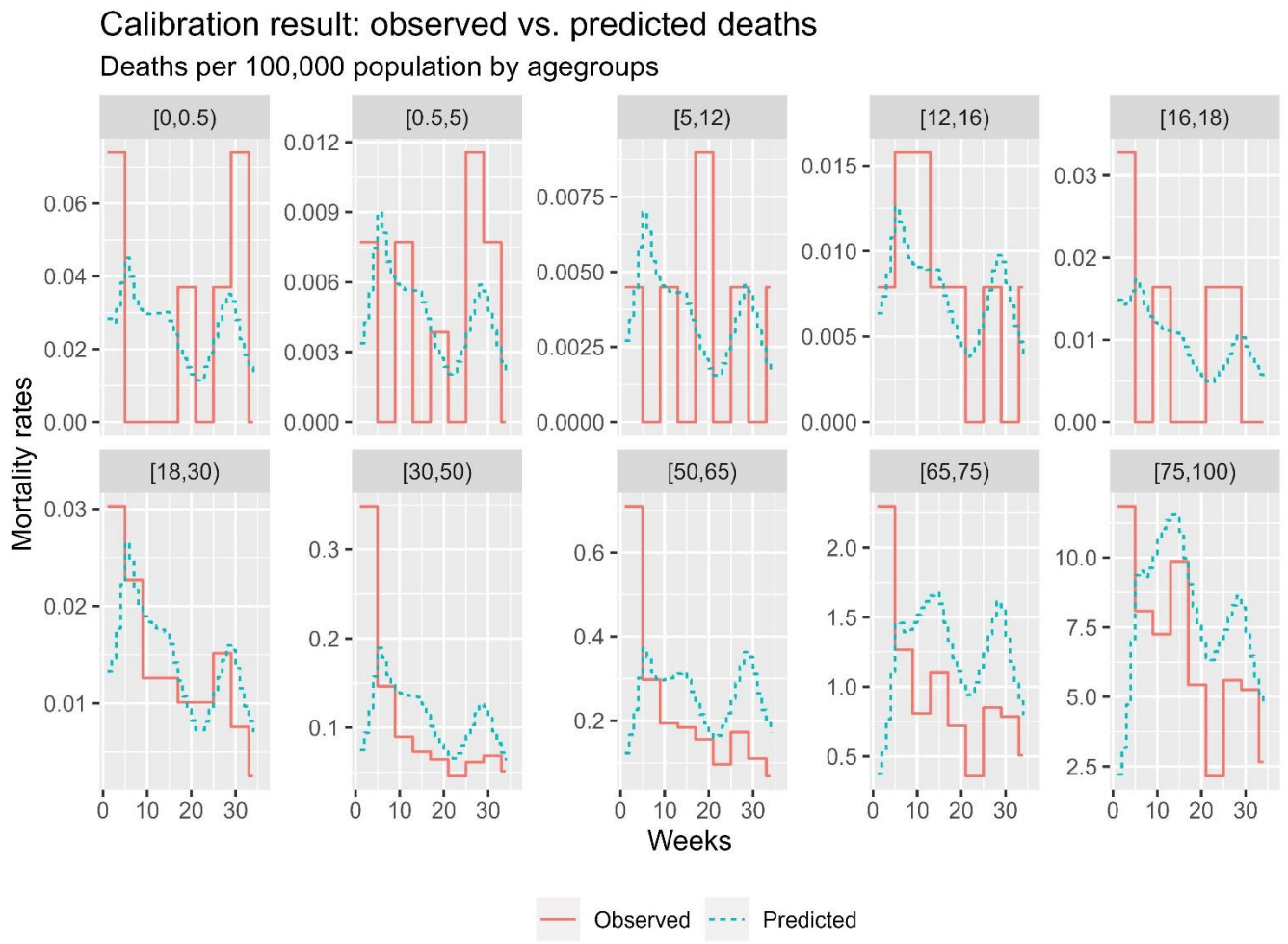

**Supplementary Figure 2: Modelled versus observed weekly prevalence of positive PCR tests per 100,000 population over the calibration period, calculated from ONS infection survey. The dashed lines show 95% confidence intervals reported in ONS infection survey.**



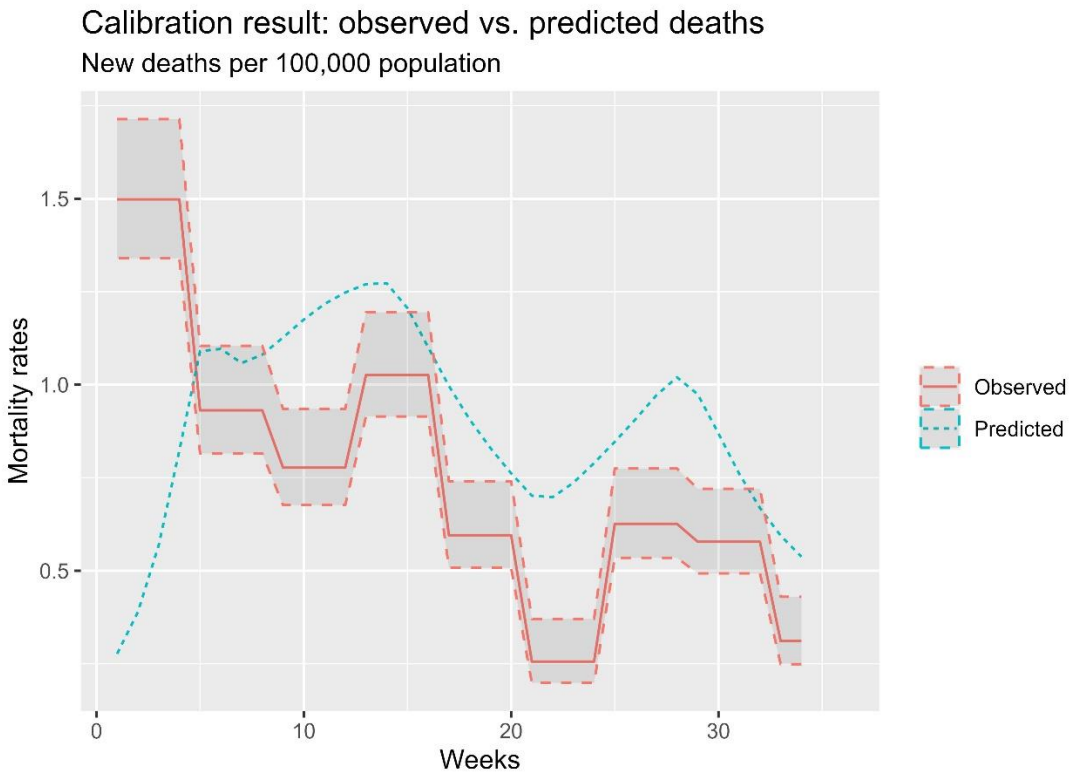

**Supplementary Figure 3: Modelled versus observed weekly new hospitalizations per 100,000 population over the calibration period, stratified by age group.**




**Supplementary Figure 4: Modelled versus observed weekly new hospitalizations per 100,000 population over the calibration period. The dashed lines show the estimated 95% binomial confidence intervals.**




**Supplementary Figure 5: Modelled versus observed weekly new deaths per 100,000 population over the calibration period, stratified by age group.**




**Supplementary Figure 6: Modelled versus observed weekly new cumulative deaths per 100,000 population over the calibration period. The dashed lines show the estimated 95% binomial confidence intervals.**

**Supplementary Table 1: Vaccine effectiveness in adults across all vaccinated compartments**

| Age | Dose 1 | Dose 2 | Booster monovalent | Waned booster** | Bivalent booster |
|---|---|---|---|---|---|
| Effectiveness against infection, % | | | | | |
| 18-30 | 30.00[24] | 30.00[24] | 37.00[25] | 0.00 | 37.00[25] |
| 30-50 | 30.00[24] | 30.00[24] | 37.00[25] | 0.00 | 37.00[25] |
| 50-65 | 30.00[24] | 30.00[24] | 37.00[25] | 0.00 | 37.00[25] |
| 65-75 | 30.00[24] | 30.00[24] | 37.00[25] | 0.00 | 37.00[25] |
| 75-100 | 30.00[24] | 30.00[24] | 37.00[25] | 0.00 | 37.00[25] |
| Effectiveness against symptomatic disease, % | | | | | |
| 18-30 | 48.90[26] | 46.52[26] | 65.00[26] | - | 65.83* |
| 30-50 | 48.90[26] | 46.52[26] | 65.00[26] | - | 65.83* |
| 50-65 | 48.90[26] | 46.52[26] | 65.00[26] | - | 65.83* |
| 65-75 | 48.90[26] | 46.52[26] | 65.00[26] | - | 65.83* |
| 75-100 | 48.90[26] | 46.52[26] | 65.00[26] | - | 65.83* |
| Effectiveness against hospitalization, % | | | | | |
| 18-30 | 31.70[24] | 63.11[24] | 77.75[24] | - | 78.74* |
| 30-50 | 31.70[24] | 63.11[24] | 77.75[24] | - | 78.74* |
| 50-65 | 31.70[24] | 63.11[24] | 77.75[24] | - | 78.74* |
| 65-75 | 47.10[24] | 69.03[24] | 85.81[24] | - | 93.83* |
| 75-100 | 47.10[24] | 69.03[24] | 85.81[24] | - | 93.83* |
| Effectiveness against ICU admission, % | | | | | |
| 18-30 | 59.80[24] | 57.32[24] | 87.21[24] | - | 88.32* |
| 30-50 | 59.80[24] | 57.32[24] | 87.21[24] | - | 88.32* |
| 50-65 | 59.80[24] | 57.32[24] | 87.21[24] | - | 88.32* |
| 65-75 | 52.60[24] | 81.22[24] | 89.02[24] | - | 97.34* |
| 75-100 | 52.60[24] | 81.22[24] | 89.02[24] | - | 97.34* |
| Effectiveness against mortality, % | | | | | |
| 18-30 | 59.00[24] | 59.00[24] | 82.03[24] | - | 83.08* |
| 30-50 | 59.00[24] | 59.00[24] | 82.03[24] | - | 83.08* |
| 50-65 | 59.00[24] | 59.00[24] | 82.03[24] | - | 83.08* |
| 65-75 | 59.00[24] | 59.00[24] | 82.03[24] | - | 83.08* |
| 75-100 | 59.00[24] | 59.00[24] | 82.03[24] | - | 83.08* |
| Effectiveness against infection from natural and hybrid immunity for all,[27] %§ | | | | | |
| Natural immunity | Hybrid immunity primary dose 1 | Hybrid immunity primary dose 2 | Hybrid immunity booster | | Hybrid immunity booster |
| 38.49% | 43.72% | 43.72% | 65.53% | | 65.53% |

All VE data followed UKHSA reports. The monovalent and bivalent vaccine effectiveness (VE) were calculated using a 3-month average data, while the VE for the primary doses were from a 6-month average data.
*The incremental effectiveness of bivalent boosters against hospitalizations[24] was used to estimate the bivalent absolute VE. Moreover, the VE for bivalent booster against infection, ICU, and death were calculated by keeping the same scaling factor between monovalent VE for infection, ICU, and death to monovalent VE for hospitalization.
**Waned vaccine strata ($V_{k=4}$, $V_{k=6}$) only have inputs for VE against infection as once infected patients rejoin the boosted vaccine strata ($V_{k=3}$, $V_{k=5}$) and have the same protection against severe COVID-19 outcomes.
[§]Natural and hybrid immunity estimates were calculated based on a 15-month period
The VEs for children are assumed to be same as that of the adults in 18-30 age group.

**Supplementary Table 2: Vaccine uptake rates across age groups**

Strategy I: factual Autumn 22/Spring 23 booster camapign. Strategy II: Autumn 22 booster only. Strategy III: Autumn 2022/Spring 2023 with improved uptake. Strategy IV: Expanded Autumn and expanded Spring. Strategy V: Expanded Autumn and expanded Spring with improved uptake. Strategy IV: No booster campaign

| Age (years) | Strategy (i) | Strategy (ii) | Strategy (iii) | Strategy (iv) | Strategy (v) | Strategy (vi) | Source for factual strategy (i) |
|---|---|---|---|---|---|---|---|
| Spring 2022 | | | | | | | |
| 0-0.5 | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | COVID 19 autumn 2023 booster program: impact assessment[28] |
| 0.5-5 | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | |
| 5-12 | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | |
| 12-16 | 0.69% | 0.69% | 0.69% | 0.69% | 0.69% | 0.69% | |
| 16-18 | 0.82% | 0.82% | 0.82% | 0.82% | 0.82% | 0.82% | |
| 18-30 | 1.51% | 1.51% | 1.51% | 1.51% | 1.51% | 1.51% | |
| 30-50 | 3.29% | 3.29% | 3.29% | 3.29% | 3.29% | 3.29% | |
| 50-65 | 5.42% | 5.42% | 5.42% | 5.42% | 5.42% | 5.42% | |
| 65-75 | 7.74% | 7.74% | 7.74% | 7.74% | 7.74% | 7.74% | |
| 75-100 | 74.64% | 74.64% | 74.64% | 74.64% | 74.64% | 74.64% | UKHSA week 27 data[29] |
| Autumn 2022 | | | | | | | |
| 0-0.5 | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | COVID 19 autumn 2023 booster program: Impact assessment[28] |
| 0.5-5 | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | |
| 5-12 | 7.48% | 7.48% | 7.48% | 7.48% | 7.48% | 0.00% | |
| 12-16 | 7.98% | 7.98% | 7.98% | 33.12% | 83.79% | 0.00% | |
| 16-18 | 9.41% | 9.41% | 9.41% | 48.26% | 83.79% | 0.00% | |
| 18-30 | 14.20% | 14.20% | 14.20% | 35.58% | 83.79% | 0.00% | |
| 30-50 | 22.09% | 22.09% | 22.09% | 53.94% | 83.79% | 0.00% | |
| 50-65 | 51.40% | 51.40% | 83.79% | 51.40% | 83.79% | 0.00% | UKHSA week 31 data[1] |
| 65-75 | 76.16% | 76.16% | 83.79% | 76.16% | 83.79% | 0.00% | |
| 75-100 | 83.79% | 83.79% | 83.79% | 83.79% | 83.79% | 0.00% | |
| Spring 2023 | | | | | | | |
| 0-0.5 | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | COVID 19 autumn 2023 booster program: Impact assessment[28] |
| 0.5-5 | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | |
| 5-12 | 0.65% | 0.00% | 0.65% | 0.65% | 0.65% | 0.00% | |
| 12-16 | 0.69% | 0.00% | 0.69% | 33.12% | 71.16% | 0.00% | |
| 16-18 | 0.82% | 0.00% | 0.82% | 48.26% | 71.16% | 0.00% | |
| 18-30 | 1.51% | 0.00% | 1.51% | 35.58% | 71.16% | 0.00% | |
| 30-50 | 3.29% | 0.00% | 3.29% | 53.94% | 71.16% | 0.00% | |
| 50-65 | 5.42% | 0.00% | 5.42% | 51.40% | 71.16% | 0.00% | |
| 65-75 | 7.74% | 0.00% | 7.74% | 76.16% | 71.16% | 0.00% | |
| 75-100 | 71.16% | 0.00% | 71.16% | 71.16% | 71.16% | 0.00% | UKHSA week 31 data[1] |

**Supplementary Table 3: Assumptions and sources for uptake rate calculation for counterfactual strategies**
Abbreviations: IS: immunosuppressed.

| Strategy | Autumn 2022 | | | Spring 2023 | | |
|---|---|---|---|---|---|---|
| | **Eligibility** | **Uptake rate estimation** | **Source** | **Eligibility** | **Uptake rate estimation** | **Source** |
| (ii) Autumn only | 5-49 years at high risk | 84% of population at risk of severe COVID-19 | *COVID 19 autumn 2023 booster program: Impact assessment*[28] | No eligible age or risk groups | - | - |
| | ≥50 years | Observed Autumn 2022 uptakes rates | *UKHSA week 31 data*[1] | | | |
| (iii) Autumn/ Spring with improved uptake | 5-49 years at high risk | 84% of population at risk of severe COVID-19 | *COVID 19 autumn 2023 booster program: Impact assessment*[28] | 5-74 years with IS | 84% of IS population | *COVID 19 autumn 2023 booster program: Impact assessment*[28] |
| | ≥50 years | Highest observed uptake rate from Autumn 2022 (83.8%) | *National Flu and COVID-19 surveillance week 31 data*[30] | All adults ≥75 years | Observed Spring 2023 uptakes rates | *National Flu and COVID-19 surveillance week 31 data*[30] |
| (iv) Expanded Autumn and expanded Spring | 5-11 years at high risk | 84% of population at risk of severe COVID-19 | *COVID 19 autumn 2023 booster program: Impact assessment*[28] | 5-11 years with IS | 84% of IS population | *COVID 19 autumn 2023 booster program: Impact assessment*[28] |
| | 12-17 years | Observed primary dose uptake | *National Flu and COVID-19 surveillance week 31 data*[30] | 12-17 years | Observed primary dose uptake | *National Flu and COVID-19 surveillance week 31 data*[30] |
| | 18-49 years | Observed dose 3 uptake | | 18-74 years | Observed dose 3 uptake | |
| | ≥50 years | Observed Autumn 2022 uptakes rates | | ≥75 years | Observed Spring 2023 uptakes rates | |
| (v) Expanded Autumn and expanded Spring with improved uptake | 5-11 years at high risk | 84% of population at risk of severe COVID-19 | *COVID 19 autumn 2023 booster program: Impact assessment*[28] | 5-11 years with IS | 84% of IS population | *COVID 19 autumn 2023 booster program: Impact assessment*[28] |
| | ≥12 years | Highest observed uptake rate from Autumn 2022 (83.8%) | *National Flu and COVID-19 surveillance week 31 data*[30] | ≥12 years | Highest observed uptake rate from Spring 2023 (71.2%) | *National Flu and COVID-19 surveillance week 31 data*[30] |

**Supplementary Table 4: Beta time windows throughout the calibration period and time horizon corresponding to real-world events assumed to impact contact rates.**

| β(t) | Date | Description |
|---|---|---|
| $\boldsymbol{\beta_{c1}}$ | 03/01/2022 | End of Christmas break |
| $\boldsymbol{\beta_{c2}}$ | 14/02/2022 | Half-term |
| $\boldsymbol{\beta_{c3}}$ | 21/02/2022 | End of half-term/ all COVID-19 restrictions lifted |
| $\boldsymbol{\beta_{c4}}$ | 04/04/2022 | Easter break |
| $\boldsymbol{\beta_{c5}}$ | 18/04/2022 | End of Easter break |
| $\boldsymbol{\beta_{c6}}$ | 30/05/2022 | Half-term |
| $\boldsymbol{\beta_{c7}}$ | 06/06/2022 | End of half-term |
| $\boldsymbol{\beta_{c8}}$ | 25/07/2022 | Summer break |
| $\boldsymbol{\beta_{c9}}$ | 05/09/2022 | End of summer break |
| $\boldsymbol{\beta_{10}}$ | 24/10/2022 | Half-term |
| $\boldsymbol{\beta_{11}}$ | 31/10/2022 | End of half-term |
| $\boldsymbol{\beta_{12}}$ | 19/12/2022 | Christmas break |
| $\boldsymbol{\beta_{13}}$ | 02/01/2023 | End of Christmas break |
| $\boldsymbol{\beta_{14}}$ | 13/02/2023 | Half-term |
| $\boldsymbol{\beta_{15}}$ | 20/02/2023 | End of half-term |
| $\boldsymbol{\beta_{16}}$ | 03/04/2023 | Easter break |
| $\boldsymbol{\beta_{17}}$ | 17/04/2023 | End of Easter break |
| $\boldsymbol{\beta_{18}}$ | 29/05/2023 | Half-term |
| $\boldsymbol{\beta_{19}}$ | 05/06/2023 | End of half-term |
| $\boldsymbol{\beta_{20}}$ | 24/07/2023 | Summer break |

**Supplementary Table 5: Age mapped baseline probabilities from Knock et al.**

| Age | Probability of hospitalization (general ward)[5] given symptomatic infection | Probability of ICU[5] given symptomatic infection* | Probability of death[5] given hospitalization | Probability of death[5] given ICU admission |
|---|---|---|---|---|
| 0-0.5 | 2.93% | 0.09% | 0.90% | 9.45% |
| 0.5-5 | 2.93% | 0.09% | 0.90% | 9.45% |
| 5-12 | 0.18% | 0.01% | 0.84% | 9.63% |
| 12-16 | 0.50% | 0.02% | 0.81% | 9.81% |
| 16-18 | 0.67% | 0.03% | 0.81% | 10.02% |
| 18-30 | 2.22% | 0.12% | 0.85% | 10.59% |
| 30-50 | 5.27% | 0.48% | 2.02% | 15.49% |
| 50-65 | 16.55% | 1.96% | 6.70% | 25.19% |
| 65-75 | 39.44% | 3.55% | 13.53% | 31.29% |
| 75-100 | 69.54% | 1.94% | 21.35% | 31.92% |

*Probability of ICU given symptomatic infection is calculated from probability of ICU given general ward admission and probability of general ward given symptomatic infection.

The age groups were mapped into model age groups by estimating the weights using the UK age distribution.[31]

**Supplementary Table 6: Calibrated model parameters**

| Parameter | Description | Final value |
|---|---|---|
| $\beta_{c1}$ | Transmission in first time window within calibration period | 0.82 |
| $\beta_{c2}$ | Transmission in second time window within calibration period | 0.0001 |
| $\beta_{c3}$ | Transmission in third time window within calibration period | 0.44 |
| $\beta_{c4}$ | Transmission in fourth time window within calibration period | 0.45 |
| $\beta_{c5}$ | Transmission in fifth time window within calibration period | 0.28 |
| $\beta_{c6}$ | Transmission in sixth time window within calibration period | 0.21 |
| $\beta_{c7}$ | Transmission in seventh time window within calibration period | 0.58 |
| $\beta_{c8}$ | Transmission in eighth time window within calibration period | 0.26 |
| $\beta_{c9}$ | Transmission in ninth time window within calibration period | 0.40 |
| Age stratified proportion waned to susceptible ($V_{k=0}$) in initial population | | |
| 16-18 | | 0.36 |
| 18-30 | | 1 |
| 30-50 | | 1 |
| 50-65 | | 1 |
| 65-75 | | 1 |
| 75-100 | | 1 |
| Age stratified proportion waned to booster waned ($V_{k=4}$) in initial population | | |
| 16-18 | | 0.01 |
| 18-30 | | 1 |
| 30-50 | | 0.001 |
| 50-65 | | 0.001 |
| 65-75 | | 1 |
| 75-100 | | 1 |
| Age stratified severity multipliers for hospitalization or ICU admission given infection | | |
| 0-0.5 | | 0.21 |
| 0.5-5 | | 0.26 |
| 5-12 | | 0.73 |
| 12-16 | | 0.62 |
| 16-18 | | 0.75 |
| 18-30 | | 0.56 |
| 30-50 | | 0.23 |
| 50-65 | | 0.10 |
| 65-75 | | 0.12 |
| 75-100 | | 0.25 |
| Age stratified severity multipliers for death given severe infection | | |
| 0-0.5 | | 0.90 |
| 0.5-5 | | 0.14 |
| 5-12 | | 0.35 |
| 12-16 | | 0.83 |
| 16-18 | | 0.50 |
| 18-30 | | 0.63 |
| 30-50 | | 1.61 |
| 50-65 | | 0.72 |
| 65-75 | | 1.15 |
| 75-100 | | 1.07 |

**Supplementary Table 7: Conditional probabilities of long COVID given infection,[32] stratified by age group and level of care received.**

| | <18 years | ≥18 years |
|---|---|---|
| **Long COVID ongoing symptomatic (from 4 weeks to 12 weeks)** | | |
| Patient received outpatient care | 2.70% | 5.70% |
| Patient received inpatient care – general ward | 27.50% | 27.50% |
| Patient received inpatient care – intensive care unit | 43.10% | 43.10% |
| **Post-COVID syndrome (more than 12 weeks)** | | |
| Patient received outpatient care | 10.00% | 0.70% |
| Patient received inpatient care – general ward | 10.00% | 11.10% |
| Patient received inpatient care – intensive care unit | 10.00% | 20.50% |

**Supplementary Table 8: Deterministic sensitivity analysis parameters**

| Number | Parameter | | Base case value | Range | Source |
|---|---|---|---|---|---|
| 1 | Relative infectiousness of symptomatic/asymptomatic cases | | 3.85 | 2.06 - 7.19 | Sayampanathan et al. 2021[33] |
| 2 | Duration of vaccine protection (months) | | 6.00 | 4.00 – 8.00 | Assumption[34] |
| 3a | Mean duration of recovery (days) | Symptomatic infection | 6.87 | 6.72 - 7.01 | Range calculated from SD of 5.21 days (mean+/-1.96*SEM)[35] |
| 3b | | Asymptomatic infection | 6.87 | 6.72 - 7.01 | |
| 4a | Risk ratio | Hospitalization | 1.70 | 1.30 - 2.20 | Sapey et al. 2020[36] |
| 4b | | ICU | 1.12 | 0.86 - 1.47 | Mason et al. 2021[37] |
| 4c | | Death | 2.15 | 1.50 - 3.09 | Mason et al. 2021[37] |
| 5a | Duration | Hospitalized | 9.10 | 8.7 - 9.5 | Vekaria et al. 2021[38] |
| 6b | | Intensive care | 14.25 | 11.8 - 16.9 | Hospital episode stat gives range from 3.1 - 7.4 days, (LB and UB from these limits added to the hospitalization duration ranges)[39] |

**Supplementary Table 9: Population size and proportion of high risk**

| Age group | Population size[31] | Share of high risk[40] (%) | Standard risk | High risk |
|---|---|---|---|---|
| 0-0.5 | 350,949 | 5.20 | 332,699 | 18,249 |
| 0.5-5 | 3,431,382 | 5.20 | 3,252,950 | 178,432 |
| 5-12 | 5,790,780 | 8.90 | 5,275,401 | 515,379 |
| 12-16 | 3,154,459 | 9.50 | 2,854,785 | 299,674 |
| 16-18 | 1,463,621 | 11.20 | 1,299,695 | 163,926 |
| 18-30 | 10,077,135 | 16.90 | 8,374,099 | 1,703,036 |
| 30-50 | 17,321,585 | 26.30 | 12,766,008 | 4,555,577 |
| 50-65 | 12,982,686 | 40.50 | 7,724,698 | 5,257,988 |
| 65-75 | 6,719,287 | 58.40 | 2,795,223 | 3,924,064 |
| 75-100 | 5,780,517 | 76.20 | 1,375,763 | 4,404,754 |

**Supplementary Table 10: Distribution of vaccination coverage in the starting population by age**

| Age | Not vaccinated | Dose 1 ($V_{k=1}$) | Dose 2 ($V_{k=2}$) | Booster ($V_{k=3}$) | Source |
|---|---|---|---|---|---|
| 0-0.5 | 100% | 0.00% | 0.00% | 0.00% | GOV.UK Dashboard[41] |
| 0.5-5 | 100% | 0.00% | 0.00% | 0.00% | |
| 5-12 | 100% | 0.00% | 0.00% | 0.00% | |
| 12-16 | 67% | 30.70% | 2.10% | 0.00% | |
| 16-18 | 46% | 40.90% | 13.30% | 0.30% | |
| 18-30 | 50% | 6.21% | 25.95% | 17.84% | |
| 30-50 | 27% | 4.03% | 26.82% | 41.93% | |
| 50-65 | 12% | 1.75% | 13.79% | 72.20% | |
| 65-75 | 7% | 1.05% | 5.80% | 85.85% | |
| 75-100 | 5% | 0.70% | 4.08% | 90.44% | |
| For k >4, the initial population is zero and the population size of waned booster compartment (k=4) is estimated through calibration. | | | | | |

**Supplementary Table 11: Obtained probabilities of hospitalisation and death during Omicron period**

| Age | Probability of hospitalisation general ward | | Probability of ICU | | Probability of death given general ward admission | | Probability of death given ICU admission | |
|---|---|---|---|---|---|---|---|---|
| | low risk | high risk | low risk | high risk | low risk | high risk | low risk | high risk |
| 0-0.5 | 0.22% | 0.38% | 0.01% | 0.01% | 0.26% | 0.55% | 2.70% | 5.80% |
| 0.5-5 | 0.28% | 0.48% | 0.01% | 0.01% | 0.04% | 0.08% | 0.42% | 0.90% |
| 5-12 | 0.05% | 0.09% | 0.00% | 0.00% | 0.09% | 0.20% | 1.08% | 2.32% |
| 12-16 | 0.12% | 0.20% | 0.01% | 0.01% | 0.21% | 0.45% | 2.57% | 5.53% |
| 16-18 | 0.19% | 0.32% | 0.01% | 0.01% | 0.13% | 0.27% | 1.58% | 3.41% |
| 18-30 | 0.46% | 0.79% | 0.03% | 0.04% | 0.17% | 0.37% | 2.12% | 4.56% |
| 30-50 | 0.46% | 0.77% | 0.05% | 0.06% | 1.03% | 2.22% | 7.94% | 17.07% |
| 50-65 | 0.62% | 1.06% | 0.09% | 0.10% | 1.53% | 3.30% | 5.77% | 12.40% |
| 65-75 | 1.74% | 2.97% | 0.20% | 0.22% | 4.94% | 10.62% | 11.43% | 24.56% |
| 75-100 | 6.49% | 11.03% | 0.23% | 0.26% | 7.28% | 15.66% | 10.89% | 23.41% |

**Supplementary Table 12: Eligibility criteria for Spring 2022, Autumn 2022, and Spring 2023 vaccination cohorts**

| Group | Eligibility criteria | Source |
|---|---|---|
| Spring 2022 eligibility | • Adult care residents<br>• Individuals aged 12 and over who are immunosuppressed<br>• All adults aged 75 years and over | JCVI statement for Spring 2022 COVID vaccine programme[42] |
| Autumn 2022 eligibility | • Resident in a care home for older adults and staff working in care homes for older adults<br>• Frontline health and social care workers<br>• All adults aged 50 years and over<br>• Persons aged 5 to 49 years in a clinical risk group, as set out in the Green Book<br>• Persons aged 5 to 49 years who are household contacts of people with immunosuppression<br>• Persons aged 16 to 49 years who are carers, as set out in the Green Book | JCVI statement for Autumn 2022 COVID vaccine programme[43] |
| Spring 2023 eligibility | • Residents in care homes for older people<br>• Persons aged 5 years and over with a weakened immune system<br>• All adults aged 75 years and older | JCVI statement for Spring 2023 COVID vaccine program[44] |

**Supplementary Table 13: Fixed and calculated model parameters**

| Parameter | Description | Stratified by | Value | Source |
|---|---|---|---|---|
| $\alpha$ | Relative infectiousness | | 0.26 | Sayapanathan et al. 2021[33] |
| $\varepsilon_{1,2,B}$ | Probability of displaying symptoms | Vaccination status | | Davies et al. 2020[45] |
| $\kappa$ | Rate of progression to infectious disease | None | 0.278 | Calculated by 1/latency period[46] |
| $\lambda$ | Force of infection | Age | n/a | Calculated from $\beta$ and the contact matrix |
| 1/ψ | Duration of protection due to natural immunity | None | 2.04 months | The duration of natural immunity is calculated to be 2.04 months following Mendes et al. (2023)[8] |
| | Duration of protection due to hybrid immunity | None | 2.04 months | We assume that the rate of waning with natural immunity and hybrid immunity similar to avoid double counting as the cohorts who lose the immunity from hybrid compartments will move to vaccinated strata with the protection from vaccination still continuing. |
| | Duration of protection due to primary doses of vaccination | None | 6.00 months | The duration of vaccine protection is assumed to be 6 months[8] |
| | Duration of protection due to booster dose of vaccine against infection | None | 5.43 months | The duration of protection against infection disease is assumed to be same as that estimated from the rate of loss of protection of BNT162b2 or mRNA-1273 boosters[8] |
| | Duration of protection due to booster dose of vaccine against symptomatic disease (waned compartment) | None | 4.30 months | The duration of protection against symptomatic disease is assumed to be same as that estimated from the rate of loss of protection of BNT162b2 or mRNA-1273 boosters[8] |

| Parameter | Description | Stratified by | Value | Source |
|---|---|---|---|---|
| $1/\gamma_{IA}$ | Duration in infectious asymptomatic state | None | 6.87 days | Menni et al. 2022[35] |
| $1/\gamma_{IS}$ | Duration in infectious asymptomatic state | None | 6.87 days | Menni et al. 2022[35] |
| $1/\gamma_{H}$ | Duration in hospital (general ward) | None | 9.10 days | Vekaria et al. 2021[38] |
| $1/\gamma_{ICU}$ | Duration in ICU | None | 14.25 days | The average number of days of stay in ICU only are 5.15 days ICNARC report 2023[47] and hospital adult critical care activity, with an additional 9.1 days in general ward.[39] |
| Risk ratio for hospitalization | | | | Sapey et al. 2020[36] |
| Risk ratio for ICU | | | 1.12 | Mason et al. 2021[37] |
| Risk ratio for fatality rate | | | 2.15 | Mason et al. 2021[37] |
| Latency period in days | | None | 3.6 | Du et al. 2022[48] |
| Baseline hospitalization rate | | Age | n/a | Calculated from the baseline probabilities of hospitalization obtained from Knock et al[5] and the rate of movement from symptomatic compartment |
| Baseline ICU admission rate | | Age | n/a | Calculated from the baseline probabilities of ICU admission from Knock et al[5] and the rate of movement from symptomatic compartment |
| Baseline fatality rate from hospital | | Age | n/a | Calculated from the baseline probabilities of death from general ward from Knock et al[5] and the rate of movement from general ward |
| Baseline fatality rate from ICU | | Age | n/a | Calculated from the baseline probabilities of death from ICU from Knock et al[5] and the rate of movement from ICU |
| Contact matrix | | Age | | POLYMOD[49] |
| $\eta$ | Hospitalization rate | Age, risk, vaccination status | n/a | Calculated from baseline hospitalization rate and severity multiplier for hospitalization. The baseline hospitalization rates for each age group are obtained from Knock et al[5] corresponding to the first epidemic wave in 2020 before the Omicron period. Thus, to obtain the rates for the Omicron period, these base line rates are multiplied with age stratified scaling factors (calibrated). For each vaccination strata, the rate is further reduced depending on the vaccine effectiveness for the hospitalization for the specific booster considered |

| | | | | |
|---|---|---|---|---|
| $\xi$ | ICU admission rate | Age, risk, vaccination status | n/a | Calculated from baseline ICU admission rate and severity multiplier for ICU admission. The baseline ICU rates for each age group are obtained from Knock et al[5] corresponding to the first epidemic wave in 2020 before the Omicron period. Thus, to obtain the rates for the Omicron period, these base line rates are multiplied with age stratified scaling factors (calibrated). For each vaccination strata, the rate is further reduced depending on the vaccine effectiveness for the hospitalization for the specific booster considered |
| $\zeta$ | Probability of death | Age, risk, vaccination status | n/a | Calculated from baseline probability of death and severity multiplier for probability of death. The baseline probability of death for each age group are obtained from Knock et al[5] corresponding to the first epidemic wave in 2020 before the Omicron period. Thus, to obtain the rates for the Omicron period, these base line values are multiplied with age stratified scaling factors (calibrated). For each vaccination strata, the rate is further reduced depending on the vaccine effectiveness for the hospitalization for the specific booster considered |

**Supplementary Table 14: Percentage of individuals with hybrid immunity in starting population**

| Age | Starting population in HI compartment (%) |
|---|---|
| 0-0.5 | 0.00 |
| 0.5-5 | 0.00 |
| 5-12 | 0.00 |
| 12-16 | 18.45 |
| 16-18 | 14.16 |
| 18-30 | 22.01 |
| 30-50 | 16.51 |
| 50-65 | 7.00 |
| 65-75 | 2.89 |
| 75-100 | 0.94 |
| Average | 10.52 |
| The average starting populations is determined by calculating the total number of individuals in each HI compartment for vaccinated and boosted strata and divided by the total population. | |

**Supplementary Table 15: Absolute numbers per clinical outcome across all scenarios.**

| Scenario | Asymptomatic infections n | Symptomatic infections n | Long COVID n | Hospitalizations | | Hospital bed days | | Deaths n |
|---|---|---|---|---|---|---|---|---|
| | | | | General ward admissions n | ICU n | General ward n | ICU n | |
| (i) Autumn/Spring | 18,260,553 | 10,414,754 | 939,504 | 103,280 | 6,180 | 1,471,745 | 88,058 | 8,344 |
| (ii) Autumn only | 18,253,682 | 10,531,437 | 949,328 | 108,429 | 6,396 | 1,545,108 | 91,143 | 8,817 |
| (iii) Autumn/Spring with improved uptake | 18,419,749 | 10,303,733 | 932,959 | 101,917 | 5,993 | 1,452,317 | 85,402 | 8,281 |
| (iv) Expanded Autumn/ expanded Spring | 17,920,059 | 9,397,140 | 858,096 | 96,036 | 5,476 | 1,368,506 | 78,028 | 8,023 |
| (v) Expanded Autumn/ expanded Spring with improved uptake | 17,845,777 | 8,773,259 | 809,554 | 92,559 | 5,079 | 1,318,968 | 72,374 | 7,930 |
| (vi) No booster | 16,946,123 | 10,793,039 | 961,797 | 119,930 | 7,315 | 1,708,998 | 104,242 | 9,808 |

**Supplementary Table 16: Absolute numbers of per clinical outcome across all scenarios.**

| Scenario | Productivity loss associated to non-fatal COVID infection | | Productivity loss associated to premature deaths due to COVID infection | |
|---|---|---|---|---|
| | Productive days lost from paid work n | Productive days lost from unpaid work n | Productive days lost from paid work n | Productive days lost from unpaid work n |
| (i) Autumn/Spring | 96,248,795 | 7,590,729 | 4,509,666 | 13,463,850 |
| (ii) Autumn only | 97,412,283 | 7,725,111 | 4,620,098 | 14,210,491 |
| (iii) Autumn/Spring with improved uptake | 95,375,880 | 7,460,185 | 4,436,298 | 13,352,051 |
| (iv) Expanded Autumn/ expanded Spring | 87,428,287 | 6,659,607 | 4,083,689 | 12,920,477 |
| (v) Expanded Autumn/ expanded Spring with improved uptake | 82,118,519 | 6,090,371 | 3,844,183 | 12,752,507 |
| (vi) No booster | 99,592,312 | 8,179,053 | 4,985,280 | 15,808,868 |

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