

COVID-19 vaccine surveillance report

Week 1

6 January 2022

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Executive summary

Four coronavirus (COVID-19) vaccines have now been approved for use in the UK. Rigorous clinical trials have been undertaken to understand the immune response, safety profile and efficacy of these vaccines 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 COVID-19: vaccine surveillance strategy (1). As with all vaccines, the safety of COVID-19 vaccines is continuously being monitored by the MHRA. They conclude that overall, the benefits of COVID-19 vaccines outweigh any potential risks (2).

Vaccine effectiveness

Several studies of vaccine effectiveness have been conducted in the UK which indicate that 2 doses of vaccine are between 65 and 95% effective at preventing symptomatic disease with COVID-19 with the Delta variant, with higher levels of protection against severe disease including hospitalisation and death. There is some evidence of waning of protection against infection and symptomatic disease over time, though protection against severe disease remains high in most groups at least 5 months after the second dose.

Population impact

The impact of the vaccination programme on the population is assessed by taking into account vaccine coverage, evidence on vaccine effectiveness and the latest COVID-19 disease surveillance indicators.

Vaccine coverage tells us about the proportion of the population that have received 1, 2 and 3 doses of COVID-19 vaccines. By 2 January 2022, the overall vaccine uptake in England for dose 1 was 68.6% and for dose 2 was 63.1%. Overall vaccine uptake in England in people with at least 3 doses was 45.6%. In line with the programme rollout, coverage is highest in the oldest age groups.

We present data on COVID-19 cases, hospitalisations and deaths by vaccination status. **This** raw data should not be used to estimate vaccine effectiveness as the data does not take into account inherent biases present such as differences in risk, behaviour and testing in the vaccinated and unvaccinated populations. Vaccine effectiveness is measured in other ways as detailed in the 'Vaccine Effectiveness' section.

Based on antibody testing of blood donors, 98.4% of the adult population now have antibodies to COVID-19 from either infection or vaccination compared to 22.7% that have antibodies from infection alone.

Vaccine effectiveness

Large clinical trials have been undertaken for each of the COVID-19 vaccines approved in the UK which found that they are highly efficacious at preventing symptomatic disease in the populations that were studied. The clinical trials have been designed to be able to assess the efficacy of the vaccine against laboratory confirmed symptomatic disease with a relatively short follow up period so that effective vaccines can be introduced as rapidly as possible.

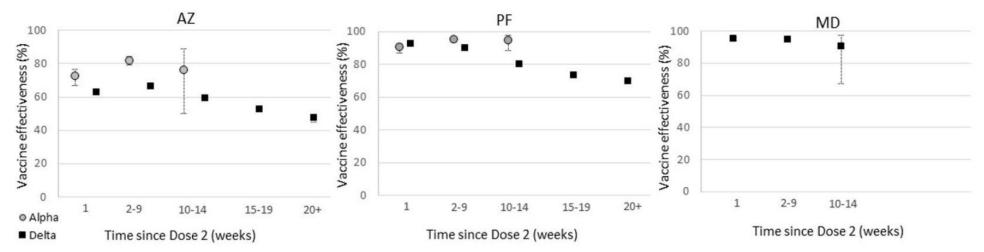
Nevertheless, understanding the effectiveness against different outcomes (such as severe disease and onwards transmission), effectiveness in different subgroups of the population and understanding the duration of protection are equally important in decision making around which vaccines should be implemented as the programme evolves, who they should be offered to and whether booster doses are required.

Vaccine effectiveness is estimated by comparing rates of disease in vaccinated individuals to rates in unvaccinated individuals. Below we outline the latest real-world evidence on vaccine effectiveness from studies in UK populations. We focus on data related to the Delta variant which is currently dominant in the UK. The findings are also summarised in <u>Table 1</u>.

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 Infection Survey and GP electronic health record data. After 2 doses, observed vaccine effectiveness against symptomatic disease with the Delta variant reaches approximately 65 to 70% with AstraZeneca Vaxzevria and 80 to 95% with Pfizer-BioNTech Comirnaty and Moderna Spikevax (3, 4) Vaccine effectiveness is generally slightly higher in younger compared to older age groups. With both Vaxzevria and Comirnaty, there is evidence of waning of protection over time, most notably among older adults. There is not yet enough follow-up with Spikevax to assess waning (Figures 1 and 3).

Figure 1. Vaccine effectiveness against Delta symptomatic disease among individuals aged over 16, with 2 doses of Vaxzevria (AZ), Comirnaty (PF) or Spikevax (MD) in England and 95% confidence intervals

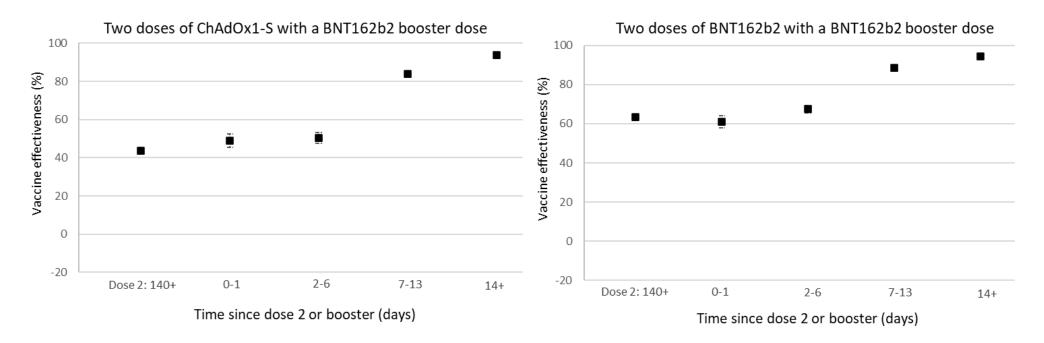


Data (based primarily on the Alpha variant) suggests that in most clinical risk groups, immune response to vaccination is maintained and high levels of VE are seen with both the Pfizer and AstraZeneca vaccines. Reduced antibody response and vaccine effectiveness were seen after 1 dose of vaccine among the immunosuppressed group, however, after a second dose the reduction in vaccine effectiveness is

smaller (5). Analyses by dosing interval suggest that immune response to vaccination and vaccine effectiveness against symptomatic disease improves with a longer (greater than 6 week interval) compared to a shorter interval of 3 to 4 weeks (Figure 1, 6, 3).

Data on booster vaccination in adults aged 50 years and older indicates that after a booster dose of the Pfizer-BioNTech vaccine, vaccine effectiveness increases to 93.8% among those who received the AstraZeneca vaccine as their primary course and 94.3% among those who received the Pfizer-BioNtech vaccine as their primary course (<u>Figure 2</u>,7).

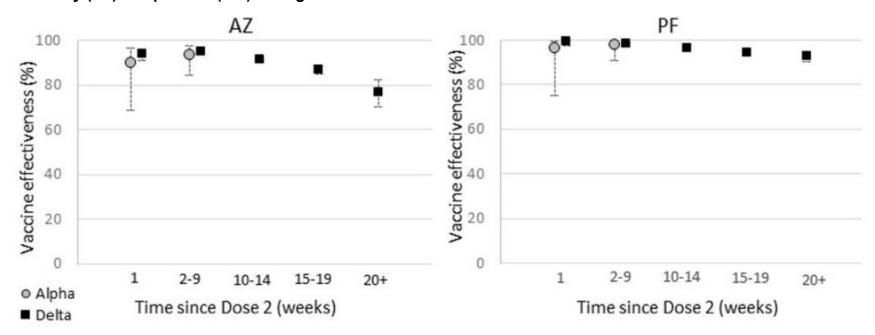
Figure 2. Vaccine Effectiveness estimates in time intervals post booster according to primary course: Unvaccinated baseline



Effectiveness against hospitalisation

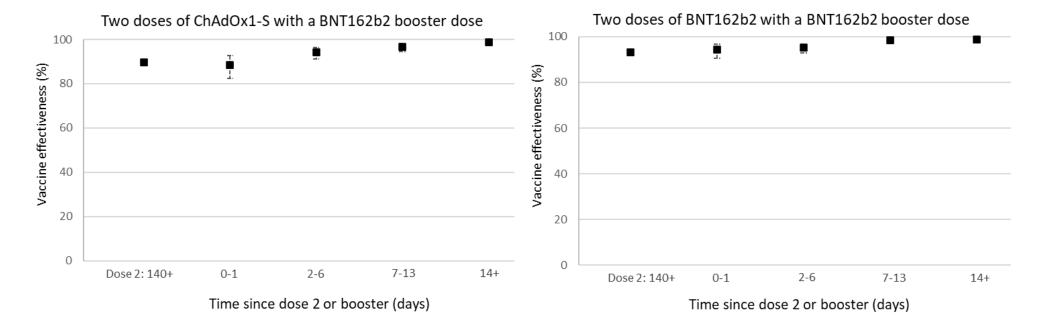
Several studies have estimated vaccine effectiveness against hospitalisation in older ages, all of which indicate higher levels of protection against hospitalisation with all vaccines against the Alpha variant (8, 9, 10, 11). Effectiveness against hospitalisation of over 90% is also observed with the Delta variant with all 3 vaccines (<u>Figure 3</u>, 3). In most groups there is relatively limited waning of protection against hospitalisation over a period of at least 5 months after the second dose. Greater waning appears to occur among those in clinical risk groups (<u>Figure 3</u>, 3).

Figure 3. Vaccine effectiveness against Delta hospitalisation among individuals aged over 16, with 2 doses of Vaxzevria (AZ), Comirnaty (PF) or Spikevax (MD) in England and 95% confidence intervals



Data on booster vaccination in adults aged 50 years and older indicates that after a booster dose of the Pfizer-BioNTech vaccine, vaccine effectiveness against hospitalisation increases to 98.8% among those who received either the AstraZeneca vaccine or the Pfizer vaccine as their primary course (Figure 4,7).

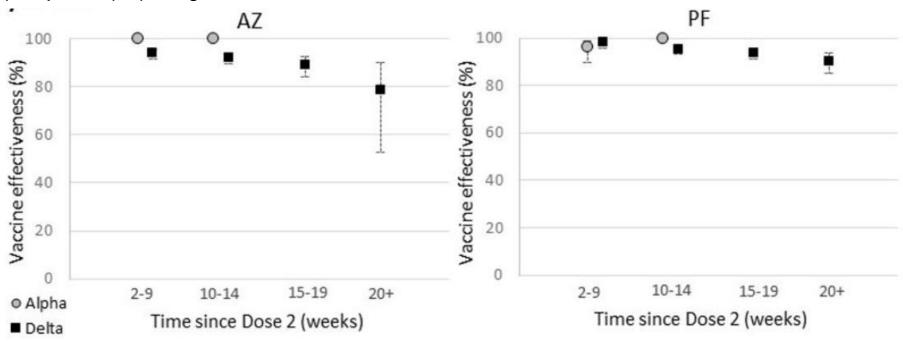
Figure 4. Vaccine Effectiveness estimates against hospitalisation in time intervals post booster according to primary course: Unvaccinated as baseline



Effectiveness against mortality

High levels of protection (over 90%) are also seen against mortality with all 3 vaccines and against both the Alpha and Delta variants (<u>Figure 5</u>, 8, 12, 3). Relatively limited waning of protection against mortality is seen over a period of at least 5 months.

Figure 5. Vaccine effectiveness against Delta death among individuals aged over 16, with 2 doses of Vaxzevria (AZ), Comirnaty (PF) or Spikevax (MD) in England and 95% confidence intervals



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 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 (13, 14, 15, 16). With the delta variant, vaccine effectiveness against infection has been estimated at around 65% with Vaxzevria and 80% with Comirnaty (4).

Effectiveness against transmission

As described above, several studies have provided evidence that vaccines are effective at preventing infection. Uninfected individuals cannot transmit. Therefore, the vaccines are also effective at preventing transmission. There may be 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). A household transmission study in England found that household contacts of cases vaccinated with a single dose had approximately 35 to 50% reduced risk of becoming a confirmed case of COVID-19. This study used routine testing data so would only include household contacts that developed symptoms and went on to request a test via pillar 2. It cannot exclude asymptomatic secondary cases or mildly symptomatic cases who chose not to request a COVID-19 test (17).

Data from Scotland has also shown that household contacts of vaccinated healthcare workers are at reduced risk of becoming a case, which is in line with the studies on infection (18). Both of these studies relate to a period when the Alpha variant dominated. An analysis from the ONS Community Infection Survey found that contacts of vaccinated index cases had around 65 to 80% reduced odds of testing positive with the Alpha variant and 35 to 65% reduced odds of testing positive with the Delta variant compare to contacts of unvaccinated index cases (19).

A summary of vaccine effectiveness evidence can be seen in <u>Table 1</u>.

Table 1. Summary of evidence on vaccine effectiveness against different outcomes Delta

	Vaccine effectiveness*			
Outcome	Pfizer-BioNTech Comirnaty	AstraZeneca Vaxzevria	Moderna Spikevax	
Infection	75-85%	60-70%		
Symptomatic disease	80-90%	65-75%	90-99%	
Hospitalisation	95-99%	90-99%	95-99%	
Mortality	90-99%	90-95%		

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 moderately level of uncertainty
Low Confidence	Little evidence is available at present and results are inconclusive

^{*} Estimates of initial vaccine effectiveness in the general population after a 2 dose course. This typically applies for at least the first 3 to 4 months after vaccination. For some outcomes there may be waning of effectiveness beyond this point.

Vaccine effectiveness against the Omicron variant

A test negative case control design was used to estimate vaccine effectiveness (VE) against symptomatic COVID-19 with the Omicron variant compared to the Delta variant. Here vaccination rates in PCR positive cases are compared to vaccination rates in those who test negative. Individuals who reported symptoms and tested in pillar 2 (community testing) between 27 November and 24 December 2021 were included in the analysis. Those who reported recent foreign travel were excluded due to differences in exposure risk and possible misclassification of vaccination status in this group.

Cases were defined as the Omicron variant or Delta variant based on whole genome sequencing, genotyping, or S-gene target status on PCR testing. The Omicron variant has been associated with a negative S-gene target result on PCR testing with the Taqpath assay whereas with the Delta variant the S-gene target is almost always positive. Vaccine effectiveness was estimated by period after dose 2 and dose 3. Results are presented for 18+ year olds.

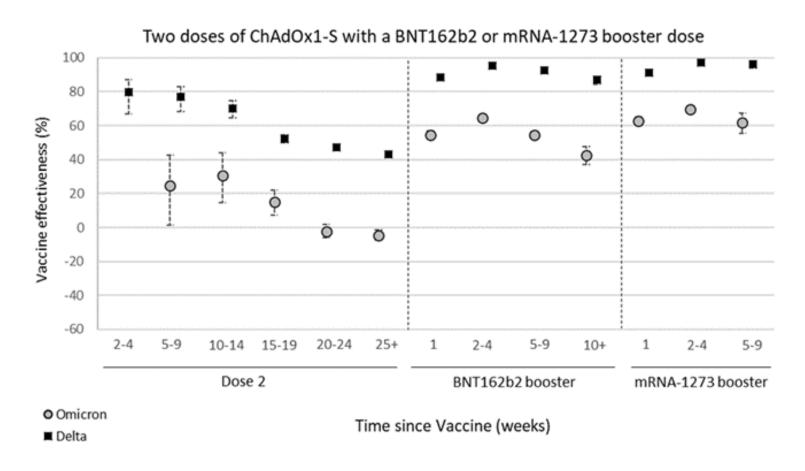
Pillar 2 symptomatic confirmed cases were then linked to the Emergency Care Dataset (ECDS) to identify admissions via emergency care 0 to 14 days after the positive test (excluding admissions due to injuries). Cox survival analysis was then used to estimate the risk of hospital admission by vaccination status. Due to small numbers all vaccine brands are considered

together. Adjustments were made for age, gender, previous positive test, region, ethnicity, clinically extremely vulnerable status, risk group status and period. To estimate vaccine effectiveness against hospitalisation the odds ratios (OR) for symptomatic disease were multiplied by the hazard ratios (HR) for hospitalisation among symptomatic cases: VEhospitalisation = 1-(ORsymptomatic disease x HRhospitalisation).

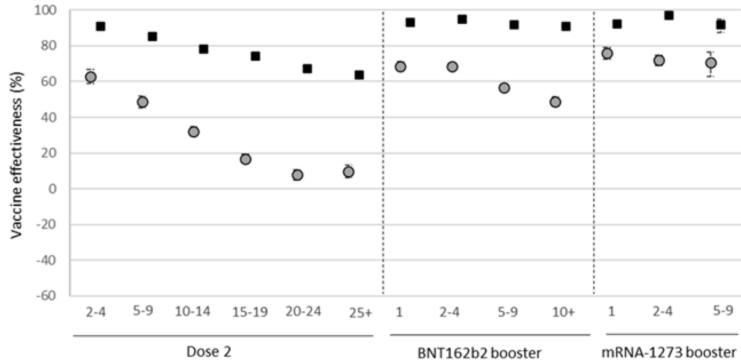
The symptomatic disease test negative case control analysis included 169,888 Delta cases and 204,036 Omicron cases. Vaccine effectiveness against symptomatic disease by period after dose 2 and dose 3 is shown in Figure 2 for those who received a primary course of the AstraZeneca vaccine (Figure 2a), Pfizer (Figure 2b) or Moderna (Figure 2c). Effectiveness of booster doses of Pfizer and Moderna are shown for AstraZeneca and Pfizer primary courses. In all periods, effectiveness was lower for Omicron compared to Delta. Among those who had received 2 doses of AstraZeneca, there was no effect against Omicron from 20 weeks after the second dose. Among those who had received 2 doses of Pfizer or Moderna effectiveness dropped from around 65-70% down to around 10% by 20 weeks after the 2nd dose. 2 to 4 weeks after a booster dose vaccine effectiveness ranged from around 65 to 75%, dropping to 55 to 70% at 5 to 9 weeks and 40-50% from 10+ weeks after the booster.

Figure 6. Vaccine effectiveness against symptomatic diseases by period after dose 1 and dose 2 for Delta (black squares) and Omicron (grey circles) for a) recipients of 2 doses of AstraZeneca(ChAdOx1-S) vaccine as the primary course and Pfizer (BNT162b2) or Moderna (mRNA-1273) as a booster; b) recipients of 2 doses of Pfizer vaccine as the primary course and Pfizer or Moderna as a booster, and c) 2 doses of Moderna as a primary course (insufficient data for boosters after a Moderna primary course)

Supplementary data is not available for this figure.



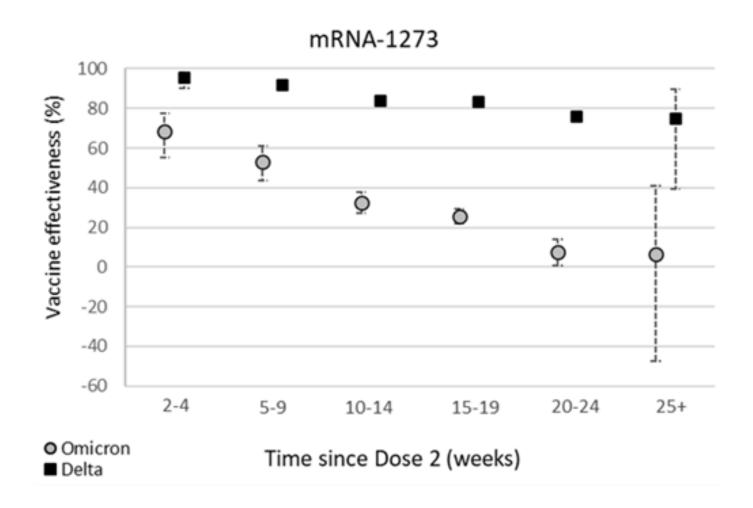
Two doses of BNT162b2 with a BNT162b2 or mRNA-1273 booster dose



Omicron

■ Delta

Time since Vaccine (weeks)



Results for hospitalisations are shown in Table 2 and Table 3. One dose of vaccine was associated with a 35% reduced risk of hospitalisation among symptomatic cases with the Omicron variant, 2 doses with a 67% reduction up to 24 weeks after the second dose and a 51% reduced risk 25 or more weeks after the second dose, and a third dose was associated with a 68% reduced risk of hospitalisation. When combined with vaccine effectiveness against symptomatic disease this was equivalent to vaccine effectiveness against hospitalisation of 52% after 1 dose, 72% 2 to 24 weeks after dose 2, 52% 25+ weeks after dose 2 and 88% 2+ weeks after a booster dose.

Table 2. Hazard ratios (HR) against hospitalisation with Omicron and Delta (all brands combined) (CI=Confidence interval)

		HR against hospitalisation (95% CI)		
Dose	Interval after dose	Omicron	Delta	
1	4+ weeks	0.65 (0.30-1.42)	0.27 (0.2-0.37)	
2	2 to 24 weeks	0.33 (0.21-0.55)	0.1 (0.09-0.13)	
2	25+ weeks	0.49 (0.30-0.81)	0.15 (0.13-0.18)	
3	2+ weeks	0.32 (0.18-0.58)	0.11 (0.09-0.14)	

Table 3. Vaccine effectiveness against hospitalisation for Omicron (all vaccine brands combined). OR = odds ratio, HR = hazard ratio, VE = vaccine effectiveness (CI=Confidence interval)

Dose	Interval after dose	OR against symptomatic disease (95% CI)	HR against hospitalisation (95% CI)	VE against hospitalisation (95% CI)
1	4+ weeks	0.74 (0.70-0.77)	0.65 (0.30-1.42)	52% (-5-78)
2	2 to 24 weeks	0.82 (0.80-0.84)	0.33 (0.21-0.55)	72% (55-83)
2	25+ weeks	0.98 (0.95-1.00)	0.49 (0.30-0.81)	52% (21-71)
3	2+ weeks	0.37 (0.36-0.38)	0.32 (0.18-0.58)	88% (78-93)

These estimates suggest that vaccine effectiveness against symptomatic disease with the Omicron variant is significantly lower than compared to the Delta variant and wanes rapidly. Nevertheless, protection against hospitalisation is much greater than that against symptomatic disease, in particular after a booster dose, where vaccine effectiveness against hospitalisation is close to 90%. Further data is needed to estimate the duration of protection against hospitalisation. Experience with previous variants suggests that this will be sustained longer than protection against symptomatic disease.

Vaccine effectiveness publications

UKHSA have published a significant amount of <u>research into vaccine effectiveness</u>, which is summarised on pages 5 to 17 and in the publications in Table 4.

Table 4. UKHSA publications on the effectiveness of COVID-19 vaccination

Publication	Subject
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 with the Omicron variant for 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.
Vaccine effectiveness and duration of protection of Comirnaty, Vaxzevria and Spikevax against mild and severe COVID-19 in the UK	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.
Higher serological responses and increased vaccine effectiveness demonstrate the value of extended vaccine schedules in combatting COVID-19 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.

Publication	Subject
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.
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 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.
Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of Long- Term Care Facilities (VIVALDI study)	The VIVALDI study found evidence that COVID-19 vaccines were associated with a substantially reduced risk of infection in care home residents.
Assessing the Effectiveness of BNT162b2 and ChAdOx1nCoV-19 COVID-19 Vaccination in Prevention of Hospitalisations in Elderly and Frail Adults: A Single Centre 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.
COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study	Early data from PHE'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.

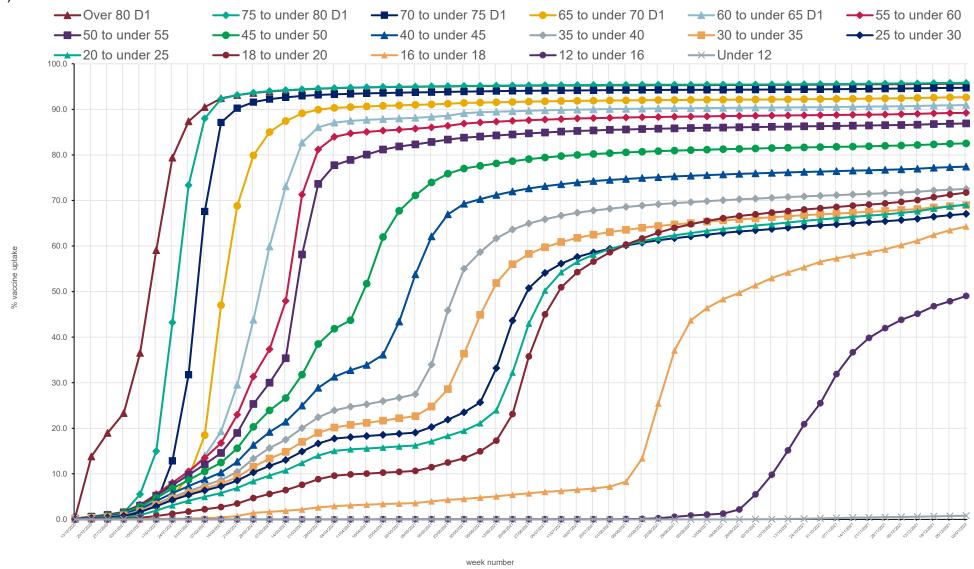
UKHSA and other government and academic partners monitor the impact of the of the vaccination programme on levels of COVID-19 antibodies in the population and different disease indicators, including hospitalisations and mortality. This is done through population-based testing and through modelling which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

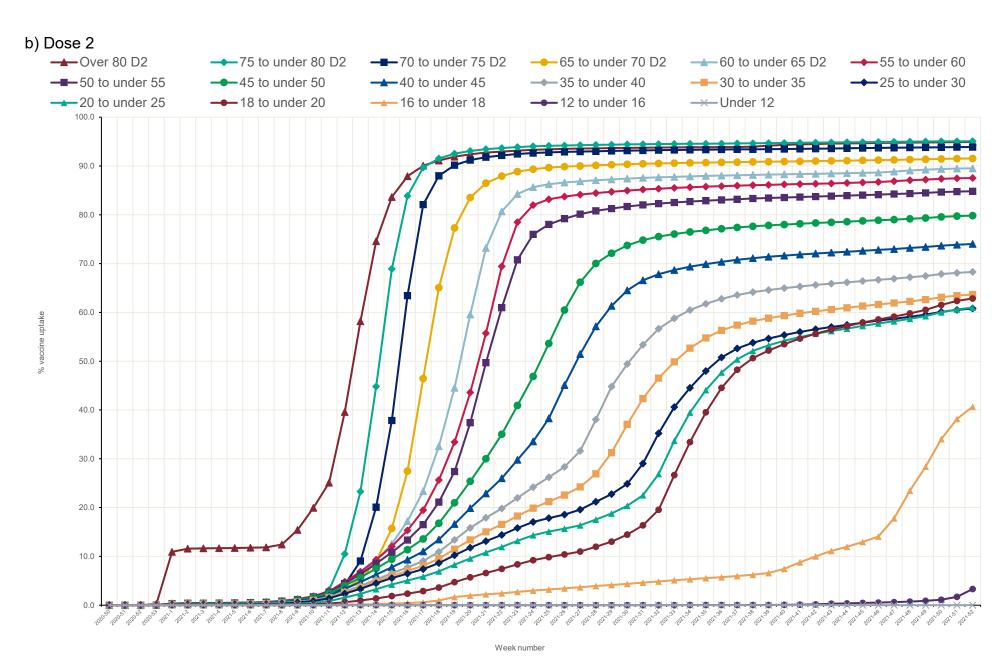
Vaccine coverage

The data in this week's report covers the period from 8 December 2020 to 2 January 2022 (week 52) (Figure 7). It shows the provisional number and percentage of living people in England who have had received 1, 2 or 3 doses of a COVID-19 vaccination by age group and week since the start of the programme. Further data on vaccine uptake by age in England can be found in the <u>national flu and COVID-19 surveillance reports</u>. Age is calculated as age on the 31 August 2021, that is, academic cohort for all ages.

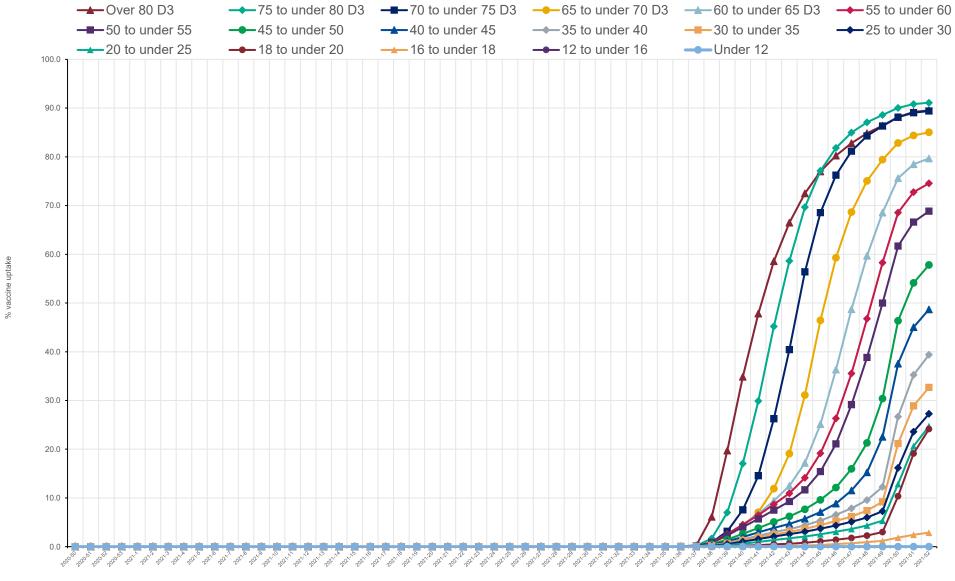
Figure 7. Cumulative weekly vaccine uptake by age

a) Dose 1









Vaccination in immunosuppressed individuals

Provisional vaccine uptake data in living and resident people identified as immunosuppressed in England to the end of week 52 can be found in Table 5. This shows that vaccine uptake in the 536,890 identified as immunosuppressed was 95.4% for at least dose 1, 93.8% for at least 2 doses and 84.8% for at least 3 doses. Data on vaccine uptake in people with at least 3 doses by age in England can be found in the National flu and COVID-19 surveillance reports.

Table 5. Vaccine uptake in people identified as immunosuppressed in England

Immuno- suppression	People in NIMs Cohort	Numbers vaccinated with at least 1 dose	vaccine	Numbers vaccinated with at least 2 doses		Numbers vaccinated with at least 3 doses	Percentage vaccine uptake with at least 3 doses
England	536,890	512,327	95.4	503,613	93.8	455,122	84.8

Detailed information on the <u>characterisation of the immunosuppressed group by NHS Digital</u> is available.

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 Royal College of Obstetricians and Gynaecologists and the Royal College of Midwives.

As of 16 April, the Joint Committee on Vaccination and Immunisation (JCVI) advice is that pregnant women should be offered COVID-19 vaccines at the same time as people of the same age or risk group. Therefore, any pregnant women not in a higher-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 age group, working back from older to younger individuals.

Prior to this, COVID-19 vaccine was delivered to priority groups based on clinical risk and risk of exposure, and delivered in order of priority. It was advised that vaccine could be offered to pregnant and breast-feeding women who were in these risk categories and at high risk of ongoing exposure or at high risk of serious complications of COVID-19 after the JCVI met on 22 December 2020. The Pfizer vaccine was rolled out from early December 2020, AstraZeneca vaccine was approved for use in the UK at the end of December 2020 and the Moderna vaccine became available from April 2021.

In England more than 80,000 women indicated that they were or could be pregnant at the time they were vaccinated by the end of September 2021 (21). In Scotland more than 14,000 women were vaccinated during pregnancy to the end of August 2021 (22) and nearly 2,000 women in Wales to the end September 2021 (23). In the USA more than 175,000 women have indicated they were pregnant at the time they received COVID-19 vaccination to 22 November 2021 (24). There is evidence of high levels of protection against SARS-CoV-2 infection in pregnant women after COVID-19 vaccination (25-27) and evidence that vaccination induces higher antibody levels than after disease (27). 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 (28).

Complications linked with COVID-19 disease in pregnancy (critical care admission and perinatal deaths) in Scotland were far more common in unvaccinated than in vaccinated pregnant women (29, 30). No safety concerns relating to COVID-19 vaccination of pregnant women have been found in published studies to date (31, 32, 33, 34). The vaccine side-effects appear to be similar in pregnant and non-pregnant populations (31).

Increased severity of COVID-19 disease in pregnant and recently pregnant women has been reported after the first SARS-CoV-2 wave in England (35, 36) and in Scotland (29). Pregnant women who develop severe disease have increased rates of admission to ICU, need for

invasive ventilation and pre-term delivery. Data from the US Centers for Disease Control and Prevention (CDC) found that pregnant women are 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 (37).

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. This report provides first the early data on COVID-19 vaccination in pregnant women and provides preliminary findings.

Vaccine coverage

COVID-19 vaccine coverage in women before they give birth has increased as more women have become eligible for vaccination. In May 2021, only 2.8% of women giving birth had received at least 1 dose of vaccine. This increased to 9.8% of women who gave birth in June, 16.0% in July and 22.2% in August 2021 (Table 6).

In the overall 8 month period between January and August 2021 a total of 355,299 women gave birth of whom 24,759 had received at least 1 dose of COVID-19 vaccine prior to delivery. For the 18,187 women where enough information was available to derive the trimester in which the vaccine was administered, 695 (3.8%) were immunised with their earliest vaccine dose in pregnancy in their first trimester, 4,487 (24.7%) were immunised in their second trimester and 13,005 (71.5%) were immunised in their third trimester.

Of all vaccinated women giving birth, 80.8% had received Pfizer vaccine, 11.1% had received AstraZeneca vaccine and 8.1% had received Moderna vaccine.

Table 6. Overall vaccine coverage in women giving birth, by month of delivery

Month	Women giving birth	Vaccinated	Unvaccinated	Unknown vaccine status
Jan-21	41,955	18 (0.0%)	41,766 (99.5%)	171 (0.4%)
Feb-21	40,105	84 (0.2%)	39,879 (99.4%)	142 (0.4%)
Mar-21	44,657	292 (0.7%)	44,230 (99.0%)	135 (0.3%)
Apr-21	43,363	495 (1.1%)	42,687 (98.4%)	181 (0.4%)
May-21	44,831	1,255 (2.8%)	43,387 (96.8%)	189 (0.4%)
Jun-21	44,822	4,383 (9.8%)	40,277 (89.9%)	162 (0.4%)
Jul-21	48,409	7,746 (16.0%)	40,468 (83.6%)	195 (0.4%)
Aug-21	47,157	10,486 (22.2%)	36,464 (77.3%)	207 (0.4%)

Table 7. Vaccine coverage by ethnicity, for women giving birth June to August 2021

Ethnicity	Women giving birth in June to August	Vaccinated	Unvaccinated
Asian	17,248	2,320 (13.5%)	14,928 (86.5%)
Black	6,736	370 (5.5%)	6,366 (94.5%)
Other	5,579	865 (15.5%)	4,714 (84.5%)
Mixed	3,311	463 (14.0%)	2,848 (86.0%)
White	100,555	17,599 (17.5%)	82,956 (82.5%)
Unknown ¹	6,395	998 (15.6%)	5,397 (84.4%)

¹ 564 women of could not be matched with a NIMS record and their ethnicity and vaccine status are therefore unknown.

Table 8. Vaccine coverage by quintile of deprivation of the small area in which the woman lived, for women giving birth June to August 2021

Quintile of deprivation	Women giving birth in June to August	Vaccinated	Unvaccinated
1 - most deprived	35,263	2,751 (7.8%)	32,512 (92.2%)
2	30,448	3,964 (13.0%)	26,484 (87.0%)
3	27,146	4,847 (17.9%)	22,299 (82.1%)
4	24,462	5,189 (21.2%)	19,273 (78.8%)
5 - least deprived	21,751	5,770 (26.5%)	15,981 (73.5%)
Unknown ¹	754	94 (12.5%)	660 (87.5%)

¹ 564 women of could not be matched with a NIMS record and their quintile of deprivation and vaccine status are therefore unknown.

Table 9. Vaccine coverage by age of mother, for women giving birth June to August 2021

Age	Women giving birth in June to August	Vaccinated	Unvaccinated
Under 20	2,463	71 (2.9%)	2,392 (97.1%)
20 to 24	15,903	738 (4.6%)	15,165 (95.4%)
25 to 29	35,417	2,915 (8.2%)	32,502 (91.8%)
30 to 34	48,655	9,164 (18.8%)	39,491 (81.2%)
35 to 39	29,719	7,709 (25.9%)	22,010 (74.1%)
40 to 44	7,246	1,924 (26.6%)	5,322 (73.4%)
45 and above ¹	420	93 (22.1%)	327 (77.9%)

¹ 564 women of could not be matched with a NIMS record and their age group and vaccine status are therefore unknown.

Using the most recent 3-month period (during which time there were 22,615 vaccinated women giving birth, accounting for 91.3% of all vaccinated women giving birth since January) there were differences in vaccine coverage by both ethnicity (<u>Table 7</u>) and by quintile of deprivation (<u>Table 8</u>). Women of Black ethnicity and women living in the most deprived areas in England were least likely to have been vaccinated with at least 1 dose of COVID-19 vaccine before they gave birth. Coverage increased as levels of deprivation decreased (<u>Table 8</u>). Vaccine coverage increased with increasing age group to those aged 40 to 44 years in whom uptake was 26.6% (<u>Table 9</u>). Women who gave birth between January and August 2021 aged 45 years or older had vaccine coverage of 22.1% and were offered vaccine earlier than the younger age groups.

Methods

Data on vaccination status is recorded in a central dataset called the National Immunisation Management Service (NIMS).¹ 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 1 record per woman, identified by her NHS Number, and the latest 'delivery episode' associated with her. These were then linked back to women in the NIMS using the NHS Number, and each woman's vaccine status was established as either vaccinated or unvaccinated (plus a small number where vaccine status was unknown), using the NIMS vaccine records. The date the vaccine was administered had to be on an earlier date than the date the woman gave birth. The ethnicity, residence and age information used to generate Tables 7 to 9 was taken from the NIMS record.

In order to establish the trimester each woman first received the vaccine, the gestational age on the date at which she gave birth was required and was used to establish the start of her pregnancy. Women recorded as receiving their earliest dose of the vaccine within 97 days of the start of their pregnancy were counted as having received the vaccine in trimester 1; women recorded as receiving their earliest dose of the vaccine between 98 and 195 days of the start of their pregnancy were counted as having received the vaccine in trimester 2 and women receiving the vaccine over 195 days (but before the day of delivery) were counted as having received the vaccine in trimester 3.

The analysis within this section was carried out on 16 November 2021. The latest HES data available is for August 2021, and HES data since April 2021 is considered provisional.

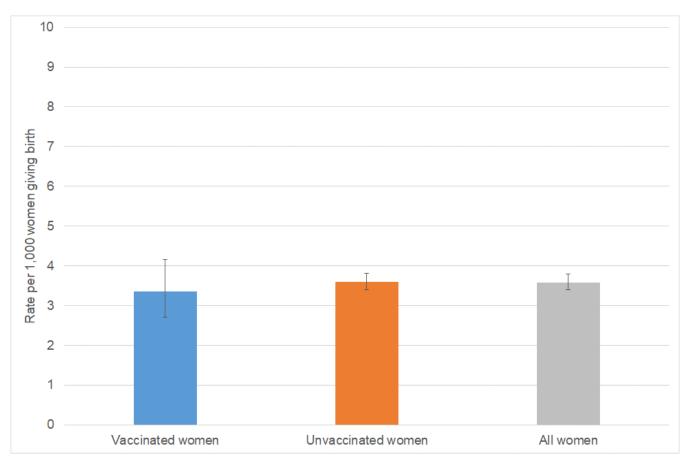
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¹ NIMS Data controllers are NHSEI and NHSD. The NIMS IT software is commissioned by NHSEI via South Central West CSU and is provided by the System C and Graphnet Care Alliance.

Pregnancy outcomes

The following figures present rates of women in England who gave birth to a stillborn baby (based on recorded diagnoses), the proportion of women giving birth to a baby with low birthweight (<2,500g) or a very low birthweight (<1,500g) and the proportion of women giving birth prematurely (<37 weeks gestation), very prematurely (<32 weeks gestation) and extremely prematurely (<28 weeks gestation). It assesses whether rates were different in women who received a COVID-19 vaccination in pregnancy compared with the unvaccinated and overall population but does not take other factors that might affect these outcomes into account, such as age and whether the woman was categorised as clinically extremely vulnerable (CEV). More detailed statistical analyses are planned. These pregnancy outcomes are routinely reported as official statistics annually by ONS. However, HES data was used to monitor outcomes more quickly than ONS data allow.

Figure 8. Stillbirths experienced by women giving birth January to August 2021



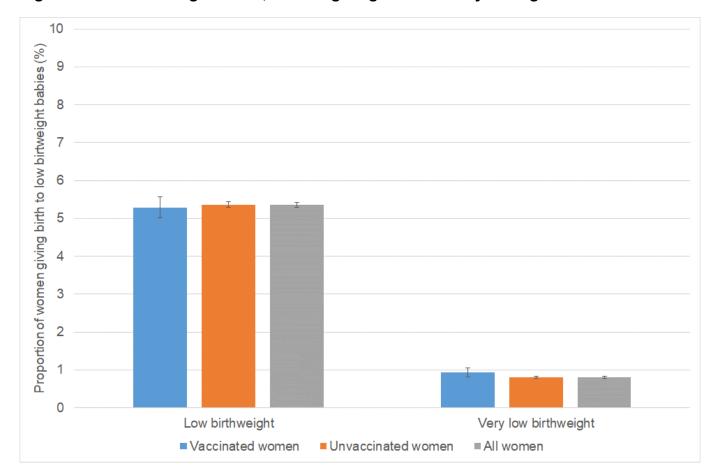


Figure 9. Low birthweight births, women giving birth January to August 2021

The stillbirth rate for vaccinated women who gave birth (3.35 per 1,000, 95%Cl 2.71 to 4.15) was similar to the rate for unvaccinated women (3.60 per 1,000, 95%Cl 3.40 to 3.81) giving birth between January and August 2021 (Figure 8). In the same period, the proportion of vaccinated women giving birth to babies with low birthweight (5.28%, 95%Cl 5.01 to 5.57) was comparable to the proportion for unvaccinated women (5.36%, 95%Cl 5.29 to 5.44) (Figure 9). Similarly, 0.93% (95%Cl 0.82 to 1.06) of vaccinated pregnant women and 0.80% (95%Cl 0.77 to 0.83) of unvaccinated pregnant women had a very low birthweight baby.

The proportion of women with premature births was 6.51% (95%CI 6.21 to 6.82) in vaccinated women and 5.99% (95%CI 5.91 to 6.08) in unvaccinated women. The proportion of women with very premature births was 1.71% (95%CI 1.55 to 1.88) in vaccinated and 1.74% (95%CI 1.70 to 1.79) in unvaccinated women. The proportion of women with extremely premature births was 1.09% (95%CI 0.97 to 1.23) in vaccinated women and 1.21% (95%CI 1.17 to 1.25) in unvaccinated women.

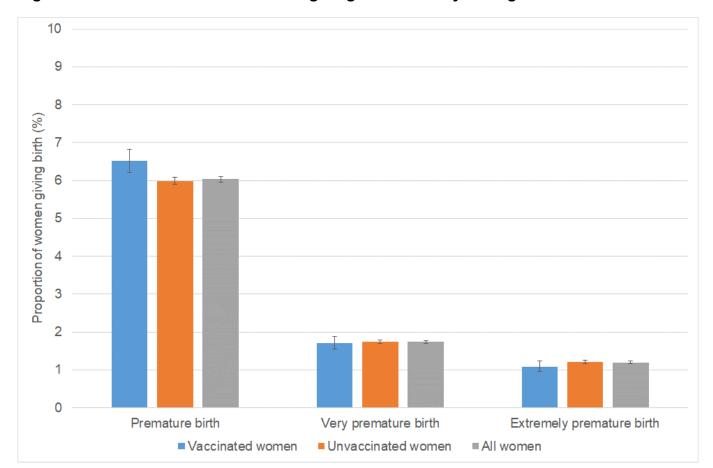


Figure 10. Premature births in women giving birth January to August 2021

The first women to be offered COVID-19 vaccine were those who were categorised as CEV and women of older age who are at increased risk of the 3 outcomes presented here (given the medical conditions that placed them in this category), together with healthcare professionals at higher risk of COVID-19 exposure. Women with underlying conditions that put them at very high risk of serious complications of COVID-19 and older pregnant women will therefore account for a relatively high proportion of early deliveries in vaccinated women. For example, whilst 26.7% of the women who gave birth were aged 35 years or older this age group accounted for 43.0% of all vaccinated women who gave birth. It is therefore very reassuring that vaccinated women had no increased risk of suffering a stillbirth or having low birthweight babies. Whilst the proportion of women with a premature birth was slightly higher in vaccinated women, this could be explained by differences in their age and underlying health risk. The proportion of very or extremely premature births, where the baby is at more risk, was similar in vaccinated and unvaccinated women.

Methods

For the analysis in this section, women aged under 50 years were identified in the NIMS data set and their vaccine status was established as either vaccinated or unvaccinated, using the NIMS vaccine records. These records were then linked, where the woman had given birth, to the de-duplicated delivery records from the HES data set by NHS number. The date the vaccine

was administered had to be on an earlier date than the date the woman gave birth. The analysis within this section was carried out on 16 November 2021. The latest HES data available is for August 2021, and HES data since April 2021 is considered provisional.

Stillbirths were identified as records where any 1 or more of the first 12 diagnoses was the following: Z37.1: Single stillbirth; Z37.3 Twins, 1 liveborn and 1 stillborn; Z37.4 Twins, both stillborn; Z37.6: Other multiple births, some liveborn; Z37.7: Other multiple births, all stillborn. Low birthweight and very low birthweight deliveries were identified as records where any of the first 4 babies born had a known birthweight between 500g and 2499g (1499g or lower for very low birthweight).

Premature deliveries were identified as records where the gestational length was less than 37 weeks (less than 32 weeks for very premature, and less than 28 weeks for extremely premature).

Low birthweight is by convention presented as a percentage of all deliveries with known birthweights, and prematurity usually presented as a percentage of all deliveries with known gestational length. However here they are presented as percentages of all deliveries, to reduce the chance of significant findings arising from a change in the overall success of recording these fields during the pandemic. Figures will therefore differ from official statistics and should be considered for surveillance purposes only.

Confidence intervals were calculated using the Wilson Score method (38). A confidence interval is a range of values that is used to quantify the imprecision in the estimate of a particular indicator. Specifically it quantifies the imprecision that results from random variation in the measurement of the indicator. A wider confidence interval shows that the indicator value presented is likely to be a less precise estimate of the true underlying value.

Main findings

COVID-19 vaccination is the safest and most effective way for women to protect themselves and their babies against severe COVID-19 disease.

COVID-19 vaccine coverage in pregnant women at delivery has increased as more women have become eligible for vaccination reaching 22.2% for women who gave birth in August 2021. This coverage is in line with the 25% of women in Scotland and 18.4% in Wales delivering in August 2021 who had received any dose and their first dose of COVID-19 vaccine respectively prior to delivery.

Coverage increased with decreasing levels of deprivation. Women of Black ethnicity had the lowest vaccine coverage.

Coverage increased with increasing age group to 40 to 44 years. This reflects the roll out of the vaccine by age group and the longer availability of vaccination in older pregnant women.

Women who had received COVID-19 vaccine and delivered between January and August 2021 were more likely to be in older age groups and to be in clinically extremely vulnerable risk groups as these women were offered COVID-19 vaccination earlier than younger women and those who were not in clinical risk categories.

It is reassuring, therefore, that vaccinated and unvaccinated women had a similar risk of stillbirth between January and August 2021. Vaccinated and unvaccinated women who gave birth in this period also had similar proportions of low and very low birthweight babies.

Whilst the proportion of premature births was slightly higher in vaccinated women, this could be explained by differences in their age and underlying health risk (as CEV women were prioritised in the earlier months of the roll-out). The proportions of very or extremely premature births, where the baby is at more risk, were similar in vaccinated and unvaccinated women.

Vaccination status in cases, deaths and hospitalisations

Vaccination status of COVID-19 cases, deaths and hospitalisations by week of specimen date over the past 4 weeks up to week 52 (up to 2 January 2022) are shown in tables 10 to 12. This data is published to help understand the implications of the pandemic to the NHS, for example understanding workloads in hospitals, and to help understand where to prioritise vaccination delivery. **This raw data should not be used to estimate vaccine effectiveness.** We have published a <u>blog post</u> to accompany this section of the vaccine surveillance report.

Methods

COVID-19 cases and deaths identified through routine collection from the Second Generation Surveillance System (SGSS) and from UKHSA EpiCell's deaths data, as described in the technical summary, were linked to the National Immunisation Management System (NIMS) to derive vaccination status, using an individual's NHS number as the unique identifier.

Attendance to emergency care at NHS trusts was derived from the Emergency Care DataSet (ECDS) managed by NHS Digital. The same data source was used to identify COVID-19 cases where the attendance to emergency care resulted in admission to an NHS trust.

ECDS is updated weekly, and cases are linked to these data twice weekly. Data from ECDS is subject to reporting delays as, although NHS trusts may update data daily, the mandatory deadline for submission is by the 21st of every month. This means that for weeks immediately following the 21st of a month, numbers may be artificially low and are likely to be higher in later versions of the report.

Data from ECDS also only reports on cases who have been presented to emergency care and had a related overnight patient admission and do not show those who are currently in hospital with COVID-19. As such, it is not appropriate for use for surveillance of those currently hospitalised with COVID-19. In addition, these data will not show cases who were directly admitted as inpatients without presenting to emergency care.

The outcome of overnight inpatient admission following presentation to emergency care, was limited to those occurring within 28 days of the earliest specimen date for a COVID-19 case. Deaths include those who died (a) within 28 days of the earliest specimen date or (b) within 60 days of the first specimen date or more than 60 days after the first specimen date with COVID-19 mentioned on the death certificate.

The rate of COVID-19 cases, hospitalisation, and deaths in fully vaccinated and unvaccinated groups was calculated using vaccine coverage data for each age group extracted at the midpoint of the reporting period from the National Immunisation Management Service.

Results

The rate of a positive COVID-19 test varies by age and vaccination status. The rate of a positive COVID-19 test is substantially lower in vaccinated individuals compared to unvaccinated individuals up to the age of 29. In individuals aged greater than 30, the rate of a positive COVID-19 test is higher in vaccinated individuals compared to unvaccinated (<u>Table 13</u>). This is likely to be due to a variety of reasons, including differences in the population of vaccinated and unvaccinated people as well as differences in testing patterns.

The rate of hospitalisation within 28 days of a positive COVID-19 test increases with age, and is substantially greater in unvaccinated individuals compared to vaccinated individuals.

The rate of death within 28 days or within 60 days of a positive COVID-19 test increases with age, and again is substantially greater in unvaccinated individuals compared to fully vaccinated individuals.

Interpretation of data

This data should be considered in the context of the vaccination status of the population groups shown in the rest of this report. In the context of very high vaccine coverage in the population, even with a highly effective vaccine, it is expected that a large proportion of cases, hospitalisations and deaths would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated and no vaccine is 100% effective. This is especially true because vaccination has been prioritised in individuals who are more susceptible or more at risk of severe disease. Individuals in risk groups may also be more at risk of hospitalisation or death due to non-COVID-19 causes, and thus may be hospitalised or die with COVID-19 rather than **from** COVID-19.

The vaccination status of cases, inpatients and deaths should not be used to assess vaccine effectiveness because of differences in risk, behaviour and testing in the vaccinated and unvaccinated populations. The case rates in the vaccinated and unvaccinated populations are crude rates that do not take into account underlying statistical biases in the data. There are likely to be systematic differences between vaccinated and unvaccinated populations, for example:

- people who are fully vaccinated may be more health conscious and therefore more likely to get tested for COVID-19 and so more likely to be identified as a case (based on the data provided by the NHS Test and Trace)
- many of those who were at the head of the queue for vaccination are those at higher risk from COVID-19 due to their age, their occupation, their family circumstances or because of underlying health issues
- people who are fully vaccinated and people who are unvaccinated may behave differently, particularly with regard to social interactions and therefore may have differing levels of exposure to COVID-19
- people who have never been vaccinated are more likely to have caught COVID-19 in the weeks or months before the period of the cases covered in the report. This gives them some natural immunity to the virus for a few months which may have contributed to a lower case rate in the past few weeks

These biases become more evident as more people are vaccinated and the differences between the vaccinated and unvaccinated population become systematically different in ways that are not accounted for without undertaken formal analysis of vaccine effectiveness. Vaccine effectiveness has been formally estimated from a number of different sources and is described on pages 5 to 17 in this report.

Denominator

The potential sources of denominator data are either the National Immunisation Management Service (NIMS) or the Office for National Statistics (ONS) mid-year population estimates. Each source has its strengths and limitations which have been described in detail on the NHS website and GOV.Wales.

NIMS may over-estimate denominators in some age groups, for example because people are registered with the NHS but may have moved abroad. However, as it is a dynamic register, such patients, once identified by the NHS, are able to be removed from the denominator. On the other hand, ONS data uses population estimates based on the 2011 census and other sources of data. When using ONS, vaccine coverage exceeds 100% of the population in some age groups, which would in turn lead to a negative denominator when calculating the size of the unvaccinated population.

UKHSA uses NIMS throughout its COVID-19 surveillance reports including in the calculation rates of COVID-19 infection, hospitalisation and deaths by vaccination status because it is a

dynamic database of named individuals, where the numerator and the denominator come from the same source and there is a record of each individual's vaccination status. Additionally, NIMS contains key sociodemographic variables for those who are targeted and then receive the vaccine, providing a rich and consistently coded data source for evaluation of the vaccine programme. Large scale efforts to contact people in the register will result in the identification of people who may be overcounted, thus affording opportunities to improve accuracy in a dynamic fashion that feeds immediately into vaccine uptake statistics and informs local vaccination efforts.

Sources of further information

UKHSA has published a blog post to accompany this section of the report.

The Office of the Statistics Regulator has published a blog post.

UKHSA has published a significant amount of <u>research into vaccine effectiveness</u> which is summarised on pages 5 to 17 of this report.

The Office for National Statistics has published research into the <u>risk of testing positive for COVID-19 by vaccination status</u>, impact of Delta on viral burden and vaccine effectiveness (<u>4</u>), and the <u>risk of death by vaccination status</u>.

Table 10. COVID-19 cases by vaccination status between week 49 and week 52 2021

Please note that corresponding rates by vaccination status can be found in <u>Table 13</u>.

Cases reported by specimen date between week 49 and week 52 2021	Total	Unlinked*	Not vaccinated	Received one dose (1 to 20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date¹
	[This data should be interpreted with caution. See information below in footnote about the correct					
	interpretation of these figures]					
Under 18	429,155	32,145	308,183	7,104	72,620	9,103
18 to 29	628,127	52,666	102,948	5,532	36,594	430,387
30 to 39	529,948	38,026	75,057	2,973	20,676	393,216
40 to 49	408,892	24,189	35,758	1,206	9,075	338,664
50 to 59	308,585	17,250	17,385	568	4,430	268,952
60 to 69	148,836	8,902	6,419	313	1,659	131,543
70 to 79	70,723	4,297	2,098	116	515	63,697
80 or over	32,314	2,589	1,214	50	395	28,066

^{*} Individuals whose NHS numbers were unavailable to link to the NIMS.

¹ In the context of very high vaccine coverage in the population, even with a highly effective vaccine, it is expected that a large proportion of cases, hospitalisations and deaths would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated and no vaccine is 100% effective. This is especially true because vaccination has been prioritised in individuals who are more susceptible or more at risk of severe disease. Individuals in risk groups may also be more at risk of hospitalisation or death due to non-COVID-19 causes, and thus may be hospitalised or die with COVID-19 rather than because of COVID-19.

Table 11. COVID-19 cases presenting to emergency care (within 28 days of a positive specimen) resulting in an overnight inpatient admission by vaccination status between week 49 and week 52 2021

Please note that corresponding rates by vaccination status can be found in <u>Table 13</u>.

Cases presenting to emergency care (within 28 days of a positive test) resulting in overnight inpatient admission, by	Total	Unlinked*	Not vaccinated	Received one dose (1 to 20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date¹
specimen date between week 49 and week 52 2021	[This data should be interpreted with caution. See information below in footnote about tinterpretation of these figures]				oout the correct	
Under 18	899	47	796	8	38	10
18 to 29	899	23	405	10	88	373
30 to 39	1,063	12	541	7	66	437
40 to 49	1,165	12	558	10	47	538
50 to 59	1,406	17	594	5	55	735
60 to 69	1,326	17	491	11	52	755
70 to 79	1,379	5	349	4	50	971
80 or over	1,844	1	322	5	52	1,464

^{*} Individuals whose NHS numbers were unavailable to link to the NIMS.

¹ In the context of very high vaccine coverage in the population, even with a highly effective vaccine, it is expected that a large proportion of cases, hospitalisations and deaths would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated and no vaccine is 100% effective. This is especially true because vaccination has been prioritised in individuals who are more susceptible or more at risk of severe disease. Individuals in risk groups may also be more at risk of hospitalisation or death due to non-COVID-19 causes, and thus may be hospitalised or die with COVID-19 rather than because of COVID-19.

Table 12. COVID-19 deaths (a) within 28 days and (b) within 60 days of positive specimen or with COVID-19 reported on death certificate, by vaccination status between week 49 and week 52 2021

Please note that corresponding rates by vaccination status can be found in <u>Table 13</u>.

(a)

Death within 28 days of positive COVID-19 test by date of death between	Total**	Unlinked*	Not vaccinated	Received one dose (1 to 20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date ¹	
week 49 and week 52 2021	[This data should be interpreted with caution. See information below in footnote about the correct interpretation of these figures]						
Under 18	5	0	4	0	0	1	
18 to 29	20	0	15	0	0	5	
30 to 39	55	0	37	0	3	15	
40 to 49	107	2	59	0	4	42	
50 to 59	229	3	102	1	11	112	
60 to 69	443	5	145	0	16	277	
70 to 79	628	9	164	2	27	426	
80 or over	1,403	7	283	3	39	1,071	

^{*} lindividuals whose NHS numbers were unavailable to link to the NIMS.

^{**} number of deaths of people who had had a positive test result for COVID-19 and either died within 60 days of the first positive test or have COVID-19 mentioned on their death certificate.

¹ In the context of very high vaccine coverage in the population, even with a highly effective vaccine, it is expected that a large proportion of cases, hospitalisations and deaths would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated and no vaccine is 100% effective. This is especially true because vaccination has been prioritised in individuals who are more susceptible or more at risk of severe disease. Individuals in risk groups may also be more at risk of hospitalisation or death due to non-COVID-19 causes, and thus may be hospitalised or die with COVID-19 rather than because of COVID-19.

(b)

(D)				1		
Death within 60 days of positive COVID-19 test by date of death between week 49 and week 52 2021	Total**	Unlinked*	Not vaccinated	Received one dose (1 to 20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date ¹
Week 43 and Week 32 2021	[This data s	should be interp	reted with caution.	See information be	low in footnote abo	out the correct
	interpretation of these figures]					
Under 18	7	0	6	0	0	1
18 to 29	22	1	16	0	0	5
30 to 39	71	0	44	0	4	23
40 to 49	140	3	78	0	5	54
50 to 59	308	3	130	1	14	160
60 to 69	561	8	172	0	21	360
70 to 79	849	11	184	2	35	617
80 or over	1,760	8	298	3	45	1,406

^{*} Individuals whose NHS numbers were unavailable to link to the NIMS.

^{**} number of deaths of people who had had a positive test result for COVID-19 and either died within 60 days of the first positive test or have COVID-19 mentioned on their death certificate.

¹ In the context of very high vaccine coverage in the population, even with a highly effective vaccine, it is expected that a large proportion of cases, hospitalisations and deaths would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated and no vaccine is 100% effective. This is especially true because vaccination has been prioritised in individuals who are more susceptible or more at risk of severe disease. Individuals in risk groups may also be more at risk of hospitalisation or death due to non-COVID-19 causes, and thus may be hospitalised or die with COVID-19 rather than because of COVID-19.

Table 13. Unadjusted rates of COVID-19 infection, hospitalisation and death in vaccinated and unvaccinated populations.

Please note that the following table should be read in conjunction with pages 34 to 36 of this report, and the footnotes provided on page 42.

	Cases reported by specimen date between week 49 and week 52 2021		Cases presenting to emergency care (within 28 days of a positive test) resulting in overnight inpatient admission, by specimen date between week 49 and week 52 2021		Death within 28 days of positive COVID-19 test by date of death between week 49 and week 52 2021		Death within 60 days of positive COVID-19 test by date of death between week 49 and week 52 2021	
		[s	see information on popul	ation bases and unadjuste	d rates in footnotes 1 and	2 below this table]		
	among persons vaccinated with 2 doses (ner among persons not vaccinated (per vaccinated with 2		Unadjusted rates among persons not vaccinated (per 100,000) ²	Unadjusted rates among persons vaccinated with 2 doses (per 100,000) ²	Unadjusted rates among persons not vaccinated (per 100,000) ²	Unadjusted rates among persons vaccinated with 2 doses (per 100,000) ²	Unadjusted rates among persons not vaccinated (per 100,000) ²	
Under 18	1,827.4	2,961.6	2.0	7.6	0.2	0.0	0.2	0.1
18 to 29	7,221.4	3,240.8	6.3	12.7	0.1	0.5	0.1	0.5
30 to 39	6,383.9	2,686.6	7.1	19.4	0.2	1.3	0.4	1.6
40 to 49	5,393.8	2,147.2	8.6	33.5	0.7	3.5	0.9	4.7
50 to 59	3,738.4	1,721.9	10.2	58.8	1.6	10.1	2.2	12.9
60 to 69	2,266.3	1,194.3	13.0	91.4	4.8	27.0	6.2	32.0
70 to 79	1,347.6	862.0	20.5	143.4	9.0	67.4	13.1	75.6
80 or over	1,055.0	981.5	55.0	260.3	40.3	228.8	52.8	240.9

¹ Comparing case rates among vaccinated and unvaccinated populations should not be used to estimate vaccine effectiveness against COVID-19 infection. Vaccine effectiveness has been formally estimated from a number of different sources and is summarised on pages 5 to 17 in this report.

The rates are calculated per 100,000 in people who have received either 2 doses of a COVID-19 vaccine or in people who have not received a COVID-19 vaccine. These figures are updated each week as the number of unvaccinated individuals and individuals vaccinated with 2 doses in the population changes.

The case rates in the vaccinated and unvaccinated populations are unadjusted crude rates that do not take into account underlying statistical biases in the data and there are likely to be systematic differences between these 2 population groups. For example:

- people who are fully vaccinated may be more health conscious and therefore more likely to get tested for COVID-19 and so more likely to be identified as a case (based on the data provided by the NHS Test and Trace)
- many of those who were at the head of the queue for vaccination are those at higher risk from COVID-19 due to their age, their occupation, their family circumstances or because of underlying health issues
- people who are fully vaccinated and people who are unvaccinated may behave differently, particularly with regard to social interactions and therefore may have differing levels of exposure to COVID-19
- people who have never been vaccinated are more likely to have caught COVID-19 in the weeks or months before the period of the cases covered in the report. This gives them some natural immunity to the virus for a few months which may have contributed to a lower case rate in the past few weeks

Unadjusted case rates among persons vaccinated have been formatted in grey to further emphasise the caution to be employed when interpreting this data.

²Case rates are calculated using NIMS - a database of named individuals from which the numerator and the denominator come from the same source and there is a record of each individuals vaccination status. Further information on the use of NIMS as the source of denominator data is presented on page 36 of this report.

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 47 2021 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 the 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. Please note that this section will be updated monthly. Last update was published on 9 December 2021. The next update will be published in January 2022.

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.

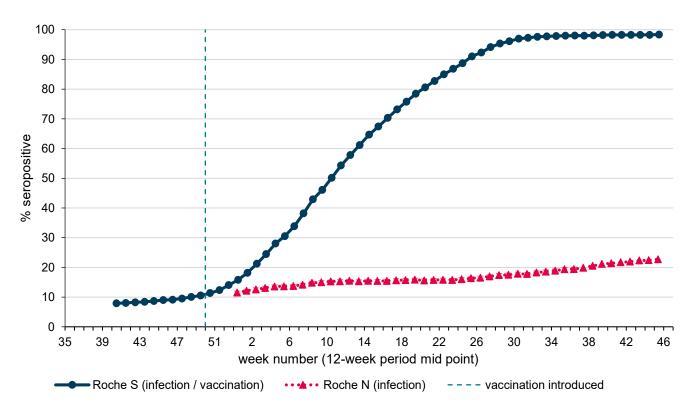
Nucleoprotein (Roche N) assays only detect post-infection antibodies, whereas spike (Roche S) assays will detect both post-infection antibodies and vaccine-induced antibodies. Thus, changes in seropositivity for the Roche N assay reflect the effect of natural infection. Increases in seropositivity as 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. Donors have been asked to defer donations for at least 7 full days post vaccination, and for at least 28 days post recovery if side-effects following vaccination or COVID-19 infection.

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. 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 22.7% (95% CI 22.0% - 23.5%) using the Roche N assay and 98.4% (95% CI 98.1% - 98.6%) using the Roche S assay for the period 4 October to 28 November (weeks 40 to 47 2021). 3,155 out of 14,453 were Roche N positive and 14,093 out of 14,324 samples were Roche S positive. This compares with 18.6% (95% CI 18.0% - 19.1%) Roche N seropositivity and 97.8% (95% CI 97.5% - 98.0%) Roche S seropositivity for the period of 12 July to 1 October 2021 (weeks 28 to 39 2021). Seropositivity (weighted by region, age group and sex) varies over time. Figure 11 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.

Figure 11. Overall 12-weekly rolling SARS-CoV-2 antibody seroprevalence (% seropositive) in blood donors



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 12).

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

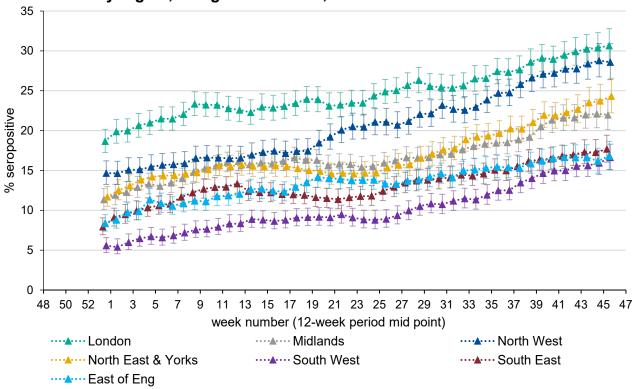


Table 14. Roche N seropositivity (95%CI) estimates by NHS region

NHS region	Weeks 28 to 39	Weeks 40 to 47	
East of England	15.1% (13.8% - 16.5%)	16.8% (15.1% - 18.7%)	
London	26.5% (24.9% - 28.1%)	30.6% (28.6% - 32.8%)	
Midlands	18.0% (16.5% - 19.6%)	22.0% (20.1% - 23.9%)	
North East and Yorkshire	19.2% (17.7% - 20.8%)	24.3% (22.2% - 26.6%)	
North West	22.9% (21.4% - 24.6%)	28.6% (26.4% -30.9%)	
South East	14.3% (13.1% - 15.7%)	17.7% (16.1% - 19.4%)	
South West	11.3% (10.2% - 12.6%)	16.6% (15.1% - 18.3%)	

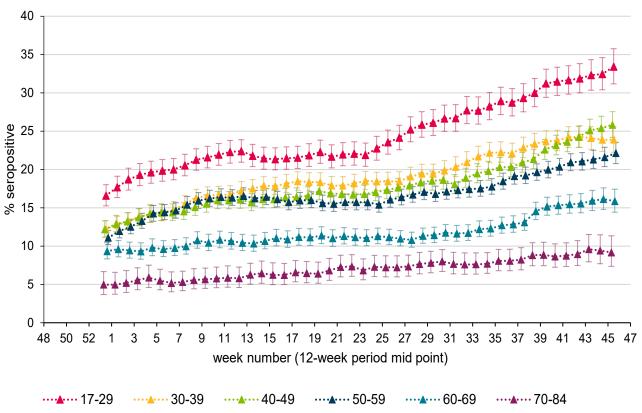
Increases in Roche N seropositivity have recently been observed across all regions (Table 14) compared to the previous 12-week period.

London has consistently seen the highest Roche N seropositivity with the lowest observed in the South West. Recently seropositivity in the North West has been increasing to similar levels as seen in London. Recent increases in seropositivity has also been observed in the South West reaching similar levels to the East of England and the South East. This is consistent with the increases in COVID-19 case rates reported for the South West (<u>Weekly national Influenza and COVID-19 surveillance report week 48</u>).

Prevalence by age group

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

Figure 13. 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 13</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.

Table 15. Roche N seropositivity (95%CI) estimates by age group

Age group	Weeks 28 to 39	Weeks 40 to 47
17 to 29	27.7% (25.9% - 29.5%)	33.4% (31.1% - 35.8%)
30 to 39	21.7% (20.4% - 23.1%)	23.9% (22.3% - 25.6%)
40 to 49	19.5% (18.3% - 20.7%)	25.8% (24.2% - 27.5%)
50 to 59	17.5% (16.5% - 18.6%)	22.1% (20.8% - 23.5%)

Age group	Weeks 28 to 39	Weeks 40 to 47
60 to 69	12.2% (11.2% - 13.3%)	15.9% (14.4% - 17.4%)
70 to 84	7.6% (6.4% - 9.1%)	9.2% (7.4% - 11.3%)

Small increases in Roche N seropositivity have recently been observed across all age groups (<u>Table 15</u>) compared to the previous 12-week period. In the most recent period seropositivity in those aged 40 to 49 is higher than those aged 30 to 39; this is a pattern that has also been observed in the COVID-19 confirmed case rates by age (<u>Weekly national Influenza and COVID-19 surveillance report week 48</u>).

Roche S seropositivity in blood donors has plateaued and is now over 96% 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) blood donors are potentially less likely to be exposed to natural infection than age matched individuals in the general population (ii) waning of the N antibody response over time and (iii) recent observations from UKHSA surveillance data that N antibody levels are lower in individuals who acquire infection following 2 doses of 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, initially amongst individuals aged 50 years and above who were prioritised for vaccination as part of the phase 1 programme and subsequently in younger adults as part of phase 2 of the vaccination programme. The impact of the booster vaccination programme 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 PHE/UKHSA surveillance over the past few months has found that over 97% 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 programme. In this week's report, groupings of antibody level ranges have been updated to better illustrate changes over time.

<u>Figure 14</u> shows monthly categorised Roche S levels in N-antibody negative individuals by age group. Almost all tested S-antibody negative during December. In the 3 oldest age groups, the impact of first vaccine dose, then second vaccine dose, can be seen from December through June, as the profile of population antibody levels increases. Then from June through September the profile of antibody levels in these cohorts gradually decreases, consistent with waning.

During October there was a small increase in percentage of donors with very high antibody levels of 10000+ AU/ml for the 50 to 84 age group, following the initiation of the booster programme. In November the proportion of donors with very high antibody levels of 10,000+ AU/ml increased further particularly in those aged 70 to 84 years. The higher profile of antibody levels in the youngest age group, is likely a result of a combination of factors including stronger immune responses in younger individuals and the higher antibody levels produced after mRNA vaccination.

<u>Figure 15</u> 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 personal factors such as underlying health conditions and age. At the start of the vaccination rollout in December antibody levels typically sat within the range of 0.8 to 2500 AU/ml, after vaccination antibody levels typically exceed 2500 AU/ml. In November more than half of donors aged 70 to 84 years had very high antibody levels of 25,000+ AU/ml. Comparing <u>Figure 14</u> with <u>Figure 15</u>, 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.

Researchers across the globe are working to better understand what antibody levels mean in terms of protection against COVID-19. Current thinking is that there is no threshold antibody level that offers complete protection against infection, but instead that higher antibody levels are likely to be associated with lower probability of infection.

Figure 14. Categorised Roche S antibody levels by age group and month in N negative samples, December 2020 to November 2021

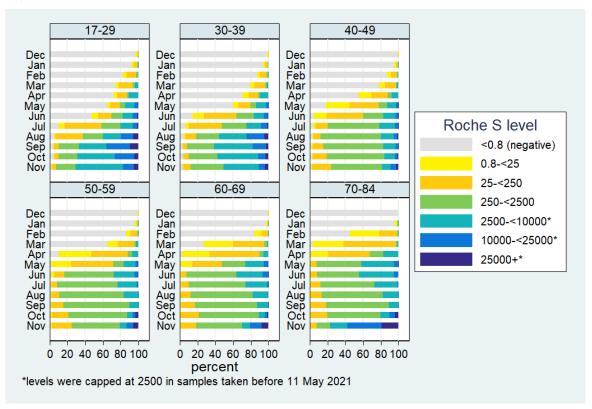
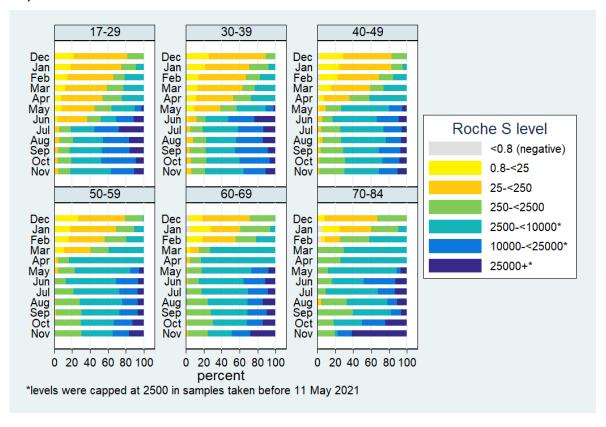


Figure 15. Categorised Roche S antibody levels by age group and month in N positive samples, December 2020 to November 2021



Summary of impact on hospitalisations, infections and mortality

UKHSA previously reported on the number of hospitalisations directly averted by vaccination. In total, around 261,500 hospitalisations have been prevented in those aged 45 years and over up to 19 September 2021.

UKHSA and University of Cambridge MRC Biostatistics Unit previously reported on the direct and indirect impact of the vaccination programme on infections and mortality. Estimates suggest that 127,500 deaths and 24,144,000 infections have been prevented as a result of the COVID-19 vaccination programme, up to 24 September.

Neither of these models will be updated going forward. This is due to these models being unable to account for the interventions that would have been implemented in the absence of vaccination. Consequently, over time the state of the actual pandemic and the no-vaccination pandemic scenario have become increasingly less comparable. For further context surrounding this figure and for previous estimates, please see previous vaccine surveillance reports.

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UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation heath secure.

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