

COVID-19 vaccine surveillance reportWeek 16

21 April 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).

Please note that from May 2022, this report will be published on a fortnightly basis.

Vaccine effectiveness

Several studies of vaccine effectiveness (VE) have been conducted in the UK against different COVID-19 variants. Vaccine effectiveness against symptomatic disease with the Omicron variant is substantially lower than against the Delta variant, with rapid waning. However, protection against hospitalisation remains high, particularly after 3 doses.

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 one, 2 and 3 doses of COVID-19 vaccines. By 17 April 2022, the overall vaccine uptake in England for dose 1 was 69.7% and for dose 2 was 65.6%. Overall vaccine uptake in England in people with at least 3 doses was 51.2%. In line with the programme rollout, coverage is highest in the oldest age groups.

Based on antibody testing of blood donors, 99.4% of the adult population have antibodies to COVID-19 from either infection or vaccination compared to 45.0% 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.

Post implementation real world vaccine effectiveness studies are needed to understand vaccine effectiveness against different outcomes (such as severe disease and onwards 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 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.

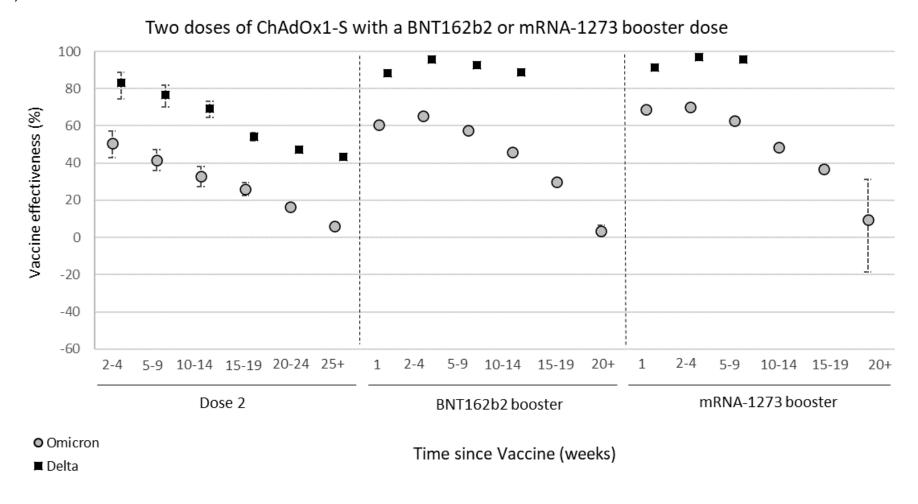
Please note that vaccine effectiveness data will be updated in this report as it becomes available. Last update was published on 13 April 2022.

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 of the AstraZeneca vaccine, vaccine effectiveness against the Omicron variant starts at 45 to 50% then drops to almost no effect from 25 weeks after the second dose. With 2 doses of Pfizer or Moderna effectiveness dropped from around 65 to 70% down to around 15% by 25 weeks after the second dose. Two to 4 weeks after a booster dose of either the Pfizer or Moderna vaccine following an AstraZeneca or Pfizer primary course, effectiveness ranges from around 60 to 75%, dropping to almost no effect from 20+ weeks after the booster. Vaccine effectiveness estimates for the booster dose are very similar, irrespective of the primary course received (3). Vaccine effectiveness is generally slightly higher in younger compared to older age groups.

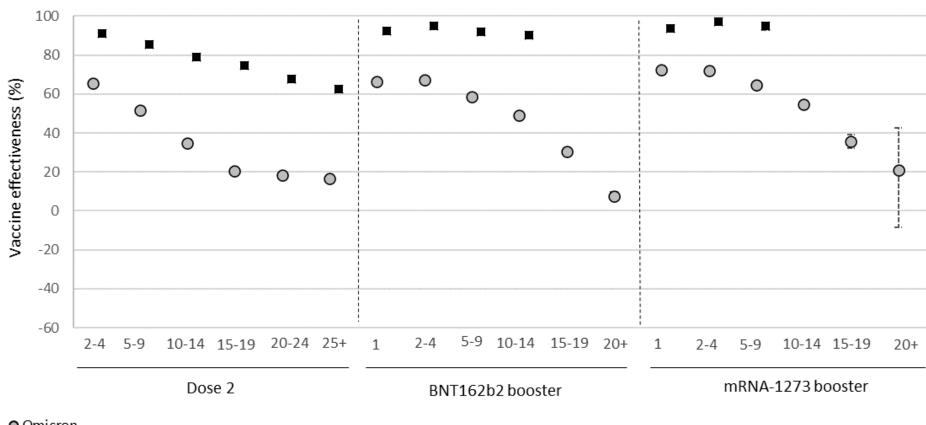
Figure 1. Vaccine effectiveness against symptomatic disease by period after the second and booster doses for Delta (black squares) and Omicron (grey circles) for a) recipients of 2 doses of AstraZeneca (ChAdOx1-S) vaccine as the primary course and Pfizer (BNT162b2) or Moderna (mRNA-1273) as a booster;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

a)



b)

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



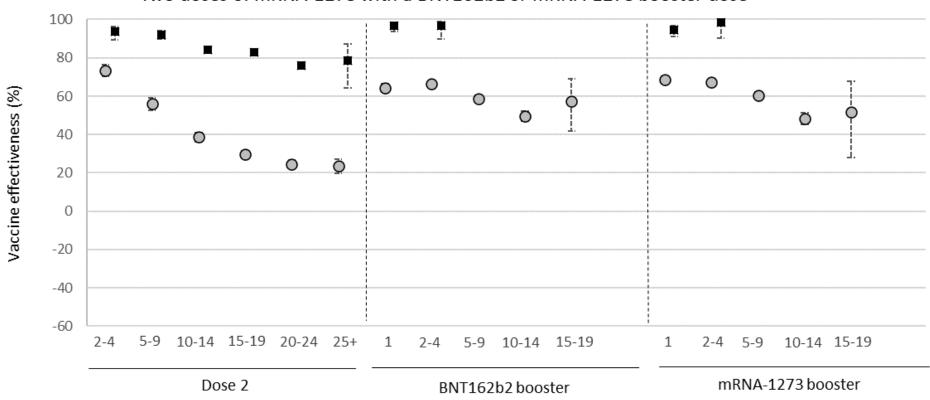
Omicron

■ Delta

Time since Vaccine (weeks)

c)





Omicron

■ Delta

Time since Vaccine (weeks)

Data (based primarily on the Alpha and Delta variants) 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 (4). 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 (5).

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 and Delta variants (6, 7, 8, 9). Vaccine effectiveness against a range of hospitalisation outcomes with the Omicron variant has been estimated using a test-negative case control study design (Table 1, 10). Among 18 to 64 year olds using all COVID-19 cases admitted via emergency care VE after a booster peaked at 82.4% and dropped to 53.6% by 15+ weeks after the booster; using all admissions for >-= 2 days with a respiratory code in the primary diagnostic field VE ranged from 90.9% down to 67.4%; further restricting to those on oxygen/ventilated/on intensive care VE ranged from 97.1% down to 75.9%. Among 65+ year olds the equivalent VE estimates were 92.4% down to 76.9%; 91.3% down to 85.3% and 95.8% down to 86.8%. Given that Omicron generally causes milder disease than previous variants, in particular among younger individuals, and that all individuals who are hospitalised for any reason in the UK are tested for COVID-19, 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. This can be seen in the vaccine effectiveness estimates against hospitalisation, whereby outcomes using broad definitions for hospitalisation give lower estimates that are likely more reflective of vaccine effectiveness against infection. Whereas definitions of hospitalisation that are more specific to severe respiratory disease give higher vaccine effectiveness estimates with less evidence of waning. This is also likely to explain the higher vaccine effectiveness against hospitalisation in 65+ year olds compared to 18 to 64 year olds. There appears to be little variation in vaccine effectiveness against hospitalisation after a booster dose according to the type of vaccine used for priming or boost (10).

Table 1. Vaccine effectiveness against hospitalisation using different definitions of hospitalisations in a) 18 to 64 year olds and b) 65 year olds and over

		ECDS symptomatic with onset date	SUS at least 2 days with ARI code in primary field	SUS at least 2 days and either oxygen, ventilation or ICU with ARI code in primary field					
18 to 64									
	Interval	VE	VE	VE					
Dose 1	0 to 27	48.5 (12.3 to 69.7)	36.2 (-33.9 to 69.6)						
	28+	48.7 (32.8 to 60.8)	44.1 (25.6 to 58)	75 (42.4 to 89.1)					
Dose 2	0 to 13	39.6 (-31.5 to 72.2)	88.9 (58.4 to 97)						
	14 to 174	54.7 (45.3 to 62.4)	69 (58.1 to 77)	86.7 (63.6 to 95.1)					
	175+	34.6 (21.7 to 45.4)	56.1 (46.4 to 64)	82.3 (67.7 to 90.3)					
Booster	0 to 6	63.9 (52.2 to 72.8)	74.3 (55.9 to 85)	90.7 (56 to 98.1)					
	7 to 13	80.1 (73.5 to 85.1)	90.9 (83.2 to 95.1)						
	14 to 34	82.4 (78.6 to 85.6)	88.6 (84.9 to 91.5)	97.1 (92.2 to 98.9)					
	35 to 69	72.7 (67.2 to 77.2)	85.8 (82.4 to 88.5)	94.3 (88.9 to 97.1)					
	70 to 104	66.9 (59.1 to 73.3)	80.2 (74.9 to 84.4)	89.9 (78.3 to 95.3)					
	105+	53.6 (36.9 to 65.9)	67.4 (53.1 to 77.4)	75.9 (15.8 to 93.1)					
		65	5+						
	Interval	VE	VE	VE					
Dose 1	0 to 27		43.9 (-41 to 77.7)						
	28+		53.4 (36.3 to 65.9)	78.3 (43.7 to 91.7)					
Dose 2	0 to 13								
	14 to 174	77.8 (45 to 91)	82.3 (74.3 to 87.8)	90.9 (72.6 to 97)					
	175+	66.7 (43.4 to 80.4)	57.7 (49.6 to 64.4)	73.4 (55.1 to 84.3)					
Booster	0 to 6	85.8 (61.5 to 94.7)	77.9 (65.3 to 85.9)	89.2 (63.1 to 96.8)					
	7 to 13	92.3 (76.3 to 97.5)	84.7 (76 to 90.2)	94.7 (71.6 to 99)					
	14 to 34	92.4 (86 to 95.8)	91.3 (89.1 to 93.1)	95.8 (91.3 to 97.9)					
	35 to 69	87 (79.2 to 91.8)	89.3 (87.3 to 90.9)	92.8 (88.4 to 95.6)					
	70 to 104	84 (74.6 to 89.9)	88.1 (86.1 to 89.9)	92.5 (88.1 to 95.2)					
	105+	76.9 (60.6 to 86.4)	85.3 (82.4 to 87.6)	86.8 (77.1 to 92.3)					

ECDS = Emergency Care Dataset (this analysis includes all admissions with a positive COVID-19 test via emergency care except for those coded as injuries). SUS = Secondary Users Service (this analysis includes all admissions to secondary care for >=2 days with a respiratory code in the first diagnostic field) (10).

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 with relatively limited waning (6, 11, 12). Vaccine effectiveness against mortality with the Omicron variant has been estimated for those aged 50 years and older by combining the risk of becoming a symptomatic case with the risk of death among symptomatic cases in vaccinated (all vaccines combined) compared to unvaccinated individuals (Table 2). At 25-plus weeks following the second dose, vaccine effectiveness was around 60% while at 2 or more weeks following a booster vaccine effectiveness was 95% against mortality.

Table 2. Hazard ratios and vaccine effectiveness against mortality (all vaccine brands combined). OR = odds ratio, HR = hazards ratio, VE = vaccine effectiveness

Dose	Interval after dose	OR versus symptomatic disease	HR versus mortality	VE versus mortality
2	25+ weeks	0.93 (0.9 to 0.96)	0.45 (0.19 to 1.03)	59% (4 to 82)
3	2+ weeks	0.41 (0.39 to 0.42)	0.12 (0.06 to 0.24)	95% (90 to 98)

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 with the Alpha and Delta variants (13, 14, 15, 16). Generally estimates are similar to or slightly lower than vaccine effectiveness estimates against symptomatic disease and there is evidence of significant waning in protection against infection over time. Estimates for vaccine effectiveness against infection with the Omicron variant are not yet available.

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 also provide some protection against 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). Several studies have provided evidence of reduced risk of household transmission from vaccinated cases compared to unvaccinated cases (17, 18, 19, 21).

Consensus vaccine effectiveness estimates

Table 3 summarises consensus estimates of vaccine effectiveness against different outcomes that have been reached by the UK Vaccine Effectiveness Expert Panel. These take into account estimates from UK studies by public health agencies and academic groups as well as international data.

Table 3. Consensus estimates of vaccine effectiveness against the Omicron variant

Vaccine product for primary course	Outcome	Second dose: 0 to 3 months	Second dose: 4 to 6 months	Second dose: 6+ months	Booster dose: All Periods	Booster dose: 0 to 3 months	Booster dose: 4 to 6 months	Booster dose: 6+ months
	All Infection	30% (10 to 50%)	0 to 35% (range only)	Insufficient data	See individual periods	50% (40 to 60%)	30% (20 to 40%)	Insufficient data
	Symptomatic	40% (30 to 50%)	20% (5 to 30%)	5% (0 to 5%)	See individual periods	60% (50 to 70%)	40% (30 to 50%)	Insufficient data
AstraZeneca	Hospitalisation	85% (60 to 90%)	70% (50 to 75%)	65% (45 to 85%)	See individual periods	90% (85 to 95%)	85% (85 to 95%)	Insufficient data
	Mortality	Insufficient data	Insufficient data	Insufficient data	See individual periods	90% (85 to 98%)	Insufficient data	Insufficient data
	Transmission	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
	All Infection	30% (20 to 40%)	Insufficient data	Insufficient data	See individual periods	50% (40 to 60%)	30% (20 to 40%)	Insufficient data
	Symptomatic	55% (35 to 75%)	30% (15 to 35%)	15% (10 to 20%)	See individual periods	65% (55 to 75%)	Insufficient data	Insufficient data
Moderna	Hospitalisation	85 to 95% (range only)	75 to 85% (range only)	55 to 90% (range only)	See individual periods	85 to 95% (range only)	Insufficient data	Insufficient data
	Mortality	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
	Transmission	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
	All Infection	30% (20 to 40%)	Insufficient data	Insufficient data	See individual periods	50% (40 to 60%)	30% (20 to 40%)	Insufficient data
Pfizer	Symptomatic	50% (30 to 65%)	20% (15 to 30%)	15% (10 to 15%)	See individual periods	65% (55 to 75%)	45% (35 to 55%)	Insufficient data
	Hospitalisation	90% (85 to 95%)	80% (75 to 85%)	70% (55 to 90%)	See individual periods	90% (85 to 95%)	85% (85 to 95%)	Insufficient data
	Mortality	Insufficient data	Insufficient data	Insufficient data	See individual periods	90% (85 to 98%)	Insufficient data	Insufficient data
	Transmission	Insufficient data	Insufficient data	Insufficient data	0 to 25% (range only)	Insufficient data	Insufficient data	Insufficient data

Booster data is based on use of the Moderna or Pfizer vaccines as a booster.

This table provides overall estimates but there may be variation by age group or other clinical or demographic factors.

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

Effectiveness against Omicron variant BA.2

The Omicron variant sub-lineage known as BA.2 was designated VUI-22JAN-01 on 19 January 2022. An increase in the number of sequences of the Omicron sub-lineage BA.2 was noted in the UK in the week starting the 3 January 2022. Vaccine effectiveness against symptomatic disease following BA.2 infection was analysed in a test-negative case control design, as compared to the Omicron BA.1 sub-lineage. Vaccine effectiveness against both symptomatic disease (Figure 2) and hospitalisation (Table 4) was similar for BA.1 and BA.2 (20). Note, in this analysis all admissions via emergency care (excluding injuries) are included – this may underestimate VE against hospitalisation as discussed in the vaccine effectiveness against hospitalisation section above.

Figure 2. Vaccine effectiveness against symptomatic disease after 2 doses or a booster dose

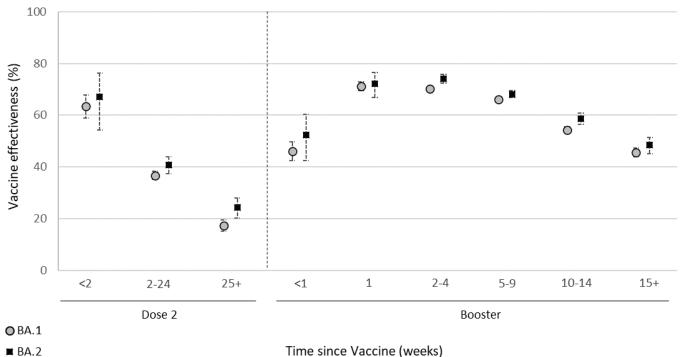


Table 4. Vaccine effectiveness against hospitalisation using the Emergency Care Dataset

Dana	luta mad (dasa)	Vaccine effectiveness (95% CI)			
Dose	Interval (days)	BA.1	BA.2		
Unvaccinated					
1	0 to 27				
	28+	24.2 (-12.5 to 48.9)	38.1 (-52.5 to 74.9)		
2	0 to 13				
	14 to 174	63.3 (47.2 to 74.6)	68.7 (26.6 to 86.6)		
	175+	32.4 (11 to 48.7)	49.9 (6.5 to 73.2)		
3	0 to 6				
	7 to 13	91.6 (65.8 to 97.9)			
	14 to 34	83.2 (75.4 to 88.5)	87.3 (57.2 to 96.2)		
	35 to 69	80.5 (74.8 to 84.9)	83.3 (70.7 to 90.5)		
	70+	72.5 (64.5 to 78.7)	70 (49.3 to 82.2)		

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 13. The publications listed in table 5 provide further results and details on the methods used.

Table 5. UKHSA publications on the effectiveness of COVID-19 vaccination

Publication	Subject
COVID-19 Vaccine Effectiveness against the Omicron BA.2 variant in England	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.

Publication	Subject
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 hospitalization in England	This study provides real world evidence of significant 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 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 supplementary appendix 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.

Publication	Subject
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 Effectiveness of BNT162b2 mRNA vaccine and	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. A study on deaths with COVID-19 indicates
ChAdOx1 adenovirus vector vaccine on mortality following COVID-19	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.
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.
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 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.

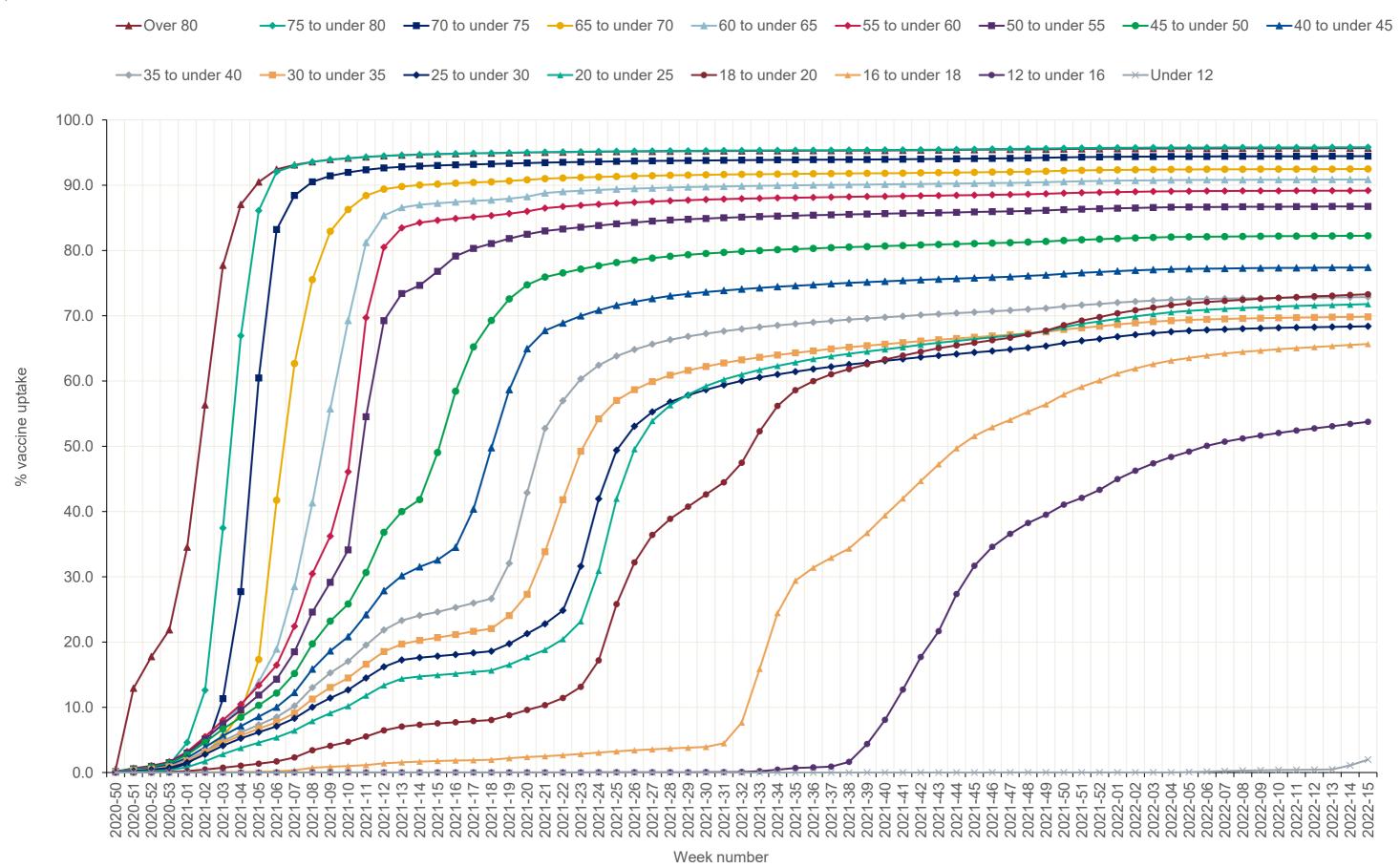
UKHSA and other government and academic partners monitor the impact of the of the vaccination programme on levels of COVID-19 antibodies in the population and different disease indicators, including hospitalisations and mortality. This is done through population-based testing and through modelling which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

Vaccine coverage

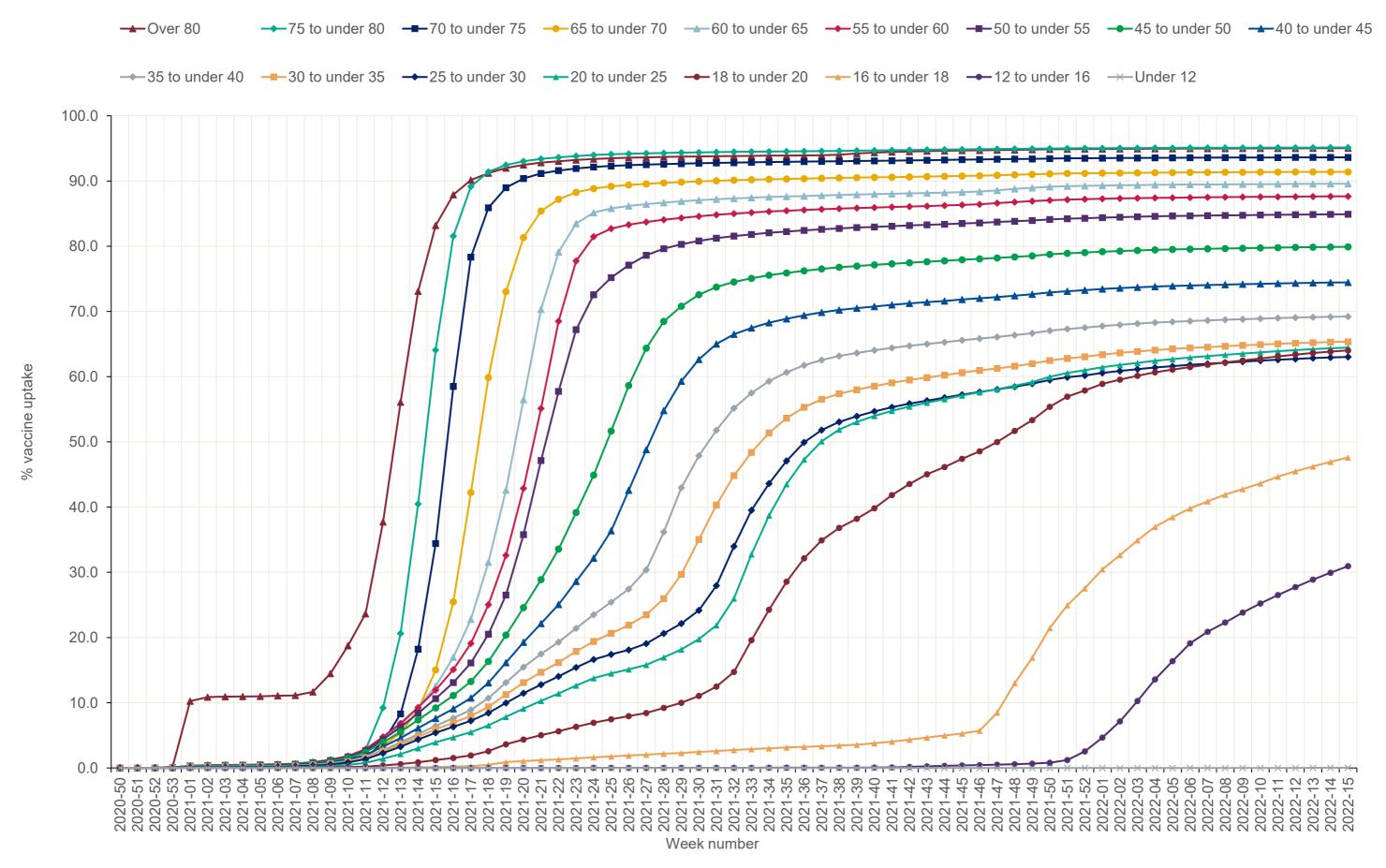
The data in this week's report covers the period from 8 December 2020 to 17 April 2022 (week 15) (Figure 3). It shows the provisional number and percentage of living people in England who have had received one, 2 or 3 doses of a COVID-19 vaccination by age group and week since the start of the programme. Further data on vaccine uptake by age in England can be found in the national flu and COVID-19 surveillance reports. Age was previously calculated as age on the 31 August 2021 (academic cohort for all ages). Please note that age is now calculated on the date data is extracted. The following weekly vaccine coverage data is extracted on a Tuesday with data capped to the previous Sunday. While this change will have an initial impact on vaccine uptake data by age, it is a positive change ensuring more accuracy and consistency in the data moving forwards.

Figure 3. Cumulative weekly vaccine uptake by age

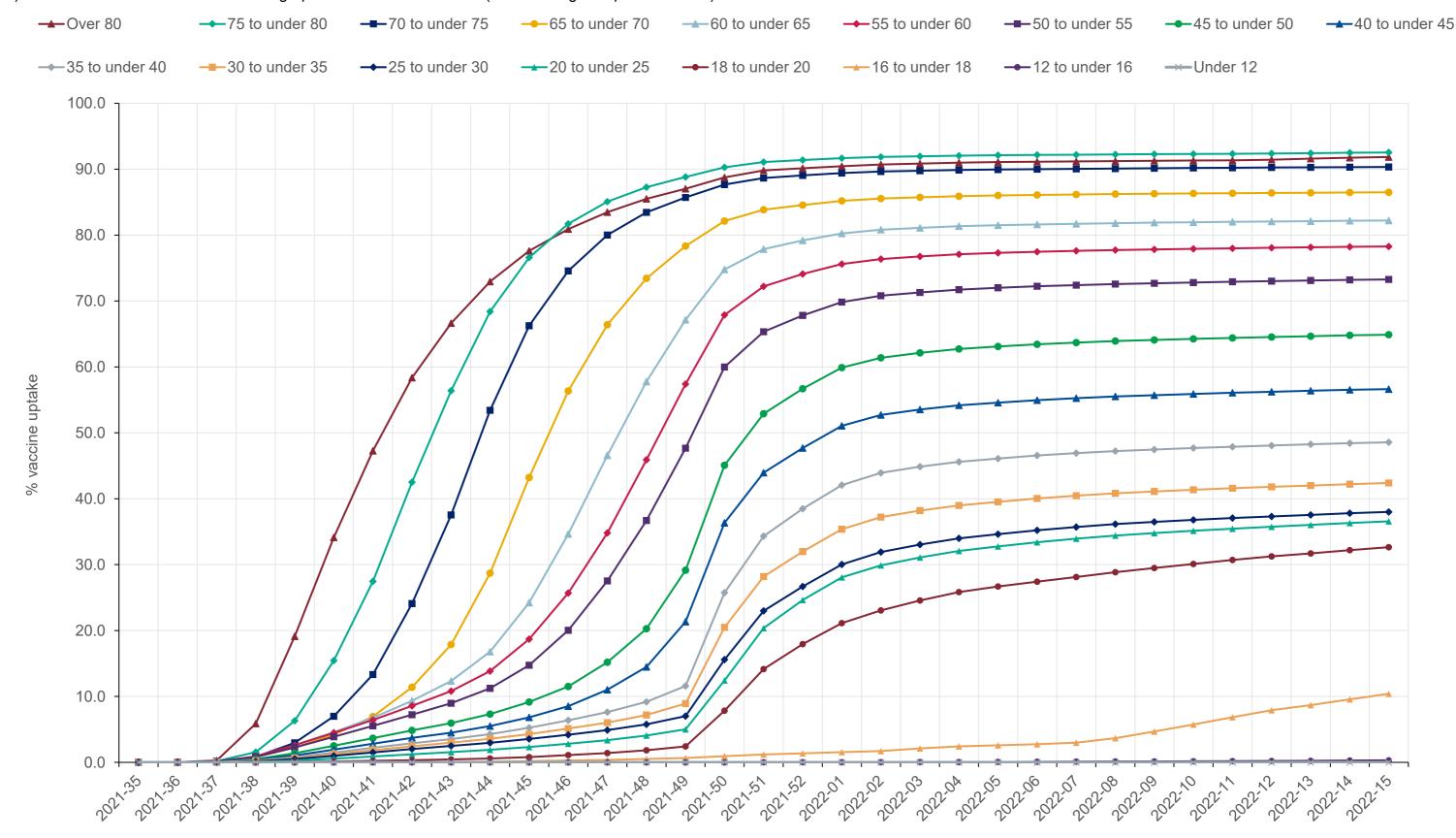
a) Dose 1



b) Dose 2



c) Dose 3. Please note the data for this graph is shown from week 35 (week ending 5 September 2021)



Week number

Vaccination in immunosuppressed individuals

Provisional vaccine uptake data in living and resident people identified as immunosuppressed in England to the end of week 14 can be found in Table 6. This shows that vaccine uptake in the 521,507 people identified as immunosuppressed was 95.7% for at least dose 1, 94.5% for at least 2 doses and 88.1% for at least 3 doses. Additional 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 6. Vaccine uptake in people identified as immunosuppressed in England

Immunosuppression	People	Numbers	Percentage	Numbers	Percentage	Numbers	Percentage
	in NIMS	vaccinated	vaccine	vaccinated	vaccine	vaccinated	vaccine
	Cohort	with at least	uptake with at	with at least	uptake with at	with at least	uptake with at
		one dose	least dose	2 doses	least 2 doses	3 doses	least 3 doses
England	521,507	498,944	95.7	492,646	94.5	459,342	88.1

Immunity derived from vaccination declines over time and many of the oldest adults received their most recent vaccine dose in September or October 2021. These individuals are at much higher risk of severe COVID-19. Therefore, as a precautionary strategy to maintain high levels of immunity, an extra spring dose is advised around 6 months provided there is at least 3 months from the previous dose for adults aged 75 years and over, residents in a care home for older adults, and individuals aged 12 years and over who are immunosuppressed, as defined in the COVID-19 healthcare guidance <u>Green Book</u>.

By the end of week 15 (week ending 17 April 2022), 8.5% (44,337/521,507) of all people identified as immunosuppressed had been vaccinated with a spring booster dose since 21 March 2022, Table 7.

Table 8 provides contextual information on how recently people identified as immunosuppressed have been vaccinated, with 49.0% (255,744/521,507) having been last vaccinated within the last 6 months and 46.6% (243,200/521,507) last vaccinated more than 6 months ago.

Table 7. Vaccine uptake in people identified as immunosuppressed in England with at least 3 doses of COVID-19 vaccine since the start of the spring booster campaign that began on the 21 March 2022 by age in England

Immunosuppression	People in NIMS cohort	Vaccinated with at least 3 doses since 21 March 2022 (spring booster)	•
England	521,507	44,337	8.5

Table 8. People identified as immunosuppressed in England vaccinated with any dose of COVID-19 vaccine in the last 3 months, 3 to 6 months, and vaccinated more than 6 months ago

Immunosuppression	•		•		accinated 3 to 6 months ago (85 to 168 days)		Vaccinated 6 months ago (169 or more days)	
	cohort	Numbers	Percentage	Numbers	Percentage	Numbers	Percentage	
		vaccinated	vaccinated	vaccinated	vaccinated	vaccinated	vaccinated	
England	521,507	243,200	46.6	157,984	30.3	97,760	18.7	

Detailed information on the characterisation of the immunosuppressed group by NHS Digital is available online.

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 College of Obstetricians and Gynaecologists and the Royal College of Midwives</u>.

Increased severity of COVID-19 disease in pregnant and recently pregnant women has been reported after the first SARS-CoV-2 wave in England (22, 23) and in Scotland (24, 25). 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 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 (26).

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 (27). 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 (27). 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 (28).

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 (29).

There is evidence of high levels of protection against SARS-CoV-2 infection in pregnant women after COVID-19 vaccination (30 to 32) and evidence that vaccination induces higher antibody levels than after disease (32). 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 (33). 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 (35). Similar findings have been reported from Scotland (25, 35) with the most recent study reporting that 90.9% (748 out of 823; 95% CI 88.7–92.7) of SARS-CoV-2 associated with

hospital admission, 98% (102 out of 104; 95% CI 92.5–99.7) 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 (24). The researchers also found high 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 28,000 pregnant women to the end of January 2021 (24) and over 6,000 women in Wales had received their first dose of vaccine before they gave birth (between 1 January 2021 and 31 January 2022) (36). In the USA more than 200,000 women have indicated they were pregnant at the time they received COVID-19 vaccination to 14 March 2022 (37).

No safety concerns relating to COVID-19 vaccination of pregnant women have been found in published studies to date (38 to 41). The rate of vaccine side-effects appears to be similar in pregnant and non-pregnant populations (38).

This report presents data on vaccine coverage and outcomes for women delivering up to the end of December 2021 and updates the early data on COVID-19 vaccination in pregnant women published in the COVID-19 vaccine surveillance report – weeks 47 of 2021, 4 of 2022 and 8 of 2022. Findings continue to be considered preliminary.

Vaccine coverage

COVID-19 vaccine coverage in women before they give birth has increased as more women have become eligible for vaccination. In November 2021, 48.6% of women giving birth had received at least one dose of vaccine. This increased to 53.7% of women who gave birth in December 2021. Of women who gave birth in November 2021, 38.3% had received 2 doses of the vaccine increasing to 43.3% of women who gave birth in December 2021 (see Table 9).

In the overall period between January and December 2021 a total of 528,362 women gave birth of whom 102,089 had received at least 1 dose of COVID-19 vaccine prior to delivery (68,952 of these women had received at least 2 doses and 4,456 women had received at least 3 doses). There were 11,492 women who had received their first dose prior to pregnancy and went on to conceive and deliver by December 2021. There were 14,895 women who were vaccinated in the first trimester, 37,916 in the second and 45,980 in the third trimester. In addition, 28,994 women were known to have received dose one before giving birth but without enough

information to establish which trimester. Of these women, 21,801 were known to have received this dose in pregnancy, and 7,143 were around the start of pregnancy.

Of all vaccinated women giving birth, 64,109 had received one or more doses of only Pfizer vaccine, 3,857 one or more doses of only Moderna, 4,598 one or more doses of only AstraZeneca and the remaining 29,525 of vaccinated women received a mixture of doses: 19,267 received a combination of Pfizer and Moderna and 10,252 received AstraZeneca with Pfizer or Moderna.

Table 9. Overall vaccine coverage in women giving birth, by month of delivery¹

Month	Women giving birth	One or more doses by time of delivery	Two or more doses by time of delivery	Unvaccinated at delivery	Unvaccinated who went on to receive dose(s) after pregnancy to 14 March 2022
Jan 2021	41,949	18 (0.0%)	1 (0.0%)	41,773 (99.6%)	32,026 (76.7%)
Feb 2021	40,093	82 (0.2%)	0 (0.0%)	39,878 (99.5%)	30,587 (76.7%)
Mar 2021	44,589	294 (0.7%)	25 (0.1%)	44,174 (99.1%)	33,630 (76.1%)
Apr 2021	42,864	492 (1.1%)	93 (0.2%)	42,217 (98.5%)	31,726 (75.1%)
May 2021	44,172	1,252 (2.8%)	306 (0.7%)	42,752 (96.8%)	31,271 (73.1%)
Jun 2021	43,815	4,354 (9.9%)	646 (1.5%)	39,321 (89.7%)	27,406 (69.7%)
Jul 2021	47,444	7,700 (16.2%)	2,201 (4.6%)	39,561 (83.4%)	26,018 (65.8%)
Aug 2021	46,202	10,482 (22.7%)	6,124 (13.3%)	35,536 (76.9%)	21,748 (61.2%)
Sep 2021	46,723	15,101 (32.3%)	10,519 (22.5%)	31,441 (67.3%)	17,395 (55.3%)
Oct 2021	46,212	19,209 (41.6%)	14,654 (31.7%)	26,808 (58.0%)	13,082 (48.8%)
Nov 2021	42,768	20,793 (48.6%)	16,389 (38.3%)	21,811 (51.0%)	8,203 (37.6%)
Dec 2021	41,531	22,312 (53.7%)	17,994 (43.3%)	19,029 (45.8%)	4,739 (24.9%)

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¹1,972 women could not be matched with a NIMS record. Their vaccine status is therefore unknown and they are excluded from these figures.

Table 10. Vaccine coverage by ethnicity, for women giving birth October to December 2021 (latest 3 months)²

	Women giving birth in October to December 2021	One or more doses by time of delivery	Two or more doses by time of delivery	Unvaccinated at delivery	Unvaccinated who went on to receive dose(s) after pregnancy to 14 March 2022
Asian	15,927	6,749 (42.4%)	4,983 (31.3%)	9,178 (57.6%)	4,227 (46.1%)
Black	6,042	1,504 (24.9%)	1,014 (16.8%)	4,538 (75.1%)	1,089 (24.0%)
Other	5,105	2,040 (40.0%)	1,658 (32.5%)	3,065 (60.0%)	990 (32.3%)
Mixed	3,111	1,197 (38.5%)	0,947 (30.4%)	1,914 (61.5%)	506 (26.4%)
White	93,595	48,075 (51.4%)	38,267 (40.9%)	45,520 (48.6%)	17,947 (39.4%)
Unknown	6,731	2,749 (40.8%)	2,168 (32.2%)	3,433 (51.0%)	1,265 (36.8%)

Table 11. Vaccine coverage by quintile of deprivation of the small area in which the woman lived, for women giving birth October to December 2021 (latest 3 months)³

	Women giving birth in October to December 2021		Two or more doses by time of delivery	Unvaccinated at delivery	Unvaccinated who went on to receive dose(s) after pregnancy to 14 March 2022
1 - most deprived	31,180	10,208 (32.7%)	6,844 (21.9%)	20,972 (67.3%)	5,962 (28.4%)
2	28,348	11,916 (42.0%)	9,009 (31.8%)	16,432 (58.0%)	5,869 (35.7%)
3	25,051	12,759 (50.9%)	10,205 (40.7%)	12,292 (49.1%)	5,116 (41.6%)
4	23,415	13,424 (57.3%)	11,015 (47.0%)	9,991 (42.7%)	4,848 (48.5%)
5 - least deprived	21,143	13,675 (64.7%)	11,721 (55.4%)	7,468 (35.3%)	4,070 (54.5%)
Unknown	1,374	332 (24.2%)	243 (17.7%)	493 (35.9%)	159 (32.3%)

² 549 women could not be matched with a NIMS record. Their vaccine status is therefore unknown and they are excluded from these figures.

³ 549 women could not be matched with a NIMS record. Their vaccine status is therefore unknown and they are excluded from these figures.

Table 12. Vaccine coverage by age of mother, for women giving birth October to December 2021 (latest 3 months)⁴

Age	Women giving birth in October to December 2021	One or more doses by time of delivery	Two or more doses by time of delivery	Unvaccinated at delivery	Unvaccinated who went on to receive dose(s) after pregnancy to 14 March 2022
Under 20	2,689	499 (18.6%)	255 (9.5%)	2,190 (81.4%)	421 (19.2%)
20 to 24	14,963	4,127 (27.6%)	2,477 (16.6%)	10,836 (72.4%)	3,024 (27.9%)
25 to 29	33,616	12,846 (38.2%)	9,102 (27.1%)	20,770 (61.8%)	7,977 (38.4%)
30 to 34	45,803	24,815 (54.2%)	20,210 (44.1%)	20,988 (45.8%)	9,249 (44.1%)
35 to 39	26,372	16,100 (61.0%)	13,697 (51.9%)	10,272 (39.0%)	4,376 (42.6%)
40 and above	6,507	3,927 (60.4%)	3,296 (50.7%)	2,580 (39.6%)	0,977 (37.9%)

⁴ 549 women could not be matched with a NIMS record. Their vaccine status is therefore unknown and they are excluded from these figures.

In the most recent 3-month period, there were 130,511 women whose vaccination record was linked and who gave birth, of whom 62,314 (47.7%) were vaccinated. These women accounted for 61.0% of all vaccinated women giving birth since January. There were differences in vaccine coverage by both ethnicity (Table 10) and by quintile of deprivation (Table 11). Overall, 38.5% of women who were unvaccinated when they gave birth in the most recent 3-month period (October to December 2021) went on to be vaccinated post-partum. This included 24.0% of Black women and 46.1% of Asian women, lower than the proportions of unvaccinated women of these ethnicities who were immunised post-partum between September and November 2021 (33.0% and 54.5% respectively). Whilst increases in coverage were observed in all groups, women of black ethnicity (in whom one dose coverage increased from 20.5% to 24.9%) and women living in the most deprived areas in England (in whom one dose coverage increased from 25.5% to 32.7%) continue to be least likely to have been vaccinated with one or 2 doses of COVID-19 vaccine before they gave birth. Coverage increased as levels of deprivation decreased (Table 11). Vaccine coverage increased with increasing age group to those aged 35 to 39 years in whom uptake was 61.0% for one dose and 51.9% for 2 doses (Table 12), with similar coverage in women who were aged 40 years or over when they gave birth.

Methods

Data on COVID-19 vaccination status together with details of each vaccine administered are recorded in a central data set called the National Immunisation Management Service (NIMS)⁵. 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. 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. 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 diagnoses 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.

⁵ 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.

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

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 14 March 2022	
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 about trimester.

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 14 March 2022
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 used to generate Tables 10 to 12 was taken from the NIMS record. The analysis within this section was carried out on 14 March 2022. The latest HES data available were for December 2021, and all HES data since April 2021 is considered provisional.

Pregnancy outcomes

The following figures present rates of women in England who:

- 1. Gave birth to one or more live-born babies at term without low birthweight: that is, they experienced none of the following adverse outcomes considered (outcomes 2 to 4), according to their delivery record.
- 2. Gave birth to a stillborn baby (based on recorded diagnoses).
- 3. Gave birth to a baby with low birthweight (less than 2,500g) or a very low birthweight (less than 1,500g). The babies with a very low birthweight are therefore a subset of the low birthweight babies.
- 4. Gave birth prematurely (less than 37 weeks gestation), very prematurely (less than 32 weeks gestation) and extremely prematurely (less than 28 weeks gestation). The very premature and extremely premature are therefore a subset of women who gave birth prematurely.

These analyses assess whether rates were different in women giving birth between January and December 2021, who received one or more COVID-19 vaccination doses during their pregnancy compared with those who did not (either because they were unvaccinated or had only received vaccine doses prior to pregnancy). The analyses do not take other factors that might affect these outcomes into account, such as age (except for outcome 1 above) and whether the woman was categorised as clinically at risk. However, women who gave birth on or after 17 April 2021 without the reported complications (outcome 1 above), were also reviewed with vaccinations given from 16 April onwards. This is a more homogenous group of pregnant women who were eligible for vaccination based solely on age and not because they were considered at high risk of exposure or severe disease. Therefore, data are also presented for women giving birth between 17 April and 31 December 2021 for comparison.

Figure 4. Women giving birth January to December 2021 to live-born babies at term without low birthweight

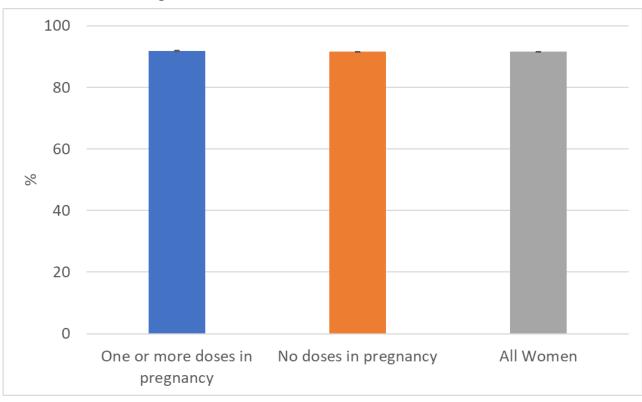


Figure 5. Women giving birth January to December 2021 to live-born babies at term without low birthweight, by age

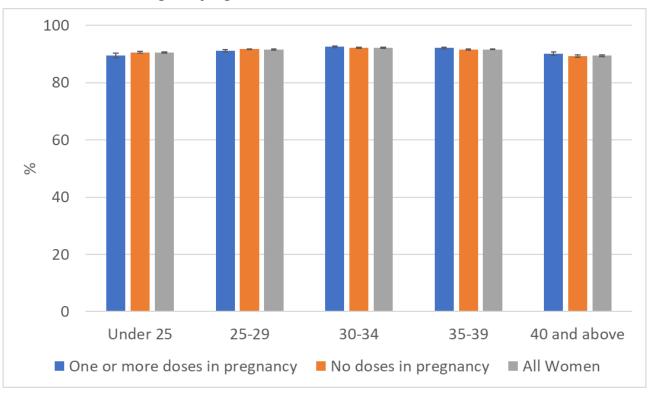


Figure 6. Women giving birth April to December 2021 to live-born babies at term without low birthweight

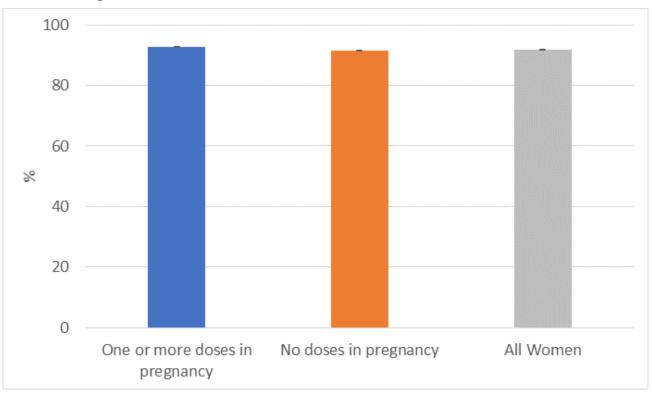


Figure 7. Women giving birth April to December 2021 to live-born babies at term without low birthweight, by age

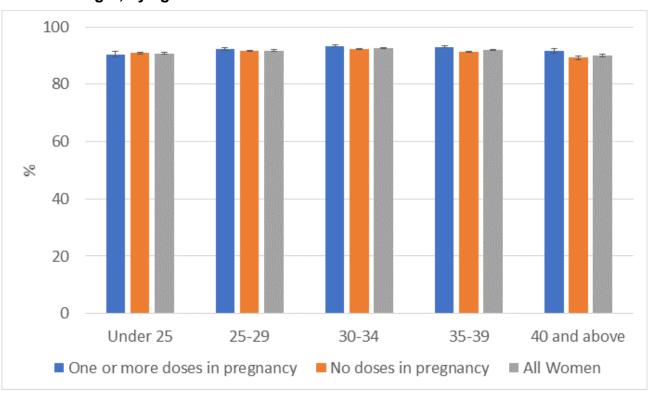


Figure 8. Stillbirths experienced by women giving birth January to December 2021

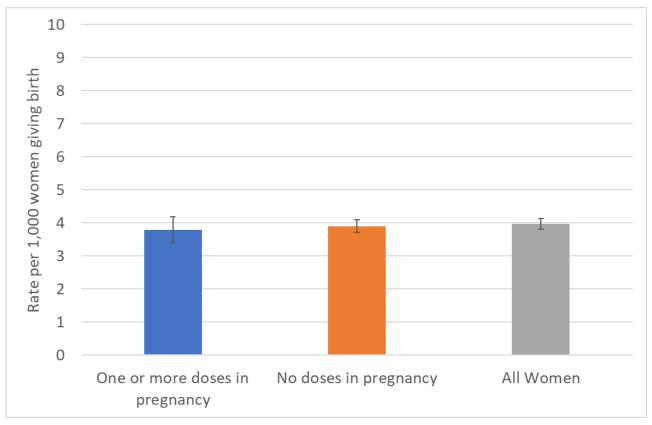
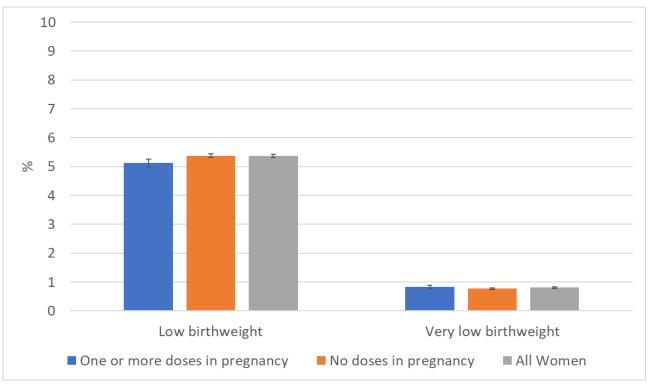


Figure 9. Low birthweight babies to women giving birth January to December 2021



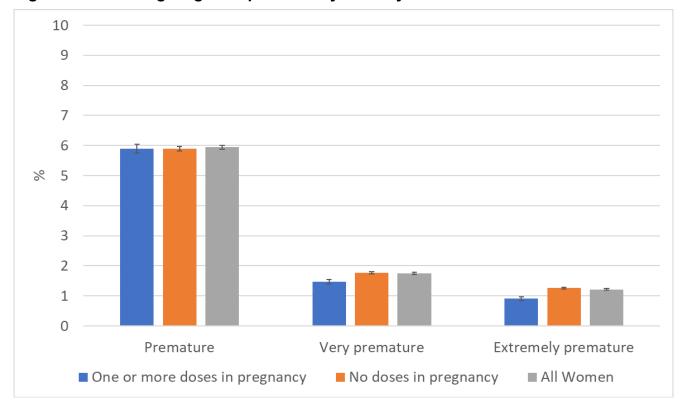


Figure 10. Women giving birth prematurely January to December 2021

The proportion of women giving birth between January and December 2021 to live-born babies at term without low birthweight (that is, with no specified adverse outcomes) having received one or more doses in pregnancy (91.8% 95%CI 91.7 to 92.0) is similar to the proportion in women who did not receive any doses in pregnancy (91.5% 95%CI 91.5 to 91.6) (Figure 4). These positive outcomes were similar across all age groups in vaccinated and unvaccinated women (Figure 5). For the more recent period (women vaccinated from 16 April and delivering from 17 April 2021), when all pregnant women were routinely offered vaccination on the basis of age, women who had received at least one dose of COVID-19 vaccine during their pregnancy were more likely to give birth without any of the reported adverse outcomes than women who had not been vaccinated in pregnancy (92.8% 95%CI 92.6 to 93.0 compared with 91.5% 95%CI 91.4 to 91.6) (Figure 6). This difference was more apparent in those aged 30 years and older (Figure 7).

The stillbirth rate for women who gave birth having received one or more doses in pregnancy (3.78 per 1,000, 95%Cl 3.41 to 4.19) was similar to the rate for those who had not received any doses in pregnancy (3.90 per 1,000, 95%Cl 3.72 to 4.09) giving birth between January and December 2021 (Figure 8). In the same period, the proportion of women who had received one or more doses in pregnancy giving birth to babies with low birthweight (5.12%, 95%Cl 4.98 to 5.26) was lower than those who had not received any doses in pregnancy (5.37%, 95%Cl 5.31 to 5.44) (Figure 6). There was no statistically significant difference between the 0.83% (95%Cl 0.78 to 0.89) of women who had received one or more doses in pregnancy and 0.77% (95%Cl 0.75 to 0.80) of those who had not, who gave birth to a very low birthweight baby (Figure 9).

The proportion of women who received one or more doses in pregnancy having premature births was 5.88% (95%CI 5.74 to 6.04), compared with 5.90% (95%CI 5.83 to 5.97) in those who had not (Figure 10). The proportion of women with very premature births was 1.46% (95%CI 1.39 to 1.54) in those who received one or more dose in pregnancy, lower than the 1.77% (95%CI 1.73 to 1.81) with a very premature birth who had not been vaccinated during pregnancy. The proportion of women with extremely premature births was 0.90% (95%CI 0.85 to 0.97) in those who received one or more dose in pregnancy: lower than the 1.26% (95%CI 1.22 to 1.29) in those who had not.

Interpretation and limitations

The first women to be offered COVID-19 vaccine were those who were categorised as at risk of severe disease and women of older age who are at increased risk of the 3 adverse 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 will thus account for a relatively high proportion of early deliveries in women who had received one or more doses of the vaccine before 16 April 2021. It is therefore very reassuring that women who had received at least one dose of the vaccine in pregnancy were more likely to deliver live born babies at term without low birthweight and had no overall increased risk of any adverse outcome through January to December.

These findings support the conclusions on vaccine safety from COVID-19 vaccine surveillance report – week 47 (COVID-19 vaccine weekly surveillance reports (week 39 2021 to week 3 2022).

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

Methods

The same methods as used to establish coverage figures were used to group records of deliveries into those who had received at least one dose of the vaccine during their pregnancy and those who had not. The definition of this second group includes any women who received dose(s) only prior to pregnancy and those who received their first dose after delivery, as well as those unvaccinated as of 14 March 2022. Outcomes are also presented by age at delivery, using the woman's date of birth as recorded in NIMS.

The following criteria were applied to identify deliveries where adverse outcomes were experienced. The outcomes are related: for example, babies born prematurely are more likely to

be born with low birthweight, and therefore a delivery may have more than one adverse outcome.

Stillbirths were identified as records where any one or more of the first 12 diagnoses was the following: Z37.1: Single stillbirth; Z37.3 Twins, one liveborn and one 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 2,499g (1,499g 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 (42). 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 53.7% for women who gave birth in December 2021 having had one or more dose before their baby was born. This is in line with coverage reported across the UK with 56% of women in Scotland (24) and 57.7% in Wales (36) delivering in December 2021 who had received any dose and their first dose of COVID-19 vaccine respectively prior to delivery.

As in the previous report, however, coverage increased with decreasing levels of deprivation and women of black ethnicity had the lowest vaccine coverage. Coverage increased with increasing age group to 35 to 39 years.

Whilst coverage has improved since the November coverage presented in the week 8 report, across all groups it continues to highlight inequalities consistent with those seen across the entire COVID-19 vaccination programme. Coverage of at least one dose increased from 5.5% in women of black ethnicity who delivered between June and August 2021 to 20.5% of these women delivering between September and November 2021 and further to 24.9% in December 2021. The difference in coverage between black and white women was 26.5 percentage points for women delivering between October to December, compared to 28.3 percentage points in the September to October period. In women living in the most deprived areas in England coverage increased from 7.8% to 25.5% to 32.7% in the same period. In addition, 24% of Black women and 28.4% of women living in the most deprived areas who were unvaccinated went on to be vaccinated post-partum.

It is very reassuring that women who had received at least one dose of the vaccine in pregnancy were as likely to deliver live born babies at term without low birthweight as women who were not vaccinated in pregnancy. In addition, the group of women who were most likely to be immunised on the basis of their age group alone (vaccinated from 16 April 2021 and giving birth from 17 April 2021) were significantly more likely to deliver live born babies at term without low birthweight than women giving birth in the same period who were not vaccinated in pregnancy.

The specific outcomes that were considered (stillbirth, low birthweight and premature delivery) were similar or lower in women who were vaccinated whilst pregnant compared to women who were not vaccinated during their pregnancy.

Vaccination status in cases, deaths and hospitalisations

Data on the vaccination status of COVID-19 cases, and deaths and hospitalisations with COVID-19, was previously 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.

From 1 April 2022, the UK Government ended provision of free universal COVID-19 testing for the general public in England, as set out in the plan for <u>living with COVID-19</u>. Such changes in testing policies affect the ability to robustly monitor COVID-19 cases by vaccination status, therefore, from the week 14 report onwards this section of the report will no longer be published. For further context and previous data, please see previous vaccine surveillance reports and our blog post.

Vaccine effectiveness is measured in other ways as detailed in the <u>vaccine effectiveness</u> section 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 week 35 2020 and week 12 2022 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. This update was published on 7 April 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. 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

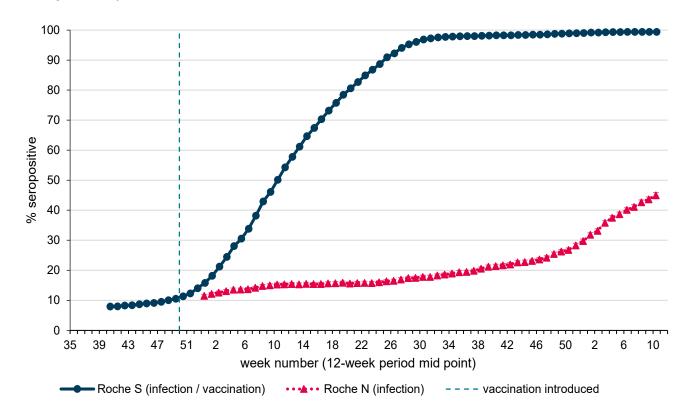
estimate of seropositivity. However, this also means the data will reflect seroprevalence several weeks previously. Seroprevalence estimates reported are based on seropositivity which are unadjusted for the sensitivity and specificity of the assays used.

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 45.0% (95% CI 44.1% - 45.9%) using the Roche N assay and 99.4% (95% CI 99.2% - 99.5%) using the Roche S assay for the period 31 January to 27 March (weeks 5 to 12 2022). 6,426 out of 14,507 were Roche N positive and 14,422 out of 14,511 samples were Roche S positive. This compares with 26.8% (95% CI 26.1% - 27.5%) Roche N seropositivity and 98.9% (95% CI 98.7% - 99.1%) Roche S seropositivity for the period of 8 November 2021 to 28 January 2022 (weeks 45 2021 to 4 2022).

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

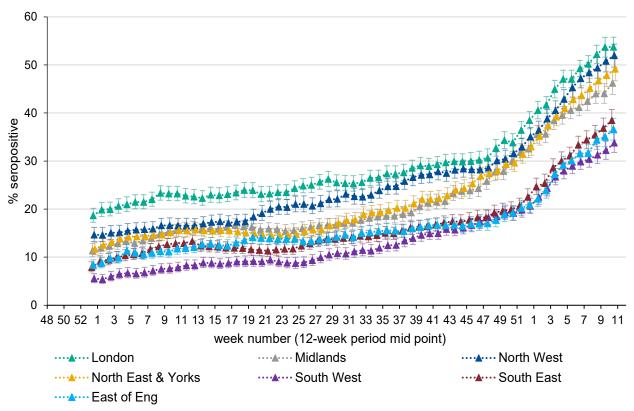


Table 13. Roche N seropositivity (95%CI) estimates by NHS region

NHS region	Weeks 45 2021 to 4 2022	Weeks 5 to 12 2022
East of England	19.2% (17.7% - 20.8%)	36.6% (34.4% - 38.9%)
London	33.8% (32.0% - 35.7%)	53.7% (51.7% - 55.8%)
Midlands	29.9% (28.3% - 31.7%)	46.2% (43.9% - 48.6%)
North East and Yorkshire	29.6% (27.9% - 31.4%)	49.2% (46.7% - 51.7%)
North West	31.6% (29.8% - 33.4%)	52.0% (49.6% - 54.3%)
South East	19.9% (18.4% - 21.5%)	38.5% (36.2% - 40.7%)
South West	19.1% (17.7% - 20.6%)	33.8% (31.8% - 35.9%)

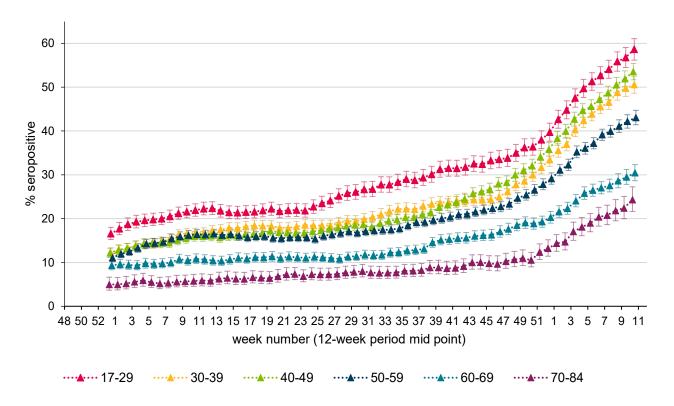
Increases in Roche N seropositivity have recently been observed across all regions (Table 13) compared to the previous 12-week period with the most notable increases in London, North West and North East and Yorkshire regions.

Whilst seropositivity has consistently been lowest in the South West, recent increases have resulted in the region now having similar levels as observed in the East of England. With the emergence of Omicron variant, cases increased considerably and peaked in week 1 2022 and then declined. In the most recent weeks, case rates have increased again across all regions. (Weekly national Influenza and COVID-19 surveillance report week 13 2022). Since it takes approximately 2 to 3 weeks to develop an antibody response following infection, recent rises in seroprevalence will likely reflect infection during the initial peak of the Omicron wave and up to early March 2022.

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 (Figure 13) 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 14. Roche N seropositivity (95%CI) estimates by age group

Age group	Weeks 45 2021 to 4 2022	Weeks 5 to 12 2022
17 to 29	36.4% (34.5% to 38.4%)	58.7% (56.2% to 61.1%)
30 to 39	30.0% (28.5% to 31.5%)	50.6% (48.6% to 52.5%)
40 to 49	32.1% (30.6% to 33.6%)	53.5% (51.7% to 55.4%)
50 to 59	26.5% (25.3% to 27.8%)	43.1% (41.4% to 44.7%)
60 to 69	18.8% (17.6% to 20.2%)	30.5% (28.7% to 32.3%)
70 to 84	10.5% (9.0% to 12.3%)	24.3% (21.6% to 27.2%)

Increases in Roche N seropositivity have recently been observed across all age groups (Table 14) compared to the previous 12-week period. In the most recent period, the largest increase in seropositivity was observed in the 3 youngest age groups. In England, COVID-19 case rates for weeks 8 to 12 2022, have increased across most adult age groups with the highest rates currently seen in individuals aged 30 to 39 followed by 40 to 49 years old (Weekly national Influenza and COVID-19 surveillance report week 13 2022).

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) 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 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 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 98% 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.

Figure 14 shows monthly categorised Roche S levels in N-antibody negative individuals by age group over the past year. In the 3 oldest age groups, the impact of first vaccine dose, then second vaccine dose, can be seen from April through June 2021, 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 10,000+ 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. In December large increases were observed in the proportion of donors aged 50 to 69 with very high antibody levels of 10,000+ au/ml. By January 2022 large increases were also observed in younger age groups as the booster programme was accelerated due to the emergence of the Omicron variant, however the slightly decreasing profile of antibody levels among all age groups in February and March shows signs of waning. Given the evidence of waning, those most at risk are being offered a booster vaccine in the spring.

Figure 15 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. In November more than half of donors aged 70 to 84 years had very high antibody levels of 25,000+ au/ml. By January 2022 increases in the proportion of donors with very high antibody levels of 25,000+ au/ml were observed across all age groups. The proportion of donors with very high antibody levels of 25,000+ au/ml remained stable during February and March 2022. Comparing Figure 14 with Figure 15, 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, April 2021 to March 2022

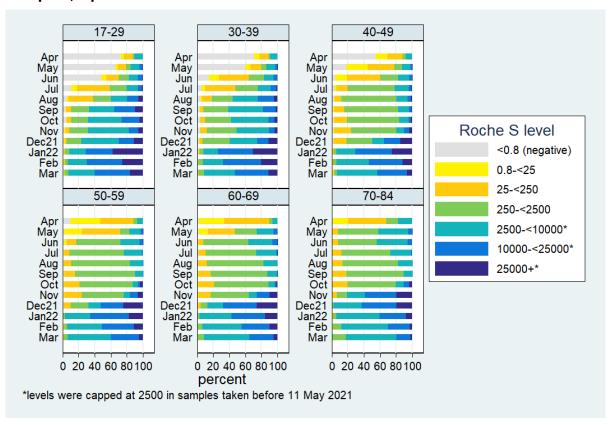
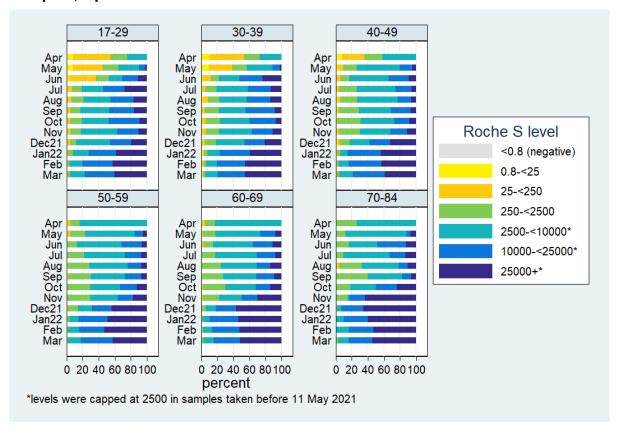


Figure 15. Categorised Roche S antibody levels by age group and month in N positive samples, April 2021 to March 2022.



Direct impact on hospitalisations

The analysis estimates the number of hospitalisations averted by booster vaccinations in the period since 13 December 2021 when Omicron infections started to become more dominant. The booster vaccination programme was accelerated and expanded to all adults aged 18 years and over from November 2021 in response to a rapid increase in Omicron infections.

The number of hospitalisations averted is estimated by incorporating vaccine effectiveness against hospitalisation, vaccine coverage and observed hospitalisations (the latter from UKHSA's surveillance system called SARI-Watch). The focus of the calculation in this model is hospitalisations averted in the Omicron period given the coverage of booster vaccinations. This allows us to model the expected number of hospitalisations in the absence of the booster vaccination programme.

The <u>most recent</u> estimates for vaccine effectiveness (VE) from the booster vaccines against hospitalisations are used in this analysis. These estimates are based on a specific hospitalisation end point involving at least 2 days hospital stay plus a respiratory diagnosis code, estimated for infected people aged 18 to 64 years 65 years and over. However this may overestimate the effect if a large proportion of hospitalised cases reported to SARI-watch were admitted for less than 2 days or did not have respiratory symptoms.

Due to the specific hospitalisation endpoint used, VE estimates have increased particularly in the period following the booster dose compared to previous VE estimates for the booster dose. The estimates used for 65 years and over are:

- 89% from the booster against Omicron in the period 5 to 9 weeks post booster applied to the data from 13 December 2021 to 9 January 2022
- 88% from the booster against Omicron in the period 10 to 14 weeks post booster applied to the data from 10 January 2022 to 13 February 2022
- 85% from the booster against Omicron in the period 15 weeks + post booster applied to the data from 14 February 2022 to 3 April 2022
- 58% for the second dose at 25 weeks and over applied to all dates

The estimates used for 18 to 64 years used are:

- 86% from the booster against Omicron in the period 5 to 9 weeks post booster applied to the data from 13 December 2021 to 12 February 2022
- 80% from the booster against Omicron in the period 10 to 14 weeks post booster applied to the data from 13 February 2022 to 19 March 2022
- 67% from the booster against Omicron in the period 15 weeks + post booster applied to the data from 20 March 2022 to 3 April 2022
- 56% for the second dose at 25 weeks and over applied to all dates

The same estimates are applied to the data for 25 to 44 years and 45 to 64 years.

Using these estimates, the relative effectiveness (rVE) of the booster (at 5 to 19 weeks, 10 to 14 weeks or at 15 weeks+) compared to 2 doses at 25 weeks+ can be calculated. For example, the rVE of the booster at 15 weeks+ compared to the 2 doses at 25 weeks+ for the group aged 65 years is:

$$1-(1-0.85)/(1-0.58) = 64\%$$

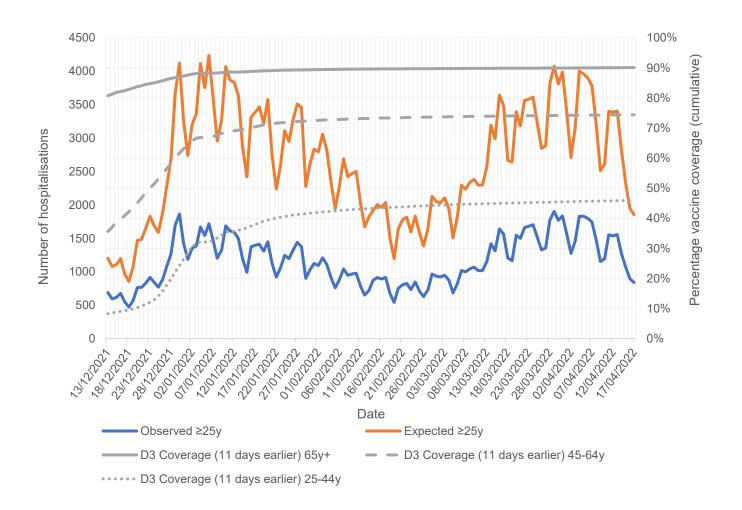
The expected cases in the absence of boosting is calculated as O_{0/1}+ [O_{2/boost} / (1- (booster cover/(booster cover + 2 dose cover))*rVE)], where O_{0/1} is observed hospitalised cases with 0 or 1 doses and O_{2/boost} is observed cases with 2 doses or more (note that these observed totals are in fact estimated using information from the subset of SARI-Watch cases where this information is ascertained, with weekly proportions with each dose number applied to the daily overall hospitalisation numbers). The daily expected cases are calculated per age group and summed for an overall total per age group in the period. The overall total per age group is summed to provide the all age total across the period. This is the same for the observed calculation. The expected number of hospitalisations is then subtracted from the total observed number of hospitalisations. The difference gives us an estimate of the number of hospitalisation events.

Based on the direct effect of the booster vaccination and booster vaccine coverage rates, UKHSA estimates that around 186,600 hospitalisations have been prevented in those aged 25 years and over in England from 13 December 2021 to 17 April 2022 inclusive. the total number averted by age group is approximately 162,300 in those aged 65 years and over, 18,100 in those aged 45 to 64 years and 6,100 in those aged 25 to 44 years as a result of the booster vaccination programme (Figure 16). All those aged 25 to 64 years in this analysis are inclusive of healthy and at-risk individuals.

Several caveats are necessary to consider. The indirect effect of protection from infection and onwards transmission is not considered. Any indirect effects are likely to be small given the low and rapidly waning vaccine effectiveness against mild disease/infection observed with the Omicron variant. Finally these estimates are likely to include some effect of spring booster vaccinations – particularly among individuals aged 75 years and over, who are one of the target groups for the latest campaign, rolled out from 21 March 2022. The other target group are younger people who are immuno-compromised - the spring booster effect may be included in the estimates for hospitalisations in those aged 25 to 64 years.

Please note this analysis will be no longer be updated after this edition of the report due to the effect of the spring booster programme appearing increasingly in uptake data for 3 doses or more. This makes it difficult to assess the impact of initial booster on hospitalisations separately from the effects of the latest campaign.

Figure 16. Estimated number of hospitalisations averted by booster vaccinations since 13 December 2021



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