

COVID-19 vaccine surveillance report Week 14

6 April 2023

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Executive summary

Rigorous clinical trials have been undertaken to understand the immune response, safety profile, and efficacy of all coronavirus (COVID-19) vaccines approved for use in the UK as part of the regulatory process. Ongoing monitoring of the vaccines as they are rolled out in the population is important to continually ensure that clinical and public health guidance on the vaccination programme is built upon the best available evidence.

UK Health Security Agency (UKHSA), formerly Public Health England (PHE), works closely with the Medicines and Healthcare Regulatory Agency (MHRA), NHS England, and other government, devolved administration, and academic partners to monitor the COVID-19 vaccination programme. Details of the vaccine surveillance strategy are set on the page <u>COVID-19: vaccine surveillance strategy (1)</u>. As with all vaccines, the safety of COVID-19 vaccines is continuously <u>being monitored by the MHRA</u>. They conclude that overall, the benefits of COVID-19 vaccines outweigh any potential risks (<u>2</u>).

Please note that this report is published monthly. The next report will be published on 4 May 2023.

This month's report contains updates on vaccine effectiveness, vaccine coverage, vaccination in pregnancy, vaccine impact on the proportion of the population with antibodies to COVID-19, and vaccination status by the time of admission through SARI-Watch.

Vaccine effectiveness

Large clinical trials were undertaken for each of the COVID-19 vaccines first approved in the UK. These found that they were highly efficacious at preventing symptomatic disease in the populations that were studied. The clinical trials were able to assess the efficacy of the vaccines against laboratory confirmed symptomatic disease caused by the strains circulating in 2020 and early 2021. They also assessed with lower power efficacy against more severe disease.

Post implementation real world vaccine effectiveness (VE) studies are needed to understand vaccine effectiveness against different outcomes (such as severe disease and onward transmission), effectiveness in different subgroups of the population and against different variants as well as to understand the duration of protection. Vaccine effectiveness is estimated by comparing rates of disease (or positivity among those tested) in vaccinated individuals to rates in unvaccinated individuals. Below we outline the latest real-world evidence on vaccine effectiveness from studies in UK populations. Where available we focus on data related to the Omicron variant which is currently dominant in the UK. Previous reports demonstrated high levels of effectiveness against Alpha and Delta variants, particularly for severe disease and death.

Please note that vaccine effectiveness data will be updated in this report as it becomes available.

Effectiveness against symptomatic disease

Vaccine effectiveness against symptomatic COVID-19 has been assessed in England based on community testing data linked to vaccination data from the National Immunisation Management System (NIMS), cohort studies such as the COVID-19 Infection Survey, and GP electronic health record data. After community testing for COVID-19 was reduced in April 2022, we were no longer able to assess vaccine effectiveness against symptomatic disease using these data but results from previous analyses are available in earlier iterations of this report. Evidence prior to April from community testing and in other studies since this time has shown that effectiveness of all COVID-19 vaccines, including after first booster doses, against symptomatic disease with Omicron BA.1 and subsequent sub-lineages of the Omicron variant is low (starting at about 50 to 60%) and wanes rapidly to near 0 by 6 months.

Effectiveness against hospitalisation

Several studies have estimated vaccine effectiveness against hospitalisation, all of which indicate higher levels of protection against hospitalisation than symptomatic disease with all vaccines against the Alpha, Delta and Omicron variants ($\underline{3}$ to $\underline{8}$). Given that Omicron generally causes milder disease than previous variants ($\underline{9}$), in particular among younger individuals, an increasing proportion of individuals hospitalised with a positive COVID-19 test are likely to have COVID-19 as an incidental finding rather than the primary reason for admission ($\underline{8}$).

We have previously found that using broader definitions of hospitalisation has given lower vaccine effectiveness estimates, reflecting outcome misclassification where cases are likely coincidentally positive whilst in hospital, without this being the primary reason for admission (and therefore these cases cannot be prevented by vaccination). We, therefore, use stricter definitions to define a COVID-19 hospitalisation.

Here, a COVID-19 hospitalisation is defined as requiring at least 2 days stay in the hospital and a respiratory code in the primary diagnostic field. To estimate effectiveness against more severe disease we also estimate effectiveness for those requiring oxygen, mechanical ventilation or ICU (Table 1). There are likely still some incidental admissions in our data, in particular among younger adults. Using data from mid-July when BA.5 sub-lineage of Omicron has been dominant shows that protection against hospitalisation is maintained to a reasonable degree long term; VE after a second dose was 40.2% after 15 or more months and 52.3% at 12 to 14 months after a first booster dose (Table 1).

Dose	Interval	VE against hospitalisation
Dose 2	2 weeks to 2 months	70.3 (30.9 to 87.2)
	3 to 5 months	71.7 (50.5 to 83.8)
	6 to 8 months	57.6 (38.6 to 70.7)
	9 to 11 months	51.2 (31.2 to 65.4)
	12 to 14 months	35.5 (23.3 to 45.8)
	15+ months	40.2 (31.0 to 48.1)
Booster (third+ dose)	2 weeks to 2 months	78.1 (75.7 to 80.3)
	3 to 5 months	65.3 (61.7 to 68.6)
	6 to 8 months	53.6 (48.8 to 58.0)
	9 to 11 months	51.1 (45.7 to 56.0)
	12 to 14 months	52.3 (43.7 to 59.6)
	15+ months	Insufficient data

Table 1. Vaccine effectiveness against hospitalisation in those aged 65 years and over.
Hospitalisation is defined as a stay of at least 2 days with a respiratory code in the
primary diagnosis field

Effectiveness of the spring 2022 booster

Spring boosters with either Pfizer BioNTech or a half dose (50µg) of Moderna were offered to those at risk and those aged 75 years and older from March 2022. VE was estimated against hospitalisation using a strict definition (at least 2 days stay with a respiratory code in the primary diagnosis field). VE was estimated against the Omicron variant, all sub-lineages (BA.1, BA.2, BA.4 and BA.5) combined since we have not found a big difference in VE between sub-lineages. Since very few individuals remained unvaccinated, VE of the fourth dose was estimated as compared to those who had a waned third dose (25 to 39 weeks past receiving their third vaccine) (Table 2). The incremental VE for the fourth dose is therefore the level of protection that the fourth dose adds in addition to the remaining protection conferred by a third dose. These estimates, therefore, appear lower and are not directly comparable with estimates where VE is calculated relative to the unvaccinated. VE against hospitalisation was enhanced by a fourth dose; the incremental VE after 2 to 4 weeks was 58.8%. This waned to 10.8% at 20 or more weeks after receiving the fourth dose.

Dose	Interval (weeks)	Vaccine effectiveness (95% CI)
3	25 to 39 weeks	Baseline
4	0 to 6 days	46.5 (37.7 to 54.2)
	7 to 13 days	45.6 (36.4 to 53.4)
	2 to 4 weeks	58.8 (54.1 to 63.0)
	5 to 9 weeks	50.1 (45.6 to 54.2)
	10 to 14 weeks	35.9 (30.2 to 41.1)
	15 to 19 weeks	21.1 (11.6 to 29.5)
	20+ weeks	10.8 (-6.2 to 25.1)

Table 2. Vaccine effectiveness against hospitalisation for fourth doses, estimated using those 25 to 39 weeks post their third dose as the baseline group

Effectiveness of the autumn 2022 bivalent booster

Bivalent boosters with either Pfizer BioNTech (Original/Omicron BA.1 Comirnaty®) or a Moderna bivalent (Spikevax® bivalent Original/Omicron vaccine) targeting both the ancestral strain and Omicron BA.1 were offered to those in clinical risk groups and those aged 50 years and older from September 2022. VE of the bivalent boosters was estimated against hospitalisation in the period following 5 September 2022 against all Omicron sub-lineages in circulation at the time. Only individuals who had received at least 2 COVID-19 vaccines before 5 September 2022 and with the last of these doses at least 6 months prior to sample date were included in analysis.

The effectiveness measured is therefore incremental effectiveness on top of at least 6 months waned protection. The incremental protection conferred by the bivalent vaccines estimated relative to those with waned immunity was 47% for Pfizer after 2 weeks, and 58% for Moderna. There was some evidence of waning after 10 or more weeks after vaccination; VE was 38% for the Pfizer booster and 34% for the Moderna booster (Table 3).

Table 3. Vaccine effectiveness of the bivalent booster vaccines against hospitalisation in those aged 50 years and older (VE = vaccine effectiveness, CI = confidence intervals)

Vaccine manufacturer	Interval after booster dose	Controls	Cases	VE (95% CI)
Pfizer	2 to 4 weeks	1,649	268	47.2 (39.4 to 54.1)
	5 to 9 weeks		678	43.7 (38.1 to 48.8)
	10+ weeks	3,086	575	38.0 (31.0 to 44.3)
Moderna	2 to 4 weeks	1,156	306	57.8 (51.6 to 63.3)
	5 to 9 weeks	3,760	644	47.5 (42.1 to 52.4)
	10+ weeks	9,888	1,913	34.1 (29.2 to 38.7)

Effectiveness against mortality (vaccines given prior to the autumn 2022 bivalent boosters)

Vaccine effectiveness against mortality with the Omicron variant (all sub-lineages using tests taken until 5 September 2022) has been estimated for those aged 65 years and older using a test-negative case control study design (all vaccines combined) (<u>Table 4</u>). At 40-plus weeks following the second dose, vaccine effectiveness was around 50%. At 2 or more weeks following third and fourth dose vaccination, effectiveness was boosted to 85.0% and 80.9%, respectively.

At 40 or more weeks after a third dose VE waned to 56.9% while at 20 or more weeks after a fourth dose (spring 2022 booster) VE waned to 68.2%. This analysis is also likely to include some incidental deaths of individuals who died with COVID-19 as opposed to from COVID-19, and we suspect the true VE against mortality is likely higher than the estimates presented here.

Table 4. Vaccine effectiveness against mortality in those aged 65 years and older (all
vaccine brands combined) (VE = vaccine effectiveness, CI = confidence intervals)

Dose	Interval after dose (weeks)	VE (95% CI)
2	40+	49.7 (41.5 to 56.7)
3	2 to 4	85.0 (80.8 to 88.2)
	5 to 9	83.1 (80.3 to 85.5)
	10 to 14	79.5 (76.6 to 82.0)
	15 to 19	75.6 (72.3 to 78.6)
	20 to 24	68.8 (64.3 to 72.7)
	25 to 39	62.6 (57.4 to 67.2)
	40+	56.9 (43.1 to 67.4)
4	2 to 4	80.9 (76.8 to 84.3)
	5 to 9	79.5 (75.8 to 82.7)
	10 to 14	71.2 (66.2 to 75.5)
	15 to 19	68.2 (61.2 to 73.9)
	20+	68.2 (58.4 to 75.7)

Effectiveness against infection

Although individuals may not develop symptoms of COVID-19 after vaccination, it is possible that they could still be infected with the virus and could transmit it to others. Understanding how effective vaccines are at preventing infection is therefore important to predict the likely impact of the vaccination programme on the wider population. In order to estimate vaccine effectiveness against infection, repeat asymptomatic testing of a defined cohort of individuals is required. Studies have now reported on vaccine effectiveness against infection in healthcare workers, care home residents and the general population with the Alpha and Delta variants (10 to 13).

Generally, estimates are similar to or slightly lower than vaccine effectiveness estimates against symptomatic disease and there is evidence of a significant waning in protection against infection over time. Effectiveness against infection with the Omicron variant is low and wanes rapidly (<u>Table 5</u>).

Effectiveness against transmission

As described above, several studies have provided evidence that vaccines provide some protection against infection. Uninfected individuals cannot transmit. Therefore, the vaccines also provide some protection against transmission.

There may be an additional benefit, beyond that due to prevention of infection, if some of those individuals who become infected despite vaccination are also at a reduced risk of transmitting (for example, because of reduced duration or level of viral shedding). Several studies have provided evidence of reduced risk of household transmission from vaccinated cases compared to unvaccinated cases (<u>14</u> to <u>18</u>) with past variants.

Consensus vaccine effectiveness estimates

Table 5. Consensus estimates of relative vaccine effectiveness against BA.4, BA.5, BQ.1 and CH1.1 Omicron for a booster dose of COVID-19 vaccine compared to 6+ months since the last dose (at least 2 doses)

Vaccine product of booster dose [Note 1]	Outcome	0 to 1 months	2 to 3 months	4 to 6 months	6+ months	Consensus narrative
Monovalent	All Infection [Note 2]	30% (20 to 40%)	20% (10 to 30%)	10% (0 to 20%)	0% (0 to 5%)	Post fourth dose estimates appear similar to pos period, restoring VE to similar levels provided by VE estimates may differ depending on whether in Some studies suggest VE estimates may be sligh BA.1/BA.2 compared to Omicron BA.4/BA.5.
Monovalent	Symptomatic [Note 2]	40% (30 to 50%)	40% (30 to 50%)	10% (0 to 20%)	Insufficient data	Post fourth dose estimates appear similar to post period, restoring VE to similar levels provided by VE estimates may differ depending on whether in
Monovalent	Hospitalisation	60% (55 to 65%)	40% (30 to 50%)	20% (15 to 25%)	0% (0 to 5%)	These estimates are based on UKHSA test negatives hospitalisations in age 75+ with 2+ days stay and absolute VE had waned to about 70% at 6+ mon would increase this back to an absolute VE of 85 studies suggest VE estimates against hospitalisation BA.4/BA.5.
Monovalent	Mortality	Insufficient data	Insufficient data	Insufficient data	Insufficient data	
Bivalent	All Infection [Note 2]	30% (20 to 40%)	20% (10 to 30%)	10% (0 to 20%)	0% (0 to 5%)	Estimates for the BA.1/BA.2 bivalent booster are seen with BA.4/BA.5 bivalent boosters.
Bivalent	Symptomatic [Note 2]	40% (30 to 50%)	40% (30 to 50%)	10% (0 to 20%)	Insufficient data	
Bivalent	Hospitalisation	55% (40 to 65%)	50% (40 to 65%)	Insufficient data	Insufficient data	Estimates for the BA.1/BA.2 bivalent booster are seen with BA.4/BA.5 bivalent boosters. There is hospitalisation is slightly lower against CH1.1 cor
Bivalent	Mortality	70% (65 to 80%)	70% (65 to 80%)	Insufficient data	Insufficient data	Current evidence based on age 65+.

The table presents estimates of VE compared to 6+ months since last dose (at least 2 doses) (estimates agreed by the vaccine expert panel).

Note 1. Refers to either Pfizer or Moderna.

Note 2. Estimates were not stratified according to monovalent or bivalent.

High confidence	Evidence from multiple studies which is consistent and comprehensive.		
Medium confidence	Evidence is emerging from a limited number of studies or with a moderate level of uncertainty.		
Low confidence	Little evidence is available, and results are inconclusive.		

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gative case control using SUS data on nd respiratory coded. Note: As onths post dose 3, a relative VE of 50% 85% compared to unvaccinated. Some sation are similar for BA.2 versus

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re not too different from what is being is some evidence that VE against compared to BA.4/BA.5.

Effectiveness against BQ.1

VE against hospitalisation for BQ.1 and BA.5 was estimated during a period of co-circulation (Table 6). This included the period from 5 September 2022 to 25 December 2022. Cases were classified as BA.5 (VOC-22APR-04) or BQ.1 (V-22OCT-01) based on sequencing information. VE was estimated for those who had received a bivalent booster vaccine as part of the autumn programme, as well as at least 2 previous doses at least 6 months previously, relative to those who were not boosted in the autumn but had at least 2 previous doses at least 6 months previously. Estimates are for those who received the booster 2 or more weeks ago. All vaccine manufacturers were combined in the analysis.

The effectiveness of the bivalent booster (manufacturers combined) against hospitalisation with BQ.1 was 52.1% as compared to 63.6% with BA.5, at 2 or more weeks after receiving the booster (Table 6). Although the effectiveness point estimate is lower for BQ.1 the confidence interval is fairly wide and overlaps the estimate for BA.5. Currently the number of BQ.1 cases in the analysis is too small to confidently assess differences in vaccine effectiveness between the 2 variants.

Variant	Vaccine	Controls	Cases	VE (95% CI)
BQ.1	Bivalent (any)	8,617	175	52.1 (40.2 to 61.6)
	Pfizer	2,730	49	54.1 (36.0 to 67.1)
	Moderna	5,887	126	51.0 (37.7 to 61.4)
BA.5	Bivalent (any)	8,617	100	63.6 (53.8 to 71.3)
	Pfizer	2,730	25	53.7 (28.5 to 70)
	Moderna	5,887	75	65.8 (55.5 to 73.7)

Table 6. VE estimates against hospitalisation with BQ.1 and BA.5 for the bivalent boosters in those aged 50 years and older

Estimates of earlier circulating Omicron sub-lineages (BA.4, BA.4.6 and BA.5) as compared to BA.2 are available in previous iterations of this report.

Effectiveness against XBB.1.5, CH.1.1 and BQ.1

Sub-lineages CH.1.1 and XBB.1.5 increased in prevalent in England in December 2022 and January 2023, respectively. VE against hospitalisation for XBB.1.5, CH.1.1. and BQ.1 was estimated during a period of co-circulation between 5 December and 19 February (<u>Table 7</u>). During this period, BA.5 was not a prominent sub-lineage. Cases were classified based on sequencing information. Cases were classified as XBB.1.5 (V-23JAN-01), CH.1.1 (V-22DEC-01) or BQ.1 (V-22OCT-01) based on sequencing information, and VE was estimated as described above.

There was some evidence that VE against hospitalisation for CH.1.1 was lower than that of BQ.1, and that VE against XBB.1.5 was lower than that of CH.1.1 and BQ.1, but confidence intervals were wide and overlapped. Currently the number of cases in the analysis is too small to confidently assess differences in vaccine effectiveness between these variants.

Variant	Bivalent booster	Controls	Cases	VE
XBB.1.5	None	34,802	108	Baseline
	2 to 4 weeks	3,215	2	56.9 (-75.9 to 89.5)
	5 to 9 weeks	19,986	15	47.3 (7.8 to 69.9)
	10 to 14 weeks	42,149	80	25.7 (-0.9 to 45.3)
	15+ weeks	30,465	220	12.3 (-12.9 to 31.9)
CH.1.1.	None	34,802	164	Baseline
	2 to 4 weeks	3,215	11	31.4 (-27.4 to 63)
	5 to 9 weeks	19,986	71	35.1 (13 to 51.6)
	10 to 14 weeks	42,149	199	28.4 (10.7 to 42.5)
	15+ weeks	30,465	164	26.3 (5.4 to 42.5)
BQ.1	None	34,802	450	Baseline
	2 to 4 weeks	3,215	23	62.6 (42.9 to 75.5)
	5 to 9 weeks	19,986	214	46.5 (36.5 to 54.9)
	10 to 14 weeks	42,149	476	40.5 (31.8 to 48.1)
	15+ weeks	30,465	258	31.3 (17.7 to 42.6)

Table 7. VE estimates against hospitalisation with XBB.1.5, CH.1.1 and BQ.1 for the bivalent boosters in those aged 50 years and older

Vaccine effectiveness publications

UKHSA and collaborators have published a significant amount of <u>research into vaccine</u> <u>effectiveness</u>, which is summarised on pages 4 to 11. The publications listed in <u>Table 8</u> provide further results and details on the methods used.

Publication	Subject
Effectiveness of the COVID-19 vaccines against severe disease with Omicron sub-	The latest evidence shows that vaccine effectiveness against hospitalisation is
lineages BA.4 and BA.5 in England	similar for the BA.4/5 variants as it is for
	BA.2. In somebody who received their

Publication	Subject
	second dose around 6 months previously, a booster dose increases protection against hospitalisation by 50 to 60%. This is the most comprehensive analysis of vaccine effectiveness against hospitalisation for BA.4/5 undertaken to date.
Effectiveness of AstraZeneca COVID-19 booster vaccination against the Omicron and Delta variants	This study estimates the effectiveness of booster vaccination with AstraZeneca against symptomatic disease and hospitalisation in individuals who were not able to receive mRNA vaccines in the UK.
<u>COVID-19 Vaccine Effectiveness against the</u> <u>Omicron BA.2 variant in England</u>	This study estimates the effectiveness of booster vaccination against symptomatic disease caused by the BA.2 sub-lineage of the Omicron (B.1.1.529) variant.
Vaccine effectiveness against hospitalisation with the Omicron variant	This study estimates vaccine effectiveness against hospitalisation with the Omicron variant and investigates the impact of using different hospitalisation outcome definitions
Effectiveness of COVID-19 vaccines against hospitalisation with the Omicron variant in adults aged 75 years and older	This study reports on vaccine effectiveness against hospitalisation with the Omicron variant in adults aged 75 years and older.
Effectiveness of BNT162b2 and ChAdOx1 against SARS-CoV-2 household transmission: a prospective cohort study in England	This study reports on vaccine effectiveness against transmission of COVID-19 with the Alpha and Delta variants.
Effectiveness of 3 doses of COVID-19 vaccines against symptomatic COVID-19 and hospitalisation in adults aged 65 years and older	Updated analysis on the effectiveness of 3 doses of COVID-19 vaccines against symptomatic COVID-19 and hospitalisation in adults aged 65 years and older.
Effectiveness of BNT162b2 COVID-19 booster vaccine against COVID-19 related symptoms and hospitalisation in England	This study provides real world evidence of significantly increased protection from the booster vaccine dose against symptomatic disease and hospitalisation irrespective of the primary course.
Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern	This study reports on the vaccine effectiveness against symptomatic disease

Publication	Subject
	with 2 dose courses of BNT1622 and ChAdOx1-S as well as booster doses of BNT162b2 following a primary course of either BNT1622 or ChAdOx1-S.
Effectiveness of BNT162b2 (Comirnaty, Pfizer- BioNTech) COVID-19 booster vaccine against COVID-19 related symptoms in England: test negative case-control study	Results from the first UK real-world study by UKHSA show significantly increased protection against symptomatic disease from a booster dose of the Pfizer-BioNTech vaccine in those aged 50 years and older.
Duration of Protection against Mild and Severe Disease by COVID-19 Vaccines	This study reports on the vaccine effectiveness and duration of protection of Comirnaty, Vaxzevria and Spikevax against mild and severe COVID-19 in the UK.
Serological responses and vaccine effectiveness for extended COVID-19 vaccine schedules in England	This study investigates the impact of different dosing schedules on immune response and vaccine effectiveness.
Pfizer-BioNTech and Oxford AstraZeneca COVID-19 vaccine effectiveness and immune response among individuals in clinical risk groups	This study reports on the immune response and clinical effectiveness of COVID-19 vaccine among individuals in clinical risk groups. A <u>supplementary appendix</u> is also available to download.
Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant	This study reports on the effectiveness of COVID-19 vaccines on hospitalisation disease with the Delta variant. A supplementary appendix is also available to download.
Effectiveness of COVID-19 Vaccines against the B.1.617.2 (Delta) Variant	This study reports on the effectiveness of COVID-19 vaccines on symptomatic disease with the Delta variant.
Effectiveness of BNT162b2 mRNA and ChAdOx1 adenovirus vector COVID-19 vaccines on risk of hospitalisation among older adults in England: an observational study using surveillance data	A study using the SARI watch surveillance system of COVID-19 hospitalisations found high levels of protection against hospitalisation after both a single dose and 2 doses of COVID-19 vaccines.
Effectiveness of BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on mortality following COVID-19	A study on deaths with COVID-19 indicates that COVID-19 vaccines offer high levels of protection against mortality.

Publication	Subject
Effect of Vaccination on Household Transmission of SARS-CoV-2 in England	Impact of vaccination on household transmission of SARS-COV-2 in England is an analysis to determine whether individuals who have received the vaccine, but still become infected with SARS-COV-2 up to 60 days after the first dose, are less likely than unvaccinated cases to transmit to their unvaccinated household contacts.
<u>Vaccine effectiveness of the first dose of</u> <u>ChAdOx1 nCoV-19 and BNT162b2 against</u> <u>SARS-CoV-2 infection in residents of Long-</u> <u>Term Care Facilities (VIVALDI study)</u>	The VIVALDI study found evidence that COVID-19 vaccines were associated with a substantially reduced risk of infection in care home residents.
Effectiveness of BNT162b2 and ChAdOx1 nCoV-19 COVID-19 vaccination at preventing hospitalisations in people aged at least 80 years: a test-negative, case-control study	The Avon CAP study, conducted in 2 hospitals in Bristol, found evidence of high levels of protection against hospitalisation in 80+ year olds with a single dose of either vaccine.
<u>COVID-19 vaccine coverage in health-care</u> workers in England and effectiveness of <u>BNT162b2 mRNA vaccine against infection</u> (<u>SIREN): a prospective, multicentre, cohort</u> study	Early data from UKHSA's SIREN study shows a promising impact on infection in healthcare workers aged under 65. Healthcare workers in the study are tested for COVID-19 every 2 weeks – whether or not they have symptoms.
Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on COVID-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study	Early data from routine COVID-19 testing in older adults shows that vaccines are effective at preventing COVID-19 disease and severe outcomes.
Impact of COVID-19 vaccination programme on seroprevalence in blood donors in England, 2021	Report on the impact of COVID-19 vaccination programme on seroprevalence in blood donors in England, 2021.

Population impact

Vaccines typically have both direct effects on those who are vaccinated and indirect effects on the wider population due to a reduced probability that people will come into contact with an infected individual. The overall impact of the vaccination programme may therefore extend beyond that estimated through vaccine effectiveness analysis.

Estimating the impact of a vaccination programme is challenging as there is no completely unaffected control group. Furthermore, the effects of the vaccination programme need to be differentiated from that of other interventions (for example, lockdowns or outbreak control measures), changes in behaviour and any seasonal variation in COVID-19 activity.

UKHSA and other government and academic partners monitor the impact of the vaccination programme on levels of COVID-19 antibodies in the population and different disease indicators, including hospitalisations and mortality. This is done through population-based testing and through modelling which combines vaccine coverage rates in different populations, estimates of vaccine effectiveness and disease surveillance indicators.

Vaccine coverage

By the end of week 10 2023 (week ending 12 March 2023), 65.7% (15,098,879 out of 22,970,162) of all people aged over 50 years old who are living and resident in England who had been vaccinated with an autumn booster dose since 1 September 2022. Vaccine uptake of those aged over 80 years old was 83.8% (2,469,906 out of 2,948,380). For further detail on the vaccine uptake and the current booster campaign, please the flu and COVID-19 weekly surveillance report.

Vaccination in pregnancy

Vaccination of pregnant women alongside their peers is recommended in the UK and other countries as an important way to protect pregnant women and their unborn children against COVID-19 disease. Vaccination of pregnant women is strongly recommended by the <u>Royal</u> <u>College of Obstetricians and Gynaecologists and the Royal College of Midwives</u>.

Increased severity of COVID-19 disease in pregnant and recently pregnant women was reported after the first SARS-CoV-2 wave in England (<u>19</u>, <u>20</u>) and Scotland (<u>21</u>, <u>22</u>). The disease is generally reported to be milder during the Omicron period with reduced risk of complications in pregnant women when compared to the Delta period (<u>23</u>,<u>24</u>). Omicron has, however, also been associated with higher rates of infection in pregnant women when compared to Delta (<u>24</u>). Pregnant women who develop the severe disease have increased rates of admission to the ICU, need for invasive ventilation and pre-term delivery.

Data from the US Centre for Disease Control and Prevention (CDC) found that pregnant women were around 3 times more likely to be admitted to ICU and nearly 3 times more likely to require invasive ventilation compared to non-pregnant women with COVID-19 disease and 25% more likely to die (25).

From 16 April 2021, the Joint Committee on Vaccination and Immunisation (JCVI) advised that pregnant women be offered COVID-19 vaccines at the same time as people of the same age or risk group (<u>26</u>). Therefore, any pregnant women not in a high-risk group would likely have received their first dose from mid-April 2021 as part of the general adult population programme in those aged under 50 years. This was offered by decreasing age group (<u>26</u>). As part of the ongoing review of the programme, the JCVI met on 2 December 2021 and considered further data on severity of SARS-CoV-2 infection in pregnant women and their pregnancies together with data on vaccine safety. As a result, pregnant women were added to the UK's priority COVID-19 vaccine list (<u>27</u>). The booster dose, made available to all individuals with severe immunosuppression from September 2021 and then extended to all eligible adults in England from 30 November 2021, is important to confer high levels of protection against Omicron strains (see report section vaccine effectiveness). Pregnant women are included as one of the priority groups to be offered the autumn 2022 COVID-19 booster dose.

Prior to 16 April 2021, COVID-19 vaccine was delivered to priority groups, based on clinical risk and risk of exposure, and delivered in order of priority. On 22 December 2020, JCVI advised that vaccine could be offered to pregnant and breast-feeding women who were in these risk categories. The Pfizer vaccine was rolled out from early December 2020, AstraZeneca vaccine was used from 4 January 2021 and the Moderna vaccine became available from April 2021. From 17 April 2021 pregnant women have been offered the Pfizer-BioNTech or Moderna (mRNA) vaccines where available for their first dose due to reassuring global safety data (28).

There is evidence of high levels of protection against SARS-CoV-2 infection in pregnant women after COVID-19 vaccination (<u>29</u> to <u>31</u>) and evidence that vaccination induces higher antibody levels than after disease (<u>31</u>). There is also evidence from a recent US study that 2-doses of mRNA COVID-19 vaccination during pregnancy might help prevent COVID-19 hospitalisations in young infants under 6 months of age (<u>32</u>). Between February and September 2021, 0.4% of 1,714 pregnant women with COVID-19 symptoms who required hospital treatment in the UK had received 2 doses of COVID-19 vaccine and, of 235 pregnant women who were admitted to intensive care with COVID-19 disease in that period, none had received 2 doses of vaccine (<u>33</u>). Similar findings have been reported from Scotland with the report that 90.9% (748 out of 823; 95% CI 88.7 to 92.7) of SARS-CoV-2 associated with hospital admission, 98% (102 out of 104; 95% CI 92.5 to 99.7) of SARS-CoV-2 associated with critical care admission and all baby deaths, occurred in pregnant women who were unvaccinated at the time of their COVID-19 diagnosis (<u>22</u>, <u>34</u>). The researchers also found a higher extended perinatal mortality rate for women who gave birth within 28 days of a COVID-19 diagnosis compared to rates across the pandemic period and in women vaccinated and going on to give birth within 28 days.

COVID-19 vaccines used in the UK programme do not contain live SARS-CoV-2 virus and therefore cannot infect a pregnant woman or her unborn child with the virus. Whilst as is commonly the case in trials of medicinal products, pregnant women were excluded from the original COVID-19 vaccine trials, there is accumulating experience and evidence of the safe and effective use of mRNA vaccines (such as the Pfizer-BioNTech or Moderna) in pregnant women. In Scotland, COVID-19 vaccine had been administered to more than 30,000 pregnant women to the end of March 2022 (21). In the USA data collected by the US Centre for Disease Control indicated that around 71% of pregnant people were fully vaccinated before or during pregnancy in week ending 20 August 2022 (35).

No safety concerns relating to COVID-19 vaccination of pregnant women have been found in published studies to date ($\underline{35}$ to $\underline{39}$). The rate of vaccine side-effects appears to be similar in pregnant and non-pregnant populations ($\underline{35}$). Studies from Norway, the USA and Scotland have found no association between COVID-19 vaccination and the risk of miscarriage ($\underline{37}$ to $\underline{40}$).

This report presents data on vaccine coverage only for women delivering up to the end of December 2022 and updates the coverage data on COVID-19 vaccination in pregnant women published in the <u>COVID-19 vaccine surveillance report</u> – weeks 47 of 2021, 4, 8, 12, 16, 19 and 35 of 2022, week 5 and week 9 of 2023. Findings continue to be provisional and are not directly comparable between reports as data is updated through the complete time period under consideration. All previous reports additionally included pregnancy outcomes (stillbirth, low birth weight and preterm deliveries) but women delivering in the most recent months with maternity data available have overwhelmingly been vaccinated with dose 1 to 3 before the pregnancy for which they are giving birth (Figure 1). These pregnancy outcomes would therefore not be expected to substantively alter previously published data. Similarly, breakdown of coverage by ethnicity, index of multiple deprivation (IMD) and maternal age group for doses 1 to 3 will no longer be updated. Data will be collated and published on women who have delivered from September 2022, after vaccination under the autumn boost programme, once numbers have accumulated.

This report is the second to include data on coverage of the autumn boost that was recommended to those at higher risk of severe COVID-19 disease in the population who had not been boosted for at least 3 months, including pregnant women. Autumn boost vaccination began in September 2022.

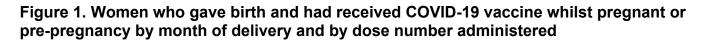
Vaccine coverage

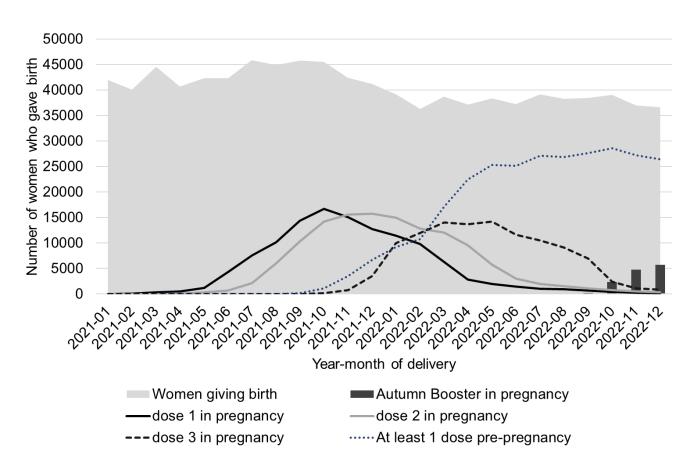
COVID-19 vaccine coverage in women at any point before they gave birth increased as more women became eligible for vaccination. In November 2021, 48.8% of women giving birth had received at least one dose of vaccine before they delivered. This increased to 53.9% of women who gave birth in December 2021, to 73.1% of women delivering by May 2022 where it stabilised with small increases to 75.1% in October 2022 (see <u>Table 9</u>). Of women who gave birth in December 2021, 43.5% had received 2 doses of the vaccine before they gave birth increasing to 66.9% of women giving birth in May 2022 and 70.1% of women who gave birth in

October 2022. By December 2022 most first, second and third doses of vaccine given to women who gave birth were administered before the start of their pregnancy (<u>Figure 1</u>).

A small proportion of women who gave birth in September (0.4%), October (6.0%), November (12.9%) and December (15.5%) 2022 had received their autumn booster dose prior to delivery. This is expected to continue to increase as more women eligible for the booster give birth over the coming months.

In the 23-month period between January 2021 and December 2022, a total of 972,766 women gave birth with linked records on vaccination status for 968,882 (99.6%) of them. Of women with linked records who gave birth over this period, 426,482 (44.0%) were known to have received at least one dose of COVID-19 vaccine prior to delivery, 365,915 (37.8%) received at least 2 doses, 111,056 (11.5%) women had received at least 3 doses and 1179 (0.1%) women received at least 4 doses but not all would have been eligible during their pregnancy.





There were 285,281 women who received their first dose prior to pregnancy and went on to conceive and deliver by December 2022. Of the 12,975 autumn boost doses administered to women who delivered between September and December, 6,593 were the Moderna bivalent vaccine and 6,382 were the Pfizer bivalent vaccine.

Table 9. Vaccine coverage in women giving birth from September 2022 (when the autumn
boost was first offered), by month of delivery ¹

Date	September 2022	October 2022	November 2022	December 2022
Women giving birth	38,435	39,022	37,007	36,602
1 or more doses by time of delivery	28,692 (74.7%)	29,314 (75.1%)	27,517 (74.4%)	26,709 (73.0%)
2 or more doses by time of delivery	26,708 (69.5%)	27,369 (70.1%)	25,670 (69.4%)	24,931 (68.1%)
3 or more doses by time of delivery	6,997 (18.2%)	2,431 (6.2%)	1,135 (3.1%)	0,828 (2.3%)
Autumn boost by time of delivery	161 (0.4%)	2,347 (6.0%)	4,780 (12.9%)	5,687 (15.5%)
Unvaccinated at delivery	9,576 (24.9%)	9,519 (24.4%)	9,290 (25.1%)	9,673 (26.4%)
Women who received autumn boost after delivery to 31 March 2023	2,433 (6.3%)	1,439 (3.7%)	428 (1.2%)	90 (0.2%)

Methods

Data on COVID-19 vaccination status together with details of each vaccine administered is recorded in a central data set called the NIMS². In addition, NHS Digital manages the Hospital Episode Statistics (HES) data sets, containing information about hospital activity in England.

Records of women giving birth ('delivery records') in the months since 1 January 2021 were identified in HES. De-duplication of delivery records resulted in a data set of women who had given birth with one record per woman, identified by her NHS Number, and the latest 'delivery episode' associated with her.

An 'earliest' and 'latest' likely pregnancy start date were assigned to each woman's record, using the known delivery date and further information from her record, where available:

¹ In this period 776 women could not be matched with a NIMS record. Their vaccine status is therefore unknown and they are excluded from these coverage figures.

² NIMS Data controllers are NHSEI and NHSD. The NIMS IT software is commissioned by NHSEI via South Central West CSU and is provided by the System C and Graphnet Care Alliance.

- Where a valid gestational age was recorded (GESTAT_1 between 24 and 42), the woman's earliest pregnancy start date was calculated by taking the number of weeks away from the delivery date, and then calculating an additional earlier week, to account for GESTAT_1 recording completed weeks of pregnancy. In a similar way, latest pregnancy start date was calculated by taking the number of weeks of GESTAT_1 away from the delivery date.
- 2. Where no valid GESTAT_1 was available, the first 12 diagnostic codes were examined to identify any with a code suggesting delivery at term (O60.2). In this case, the gestational age at delivery was assumed to be between 37 and 42 completed weeks of pregnancy, and a similar method was used to establish earliest and latest pregnancy start dates.
- 3. Where no valid GESTAT_1 was available and there were no codes suggesting term delivery, the first 12 diagnoses codes were examined to identify any suggesting preterm delivery (O60.1 or O60.3). In this case, the gestational age at delivery was assumed to be between 24 and 36 completed weeks of pregnancy, and these values were used to establish earliest and latest pregnancy start dates.
- 4. In the absence of any additional information in the woman's record (or in conflicting cases where diagnostic codes suggesting both term and pre-term delivery appeared in the same record), the gestational age at delivery was assumed to be between 24 and 42 completed weeks of pregnancy, and these values were used to establish earliest and latest pregnancy start dates.

Earliest and latest dates for the start of each trimester were established in a similar way, using the windows of trimester 1: day 0 to day 97 (where day 0 is the earliest or latest pregnancy start date, as established using the method above), trimester 2: day 98 to day 195 and trimester 3: day 196 to delivery. Each woman's delivery record was linked to her record(s) in the NIMS using the NHS Number, establishing her vaccine status as either having had one or more doses before delivery (including any prior to becoming pregnant) or not having had any doses of the vaccine prior to delivery, using the NIMS vaccine records. For a woman to be identified as having had the autumn booster dose bivalent vaccine was recorded in NIMS on or after 1 September 2022.

Dose administered pre-pregnancy	Dose administered before the earliest pregnancy start date
Dose administered in pregnancy	Dose administered after the latest pregnancy start date and before the delivery date
Dose administered post- pregnancy	Dose administered on or after the delivery date based on NIMS records extracted on 28 February 2023

For each vaccine dose (this analysis considered doses 1 to 4) the woman was known to have received, the following information was ascertained:

Dose in pregnancy: unknown	Dose administered around the start or pregnancy: after the earliest pregnancy start date and before the latest pregnancy start date
Unvaccinated	No vaccine records exist for the woman, based on NHS number

And the following information a	about trimester:
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Dose administered pre-pregnancy	Dose administered before the earliest pregnancy start date
Dose administered in trimester 1	Dose administered after the latest pregnancy start date and before the earliest pregnancy start date +97 days
Dose administered in trimester 2	Dose administered after the latest pregnancy start date +98 days and before the earliest pregnancy start date +195 days
Dose administered in trimester 3	Dose administered after the latest pregnancy start date + 196 days and before the delivery date
Dose administered post-pregnancy	Dose administered on or after the delivery date based on NIMS records extracted on 28 February 2023
Dose in trimester unknown	Dose administered in the 'gap' between trimesters, because of inaccuracy in establishing pregnancy start date
Unvaccinated	No vaccine records exist for the woman, based on NHS number

The ethnicity, residence and age information when used is taken from the NIMS record. The analysis within this section was carried out on 21 March 2023. The latest HES data available was for December 2022, and all HES data since April 2021 is considered provisional.

Interpretation and limitations

Previously published findings have supported vaccine safety in pregnancy from COVID-19 vaccine surveillance reports from week 47 2021 onwards <u>COVID-19 vaccine weekly</u> <u>surveillance reports (weeks 39 to 40, 2021 to 2022)</u> and from analyses published by Public Health Scotland <u>Outputs and information for the public – the University of Edinburgh</u>.

More detailed statistical analyses are planned (see <u>COVID-19 vaccination in pregnancy</u> <u>surveillance protocol</u>). There are recognised limitations of the data sets including the level of completeness of the relevant fields. Adverse pregnancy outcomes considered in earlier reports are routinely reported as official statistics annually by ONS, (see <u>Coronavirus (COVID-19)</u> <u>hospital admissions by vaccination and pregnancy status, England</u>), however HES data was used to monitor outcomes more quickly than ONS data allows.

Main findings

COVID-19 vaccination is the safest and most effective way for women to protect themselves and their pregnancies against severe COVID-19 disease. The JCVI has advised that women who are pregnant are in a clinical risk group within the COVID-19 vaccine programme. Unvaccinated women who become pregnant are strongly encouraged to come forward for vaccination. Women who are pregnant and have previously been vaccinated should have been offered a booster dose this autumn (Joint Committee on Vaccination and Immunisation (JCVI) updated statement on the COVID-19 vaccination programme for autumn 2022).

COVID-19 vaccine coverage in pregnant women at delivery increased as more women have become eligible for vaccination, stabilising from May 2022. Of women who gave birth in December 2022 73.0% had received one or more dose before their baby was born. In Scotland, 78% of the women delivering in July 2022 had received at least one dose of COVID-19 vaccine prior to delivery, with 73% having received at least 2 doses and 48% having received at least 3 doses (41). In Wales estimated coverage at time of delivery for 2,018 women with delivery dates during July 2022 was 81% for at least one dose, 77% for at least 2 doses and 45% for at least one booster dose (data provided by Public Health Wales). This is the second report that includes coverage data for women who received the COVID-19 autumn boost vaccination before giving birth in England between September and December 2022 with 15.5% who gave birth in December 2022 receiving this vaccine before they gave birth. In Wales the estimated coverage for women who were pregnant as of 1 February 2023 was 10.7% (95% CI 10.8 to 11.9%) for the autumn 2022 booster (data provided by Public Health Wales). Outcome data and further break down of coverage data will be generated for the autumn boost when further vaccinated pregnancies have accumulated.

Vaccine impact on proportion of population with antibodies to COVID-19

Seroprevalence

The results from testing samples provided by healthy adult blood donors aged 17 years and older, supplied by the NHS Blood and Transplant (NHS BT collection) between weeks 35 2020 and week 11 2023 are summarised. As of week 44 2020, approximately 250 samples from each geographic NHS region are tested each week.

The COVID-19 vaccination campaign began on 8 December 2020 (week 50) with a phased roll out by age and risk group. From the beginning of September 2021, a third dose was offered to individuals with severe immunosuppression. A booster dose was introduced from 16 September 2021 for individuals aged 50 years and over, frontline health and social care staff, individuals aged 16 to 49 with certain underlying health conditions and household contacts of immunosuppressed individuals.

Eligibility for booster doses was extended to individuals aged 40 years and over from 22 November and from December to those aged 18 to 39 in a phased rollout by age group. Booster doses are generally given at least 6 months after the second dose, although the minimum interval was reduced to at least 3 months from the second or third dose in an effort to accelerate the roll out with the emergence of the Omicron variant. A second booster (spring booster) was introduced from 21 March 2022 for individuals aged 75 years and older, older residents in care homes and individuals with severe immunosuppression. The spring booster was offered 3 to 6 months after the last dose. An autumn booster was introduced from 7 September 2022 for individuals aged 50 years and over, those in care homes, individuals aged 5 years and over in clinical risk groups, frontline health and social care staff, those who care for vulnerable individuals and families of individuals with weakened immune systems, with those at highest risk being vaccinated first. The autumn booster is offered at least 3 months after the last dose.

Please note that this section will be updated monthly. This update was published on 6 April 2023.

Seroprevalence in blood donors aged 17 years and older

The results presented here are based on testing samples with Roche nucleoprotein (N) and Roche spike (S) antibody assays.

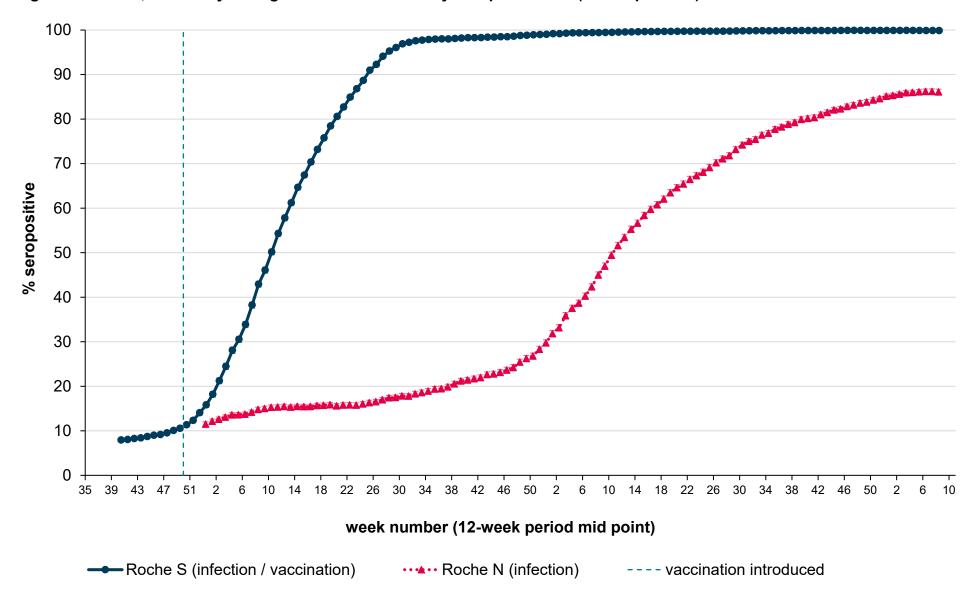
Nucleoprotein (Roche N) assays only detect post-infection antibodies, whereas spike (Roche S) assays will detect both post-infection antibodies and vaccine-induced antibodies. Thus, changes in seropositivity for the Roche N assay reflect the effect of natural infection. Increases in seropositivity as measured by S antibody reflect both infection and vaccination. Antibody responses to both targets reflect infection or vaccination occurring at least 2 to 3 weeks previously given the time taken to generate a COVID-19 antibody response. Currently donors are asked to defer donations for at least 48 hours post vaccination (previously 7 days), and for at least 10 full days after a positive COVID-19 test as well as 7 days following resolution of any symptoms (previously 28 days, changes were implemented during January 2022).

This report presents Roche N and Roche S seropositivity estimates on the same set of samples, using a 12-week rolling prevalence for national, age group and regional estimates. Seropositivity estimates are plotted using the mid-point of a 12-weekly rolling period that reduces to 8 weeks in the most recent weeks to allow for a more representative current estimate of seropositivity. However, this also means the data will reflect seroprevalence several weeks previously. Seroprevalence estimates reported are based on seropositivity which are unadjusted for the sensitivity and specificity of the assays used.

National prevalence

Overall population weighted (by age group, sex and NHS region) antibody prevalence among blood donors aged 17 years and older in England was 86.1 % (95% CI 85.4% to 86.7%) using the Roche N assay and 99.9% (95% CI 99.8% to 99.9%) using the Roche S assay for the period 25 January to 17 March 2023 (week 4 to week 11 2023). 12,548 out of 14,575 were Roche N positive and 14,558 out of 14,575 samples were Roche S positive. This compares with 83.6% (95% CI 83.0% to 84.2%) Roche N seropositivity and 99.9% (95% CI 99.8% to 99.9%) Roche S seropositivity for the period of 26 October 2022 to 20 January 2023 (weeks 43 2022 to week 3 2023).

Seropositivity (weighted by region, age group and sex) varies over time. Figure 2 shows the overall 12-weekly rolling proportion seropositive over time for the Roche N and Roche S assays. Seropositivity estimates are plotted weekly using the mid-point of a rolling 12-weekly period.

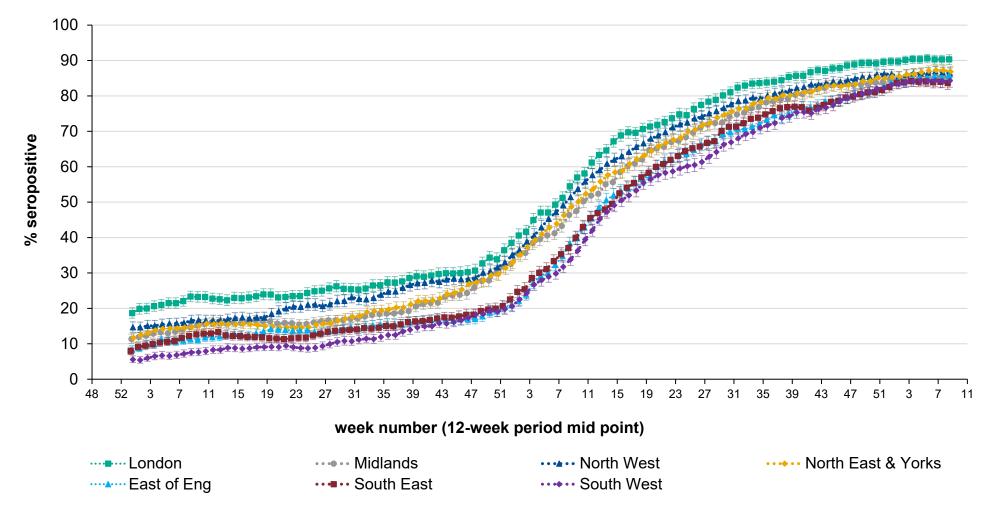




Regional prevalence of infection over time

Seropositivity (weighted by age group and sex) using the Roche N assay which detects infection only, varies by region (Figure 3).

Figure 3. 12-weekly rolling SARS-CoV-2 antibody seroprevalence (% seropositive) in blood donors by region, using Roche N test; error bars show 95% confidence intervals



NHS region	Weeks 43 2022 to 3 2023	Weeks 4 to 11 2023
East of England	80.8% (79.1% to 82.3%)	85.8% (84.1% to 87.3%)
London	89.3% (88.0% to 90.4%)	90.3% (88.8% to 91.6%)
Midlands	83.2% (81.7% to 84.6%)	85.0% (83.2% to 86.6%)
North East and Yorkshire	84.2% (82.5% to 85.7%)	86.8% (85.1% to 88.4%)
North West	85.3% (83.8% to 86.7%)	86.3% (84.5% to 87.9%)
South East	80.5% (78.9% to 82.0%)	83.6% (81.8% to 85.3%)
South West	80.6% (79.1% to 82.1%)	84.3% (82.4% to 86.0%)

Table 10. Roche N seropositivity (95%CI) estimates by NHS region

Increases in Roche N seropositivity have recently been observed across all regions (Table 10) compared to the previous 12-week period with the largest increases in the East of England and South West regions.

The difference in seropositivity by region has narrowed over time. Seropositivity was previously lowest in the South West, but was recently surpassed by the South East. The highest seropositivity has consistently been observed in London, closely followed by the North West, but in recent weeks the North West has been surpassed by the North East and Yorkshire.

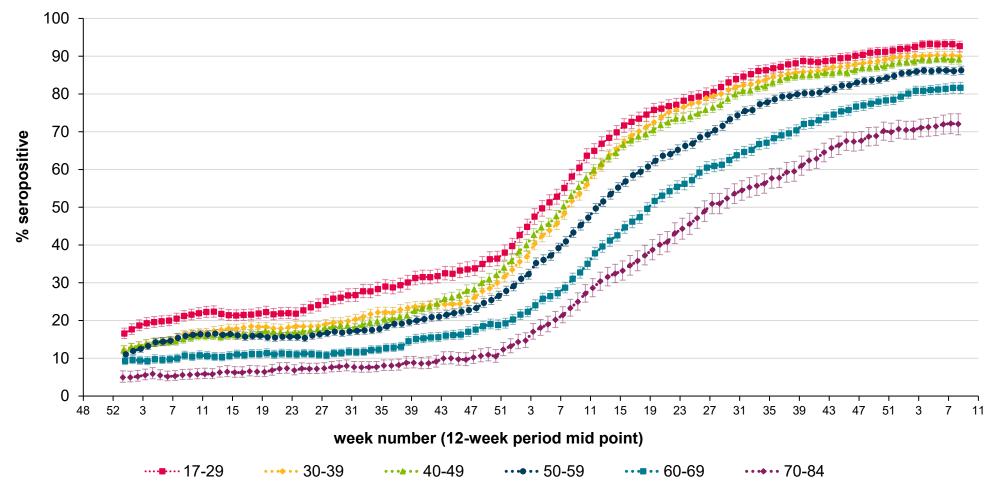
Overall COVID-19 case rates through Pillar 1 have decreased or remained stable across most regions. Overall, Pillar 1 positivity remained stable compared to the previous week. (Weekly national Influenza and COVID-19 surveillance report week 13 2023).

Pillar 1 testing is undertaken by NHS hospitals and UKHSA labs for those with a clinical need and some health and social care workers. <u>Testing recommendations</u> have been updated and routine asymptomatic testing through NHS settings has been paused since the end of August 2022, which will have an impact on Pillar 1 case rates and positivity rates. Changes in testing practices is likely to influence a range of surveillance indicators highlighting the importance of maintaining the serosurveillance programme to provide consistent data on exposure to infection and vaccine impact in the population over time.

Prevalence by age group

Seropositivity estimates by age group using the Roche N assay are presented below.

Figure 4. Population weighted 12-weekly rolling SARS-CoV-2 antibody seroprevalence (% seropositive) in blood donors from the Roche N assay by age group



Based on testing samples using the Roche N assay (<u>Figure 4</u>) as a marker of infection, the highest seropositivity continues to be observed in those aged 17 to 29 and the lowest in those aged 70 to 84.

Age group	Weeks 43 2022 to 3 2023	Weeks 4 to 11 2023
17 to 29	90.9% (89.6% to 92.2%)	92.7% (91.2% to 94.0%)
30 to 39	88.5% (87.5% to 89.5%)	90.0% (88.8% to 91.1%)
40 to 49	87.0% (85.9% to 88.0%)	89.2% (87.9% to 90.3%)
50 to 59	83.6% (82.6% to 84.6%)	86.3% (85.1% to 87.3%)
60 to 69	77.4% (76.1% to 78.7%)	81.6% (80.1% to 83.1%)
70 to 84	68.7% (66.2% to 71.1%)	72.0% (69.2% to 74.7%)

Table 11. Roche N seropositivity (95%CI) estimates by age group

Increases in N seropositivity have recently been observed across all age groups (Table 11) compared to the previous 12-week period. In the most recent period, the largest increase in seropositivity was observed in individuals aged 60 to 69 years and 70 to 84 years.

In England, Pillar 1 COVID-19 case rates for week 12 2023, decreased or remained stable across most age groups with the highest rates currently seen in individuals aged 70 years and older (Weekly national Influenza and COVID-19 surveillance report week 13 2023).

Roche S seropositivity in blood donors has plateaued and is now over 99% across all age groups. Seropositivity estimates for S antibody in blood donors are likely to be higher than would be expected in the general population and this probably reflects the fact that donors are more likely to be vaccinated. Seropositivity estimates for N antibody will underestimate the proportion of the population previously infected due to (i) waning of the N antibody response over time and (ii) observations from UKHSA surveillance data that N antibody levels are lower in individuals who acquire infection following vaccination. These lower N antibody responses in individuals with breakthrough infections (post-vaccination) compared to primary infection likely reflect the shorter and milder infections in these patients. Patients with breakthrough infections do have significant increases in S antibody levels consistent with boosting of their antibody levels.

Vaccination has made an important contribution to the overall Roche S increases observed since the roll out of the vaccination programme. The impact of the booster vaccination programmes can be assessed by monitoring Roche S antibody levels across the population over time.

Roche S levels by age group and month

The Roche S assay that the UKHSA uses for serological surveillance is fully quantitative, meaning that it measures the level of antibodies in a blood sample; an antibody level above 0.8

au/ml (approximately 1 IU/ml using the WHO standard) is deemed positive. The UKHSA surveillance since autumn 2021 has found that over 99% of the population of blood donors test positive for S-antibodies, which may have resulted from either COVID-19 infection or vaccination. With such high seropositivity, it is important to look at population antibody levels in order to assess the impact of the vaccination booster programmes.

Figure 5 shows monthly categorised Roche S levels in N-antibody negative individuals by age group over the past year. After high antibody levels following the rollout of the accelerated booster programme due to the emergence of the Omicron variant in late 2021, the decreasing profile of antibody levels among 17 to 69 year olds from April through to August shows signs of waning. From April 2022 the proportion of donors, aged 70 to 84 years, with very high antibody levels of 25,000+ au/ml increased following the introduction of the spring booster for ages 75 and older. Antibody levels in this older age group have remained consistent from May to September 2022. A further increase in highest antibody levels can be seen in October following the autumn booster in those aged 40 to 84, with the highest increase seen in those aged 70 to 84. In November 2022 the proportion of donors aged 70 to 84 with very high antibody levels of 25,000+ au/ml remained high, and the proportion of donors aged 50 to 69 years with very high antibody levels of 25,000+ au/ml remained high, and the proportion of donors, aged 50 to 69 years with very high antibody levels of 25,000+ au/ml remained high, and the proportion of donors, aged 50 to 69 years with very high antibody levels of 25,000+ au/ml remained high, and the proportion of donors, aged 50 to 69 years with very high antibody levels of 25,000+ au/ml remained high, and the proportion of donors, aged 50 to 69 years with very high antibody levels of 25,000+ au/ml remained high, and the proportion of donors, aged 50 to 69 years with very high antibody levels of 25,000+ au/ml decreased.

By the end of week 10 2023, 65.7% of all individuals aged 50 years and older had been vaccinated with an autumn booster dose (<u>Weekly national Influenza and COVID-19 surveillance</u> report week 13 2023).

Figure 6 shows categorised Roche S levels in N-antibody positive individuals, those likely to have experienced past infection. Pre-vaccination antibody levels will be influenced by time since infection, variant and severity of infection, as well as individual factors such as underlying health conditions and age. Since April 2022 the proportion of donors with very high antibody levels of 25,000+ au/ml decreased across all age groups except for those aged 70 to 84 where increases were observed in April and May 2022; however, decreases were observed between June and September 2022. Increases of the highest antibody levels are being seen across those aged 60 to 84 in October following rollout of the autumn booster. In those aged 17 to 59 very little change has been observed between June and October 2022. In November 2022 increases in the proportion of donors with very high antibody levels of 25,000+ au/ml continued to be observed in donors aged 50 to 84 years. Since January 2023 decreases were seen in the proportion of donors, aged between 50 to 84 years, with very high antibody levels of 25,000+ au/ml.

Comparing Figure 5 with Figure 6, the overall higher profile of antibody levels in those who have experienced past infection is evident; both vaccination post infection and breakthrough infection following vaccination are expected to boost existing antibody levels. Whilst it is thought that there is no threshold antibody level that offers complete protection against infection, higher antibody levels are likely to be associated with lower probability of infection.



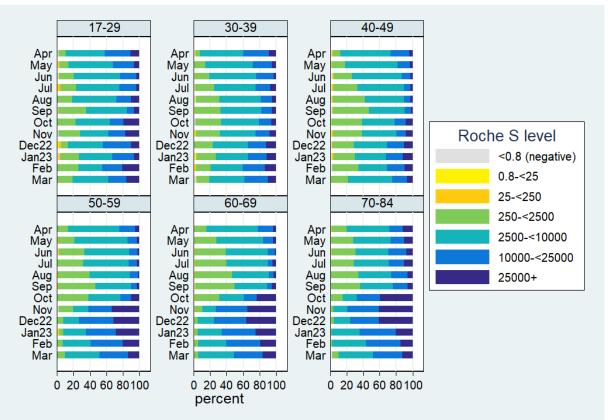
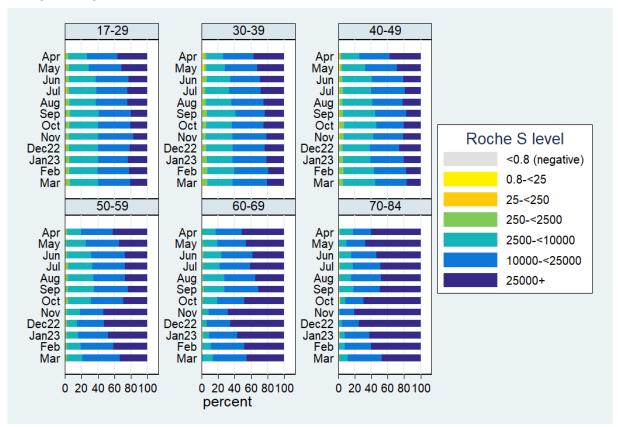


Figure 6. Categorised Roche S antibody levels by age group and month in N positive samples, April 2022 to March 2023



SARI-Watch surveillance data

SARI-Watch is a national surveillance system in England that captures aggregate and individual data on laboratory confirmed COVID-19 hospitalisations (to all level of care) and ICU or HDU admissions. The individual level data is based on hospitalisations for laboratory confirmed COVID-19 submitted by a sentinel network of acute NHS trusts.

The analyses presented are based on individual level data from the sentinel collection in England. The analysis uses data from 1 September 2022 to 26 March 2023 inclusive submitted by 10 acute NHS trusts. 1 September was the official roll out of the autumn 2022 booster campaign. The data was up to 26 February 2023 as this was last date of ISO week 12 2023. To obtain vaccine history for admitted persons, the SARI-Watch data was linked to the NIMS on 4 April 2023 using key personal identifiers. NIMS captures data on vaccination history of people in England. Data on vaccination history was used to group admissions into 4 categories. Please note that vaccination status on admission does not represent VE against hospitalisation. Vaccination is highly protective against hospitalisation as VE studies show (see vaccine effectiveness section in this report) but does not completely eliminate the risk of being hospitalised. Hence those that get hospitalised even if vaccinated tend to be the vulnerable elderly population or those with significant underlying health issues. Other caveats are that London trusts are currently under-represented in sentinel data and the most recent data is typically subject to retrospective updates after submission.

Vaccination status by time of admission by age group

Vaccination status on hospital admission was grouped into 4 categories:

- 'Unvaccinated' no evidence of previous vaccination at the time of admission
- 'D1' comprising only 1 dose of the primary course by the time of admission
- 'D2' comprising only 2 doses of the primary course by the time of admission
- 'D3 comprising 3 doses or more by the time of admission; this includes 3 doses of primary course only or 2 doses of the primary course plus any or all of the boosters (either autumn 2021, spring 2022 or autumn 2022 booster)

The unlinked group represents hospitalised cases that could not be matched to NIMS data either due to incorrect or missing personal identifiers. This accounted for <1% of data in the 1 September 2022 to 26 March 2023 period.

<u>Table 12</u> shows vaccination status by the time of admission and age group among admitted cases from 1 September 2022 to 26 March 2023 inclusive (n=7,201 admissions).

Those aged 75 years or more had the lowest proportion that were unvaccinated by the time of admission at 3.2% in this period. The highest proportion that were unvaccinated by time of admission was in <40 years at 53.1% (Table 12).

Those in the category '≥3 doses' by time of admission accounted for 92.8% of admitted cases aged 75 years or more (Table 12). This compares with 26.8% in those aged <40 years.

Age group	Data type	Unvaccinated	1 dose (primary)	3 doses (primary)	≥3 doses	Unlinked	Total
Under 40	Number	339	23	99	171	7	639
	%	53.1	3.6	15.5	26.8	1.1	
40 to 49	Number	34	11	49	135	4	233
	%	14.6	4.7	21	57.9	1.7	
50 to 64	Number	91	35	78	612	2	818
	%	11.1	4.3	9.5	74.8	0.2	
65 to 74	Number	75	19	75	982	6	1,157
	%	6.5	1.6	6.5	84.9	0.5	
Over 75	Number	139	32	132	4,041	10	4,354
	%	3.2	0.7	3	92.8	0.2	

 Table 12. Vaccination status at time of admission by age group for admissions from 1

 September 2022 to 26 March 2023, sentinel data, England

Rate of hospitalisation for COVID-19 in vaccinated people by time since vaccination (any dose) and age group

Using linked sentinel data, admissions from 27 February to 26 March 2023 inclusive were analysed as this represented 4 weeks mostly covering March 2023 (ISO weeks 9 to 12). This period will match the ISO week system used in the mandatory aggregate collection (ISO weeks 9 to 12 2023, used in second step of the calculation – see next paragraph). In this time period 9 sentinel acute NHS trusts contributed data. Time since last vaccination at the time of admission was calculated based on time in days between the last vaccination and hospital admission date. The last vaccination is irrespective of any dose whether from the primary or the booster schedule. The interval for each admitted case was grouped into <6 months, 6 to under 9

months, 9 to under 12 months and 12 months and over since last vaccination. Each month comprises 30 days. The proportion falling in each interval was calculated per age group.

The proportion by time since last vaccination and age group obtained from sentinel data was then applied to the corresponding age group for cases from the aggregate collection. Cases from the aggregate collection was used as this is a mandatory surveillance system based on wider national reporting. The mandatory surveillance is based on weekly data (based on ISO week system from Monday to Sunday). The last 4 weeks available in 2023 were used from the aggregate data (ISO weeks 9 to 12). Due to mean 70% trust coverage in the period of study (27 February to 26 March 2023 inclusive) in the aggregate collection, a corrective factor was applied to the second step of the calculation. The second step is where the proportions by age group and time since vaccination from sentinel data are applied to the cases from the aggregate collection in same age group. The corrective factor would approximate the true total cases if there was 100% trust coverage.

To estimate rates of hospitalisation among vaccinated people by time since last vaccination and age group, the NIMS denominator is needed. Using NIMS data, the time since last vaccination in days was calculated from vaccination date (any dose) capped to 26 March 2023. The time in days was grouped in the same intervals described. The same age and/time since vaccination groups are used for SARI-Watch and NIMS, with the former being the numerator and latter being the denominator. The rate of hospitalisation is calculated for each age/time since last vaccination group, expressed as hospitalised cases in the study period (27 February to 26 March 2023) per 100,000 vaccinated people in England.

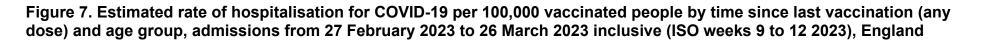
Figure 7 shows that the highest hospitalisation rates were in those aged 75 years and over for every time since last vaccination interval compared to corresponding intervals in other age groups. Usually, the lowest rate of hospitalisation has been in those vaccinated in the 6 months prior to hospitalisation as shown in previous reports. However, in this latest analysis, the rate of hospitalisation is seen in the shortest interval (vaccinated in the 6 months prior to vaccination) for most age groups. This is due to 2 reasons: an increase in cases reported via the individual case and mandatory aggregate level surveillance systems. The latter scheme showed an increase in the hospitalisation rate over this 4-week period peaking in ISO week 11 2023 (13 to 19 March inclusive), affecting people aged 75 years or more mainly. This increase coincided with ongoing increases in Omicron sublineages XBB.1.5, XBB and C.H.1.1. The second reason why the hospitalisation rate was highest in the shortest vaccination interval is that the cohort in this interval (the denominator for the rate per vaccinated) has decreased. At this stage of the vaccination campaign, most people have already received the autumn 2022 booster and shifted to the next vaccination interval.

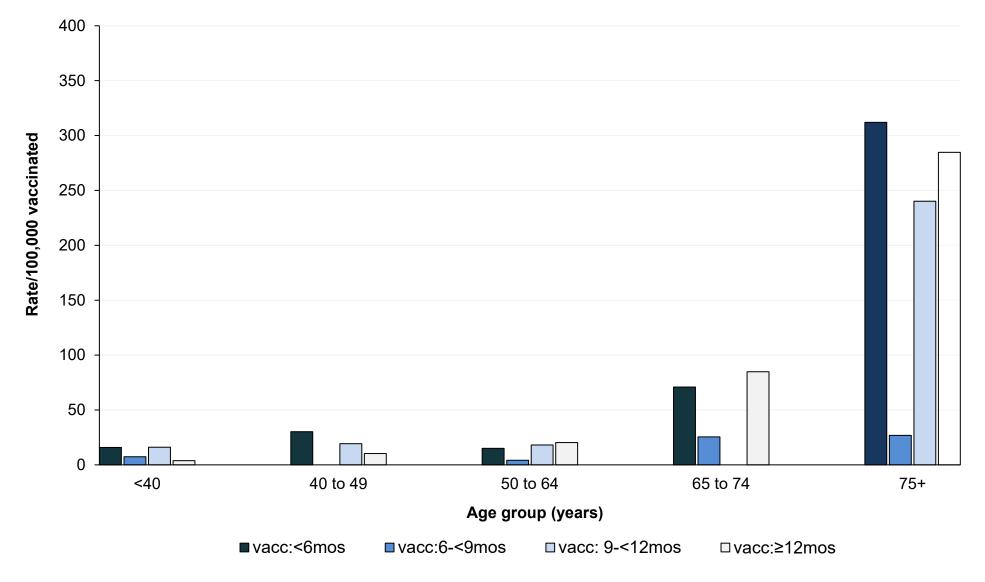
For example, among people aged 75 years or more, the hospitalisation rate was highest in the shortest interval of <6 months (312.0/100,000). This rate increased since the previous report due to reasons explained above: this interval coinciding with increases in Omicron sublineages. This in turn contributed to increases in hospitalisations in the 4-week period (based on aggregate level data from the mandatory surveillance system). Also, the NIMS data showed that

nationally 51.4% (2,796,567/5,438,723) of people aged 75 years or more had their last vaccination within 6 months of 26 March 2023. In the previous report this was 83.1%. The rate/100,000 vaccinated dropped in subsequent intervals but a gradient is observed among these 3 intervals that is the rate increased as the time since last vaccination interval increased.

The rates in younger age groups were much lower and declined with age reflecting progressively lower risk of hospitalisation. However, as in the 75 years and over analysis the lowest rate was not in the shortest interval (vaccinated <6 months) for those aged 65 to 74 years using the latest linked data. This is due to the 2 reasons as described: an increase in cases in the latest period and a decrease in NIMS denominator for the shortest vaccination interval. For this age group, the population level vaccination coverage was 57.3% (3,314,551/5,782,599) for those who had their last vaccination (any dose) within 6 months of 26 March 2023. This is a decrease from 75.7% in the last report for the same vaccination interval. However, we see a gradient in the subsequent intervals with the highest rate in the longest interval (84.8/100,000). Note there were no admitted cases reported for the 9 to <12 months interval based on the individual level linked data.

The rates in <40, 40 to 49 and 50 to 64 years requires careful interpretation as the time since last vaccination percentages derived from linked data were based on small volumes for the period under study. As seen in previous reports, for people aged <40 years for example, the rate was highest in the <6 months interval (15.8/100,000). It is possible that the clinical risk factors that make younger adults eligible for the autumn 2022 booster vaccination may also make them more pre-disposed to hospital admissions than the general age-matched population. For example, patients with immunosuppression in whom the vaccine <u>may be less effective</u>. The combined effect of these factors may have elevated the risk in the shortest interval.





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