

COVID-19 vaccine surveillance reportWeek 46

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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 and 2 doses of COVID-19 vaccines. By 14 November 2021, the overall vaccine uptake in England for dose 1 was 67.2% and for dose 2 was 61.3%. In those aged 12 to under 16, vaccine uptake for dose 1 was 35.8%. 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. **These 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, 98.1% of the adult population now have antibodies to COVID-19 from either infection or vaccination compared to 20.2% that have antibodies from infection alone.

Vaccine effectiveness

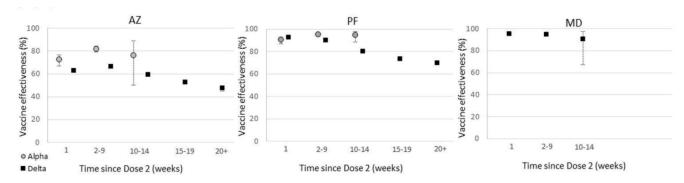
Large clinical trials have been undertaken for each of the COVID-19 vaccines approved in the UK which found that they are highly efficacious at preventing symptomatic disease in the populations that were studied. The clinical trials have been designed to be able to assess the efficacy of the vaccine 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 (Figure 1, 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

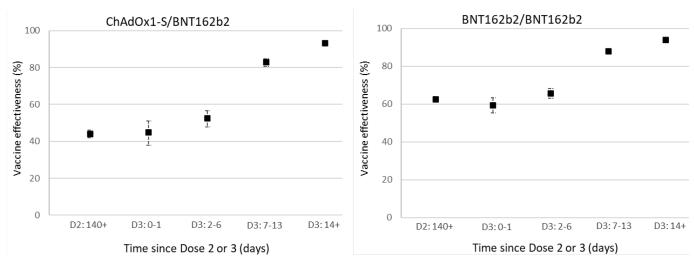


Data (based primarily on the Alpha variant) suggest that in most clinical risk groups, immune response to vaccination is maintained and high levels of VE are seen with both the Pfizer and AstraZeneca vaccines. Reduced antibody response and vaccine effectiveness were seen after 1 dose of vaccine among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

Early data on booster vaccination in adults aged 50 years and older indicate that after a booster dose of the Pfizer-BioNTech vaccine, vaccine effectiveness increases to 93.1% among those who received the AstraZeneca vaccine as their primary course and 94.0% among those who received the Pfizer-BioNtech vaccine as their primary course (Figure 2, 7)

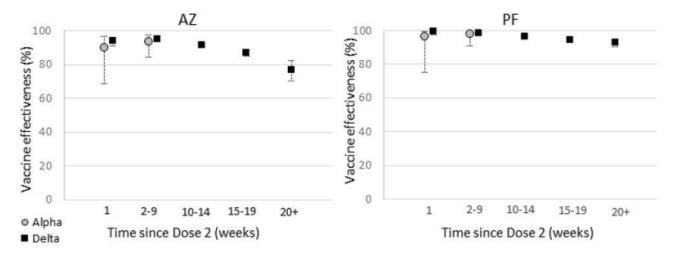
Figure 2. Vaccine Effectiveness estimates in time intervals post booster according to primary course: Unvaccinated baseline



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 (Figure 3, 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 (Figure 3, 3).

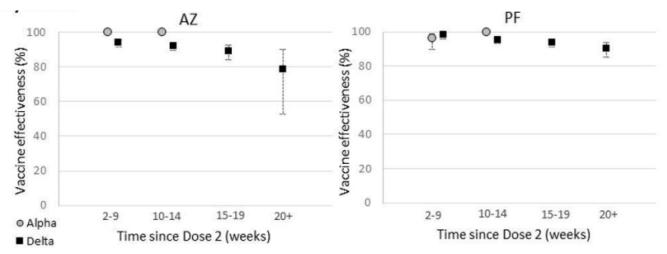
Figure 3. Vaccine effectiveness against Delta hospitalisation among individuals aged over 16, with 2 doses of Vaxzevria (AZ), Comirnaty (PF) or Spikevax (MD) in England and 95% confidence intervals



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 4</u>, <u>8</u>, <u>12</u>, <u>3</u>). Relatively limited waning of protection against mortality is seen over a period of at least 5 months.

Figure 4. 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 65-80% 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 Table 1.

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

	Vaccir			
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 publications

UKHSA have published a significant amount of <u>research into vaccine effectiveness</u>, which is summarised on pages 5 to 8 and in the publications in table 2.

Table 2. UKHSA publications on the effectiveness of COVID-19 vaccination

Publication	Subject
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 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.
Effectiveness of BNT162b2 mRNA and ChAdOx1 adenovirus vector COVID-19 vaccines on risk of hospitalisation among older adults in England: an observational study using surveillance data	A study using the SARI watch surveillance system of COVID-19 hospitalisations found high levels of protection against hospitalisation after both a single dose and 2 doses of COVID-19 vaccines.
Effectiveness of BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on mortality following COVID-19	A study on deaths with COVID-19 indicates that COVID-19 vaccines offer high levels of protection against mortality.
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

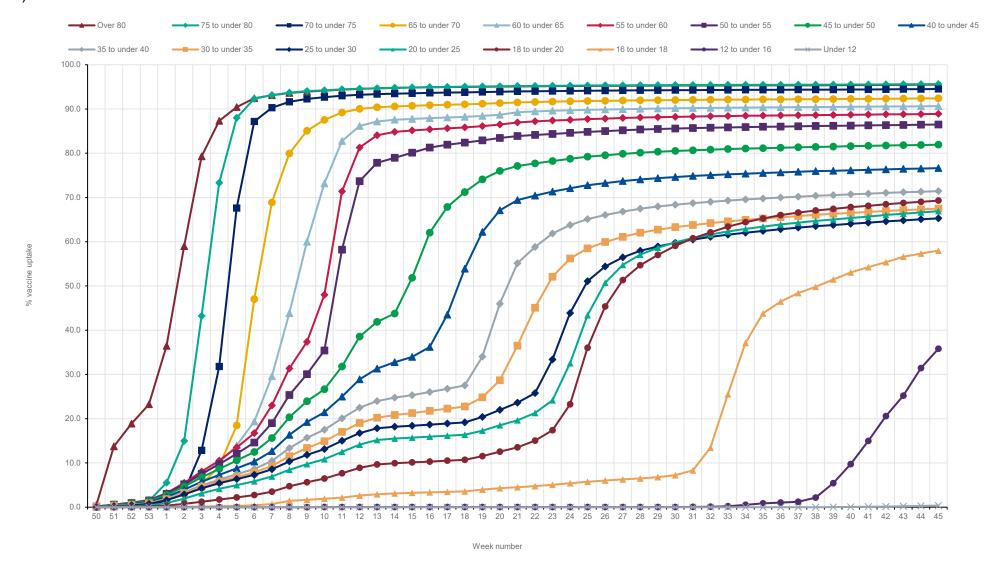
The data in this week's report covers the period from 8 December 2020 to 14 November 2021 (week 45) (Figure 5). It shows the provisional number and percentage of people in England who have had received 1 dose or 2 doses of a COVID-19 vaccination by age group and week since the start of the programme. Please note a change in the definition of age-cohorts has now been implemented and backdated in the following data on vaccine uptake. Age is calculated as age on the 31 August 2021 i.e. academic cohort for all ages.

Up to 31 October 2021 84,674 women of child-bearing age in England (under 50) who reported that they were pregnant or could be pregnant at the time, received at least 1 dose of COVID-19 vaccination and of these, 80,728 have received their second dose. This is in response to the self-reported pre-screening question "Are you or could you be pregnant?". The true number of pregnant women who have had a COVID-19 vaccination is likely to be greater than this.

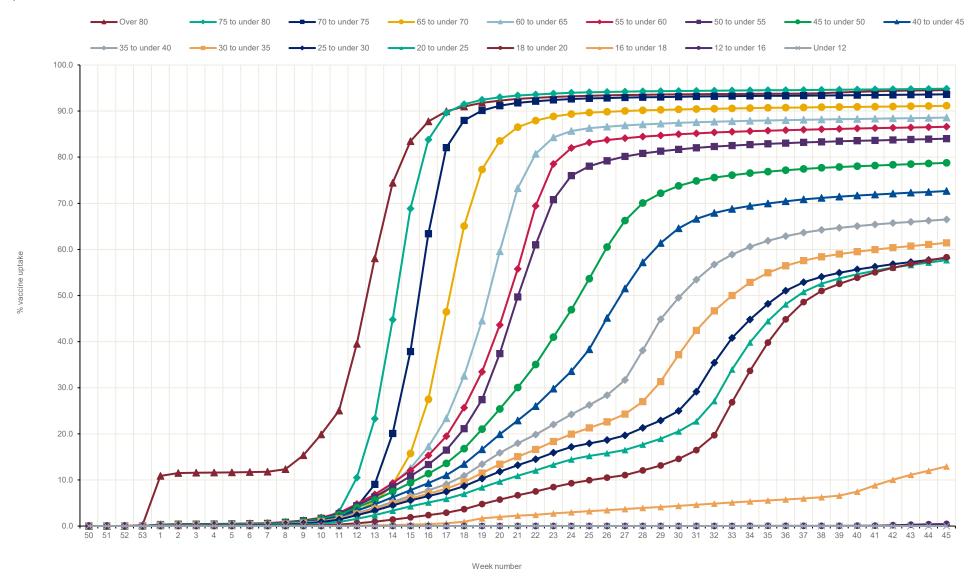
Please note that pregnant women are not a separate priority group as defined by JCVI who have advised that "women who are pregnant should be offered vaccination at the same time as non-pregnant women, based on their age and clinical risk group" therefore comparing vaccine uptake in pregnant women to other vaccination programmes is not currently appropriate. The MHRA closely monitors the safety of COVID-19 vaccine exposures in pregnancy, including Yellow Card reports for COVID-19 vaccines used in pregnancy, for the latest information please see the webpage Coronavirus vaccine – weekly summary of Yellow Card reporting.

Figure 5. Cumulative weekly vaccine uptake by age

a) Dose 1



b) Dose 2



Vaccination status

Vaccination status of COVID-19 cases, deaths and hospitalisations by week of specimen date over the past 4 weeks up to week 45 (up to 14 November 2021) are shown in <u>Tables 3 to 5</u>.

These data are 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. **These raw data should not be used to estimate vaccine effectiveness.**

We have published a blog 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 here, 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 are 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 report 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 6</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

These 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 8 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 here and here.

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 have published a blog to accompany this section of the report.

The Office of the Statistics Regulator have published a blog.

UKHSA have published a significant amount of <u>research into vaccine effectiveness</u> which is summarised on pages 5 to 8 of this report.

The Office for National Statistics have 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 (4), and the risk of death by vaccination status.

Table 3. COVID-19 cases by vaccination status between week 42 and week 45 2021 Please note that corresponding rates by vaccination status can be found in Table 6.

Cases reported by specimen date between week 42 and week 45 2021	Total	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date¹
Under 18	313,716	19,133	255,755	19,103	18,886	839
18-29	84,503	8,379	26,714	725	8,937	39,748
30-39	122,367	8,981	27,457	646	7,325	77,958
40-49	154,671	8,503	15,920	270	4,042	125,936
50-59	117,722	5,890	7,152	98	1,947	102,635
60-69	68,181	3,425	2,739	45	863	61,109
70-79	34,455	1,891	1,067	14	251	31,232
≥80	11,863	838	540	11	176	10,298

^{*}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 4. 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 42 and week 45 2021

Please note that corresponding rates by vaccination status can be found in <u>Table 6</u>.

Cases presenting to emergency care (within 28 days of a positive test) resulting in overnight inpatient admission, by specimen date between week 42 and week 45 2021	Total	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date¹
Under 18	553	14	508	15	16	0
18-29	398	8	278	6	28	78
30-39	807	7	489	10	56	245
40-49	1,117	15	534	2	45	521
50-59	1,497	13	550	2	51	881
60-69	1,591	7	376	4	26	1,178
70-79	2,047	5	261	3	26	1,752
≥80	1,821	2	204	1	36	1,578

^{*}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 5. 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 42 and week 45 2021

Please note that corresponding rates by vaccination status can be found in Table 6.

(a)

Death within 28 days of positive COVID-19 test by date of death between week 42 and week 45 2021	Total**	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date¹
Under 18	11	1	10	0	0	0
18-29	12	0	9	0	2	1
30-39	40	1	25	0	4	10
40-49	91	3	44	0	3	41
50-59	232	5	102	0	9	116
60-69	548	4	151	0	20	373
70-79	991	7	153	0	16	815
≥80	1,751	5	181	3	43	1,519

(b)

Death within 60 days of positive COVID-19 test by date of death between week 42 and week 45 2021	Total**	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date ¹
Under 18	14	1	12	0	1	0
18-29	13	0	9	0	2	2
30-39	51	1	32	0	4	14
40-49	120	3	55	0	6	56
50-59	286	5	123	0	11	147
60-69	661	5	185	0	21	450
70-79	1,157	8	166	0	23	960
≥80	2,057	5	201	4	57	1,790

^{*}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 6. 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 14-16 of this report, and the footnotes provided on

page 22.

page	Cases reported specimen date to week 42 and we	oetween	Cases presenting to emergency care (within 28 days of a positive test) resulting in overnight inpatient admission, by specimen date between week 42 and week 45 2021		Death within 28 days of positive COVID-19 test by date of death between week 42 and week 45 2021		Death within 60 days of positive COVID-19 test by date of death between week 42 and week 45 2021	
	Unadjusted rates among persons vaccinated with 2 doses (per 100,000) ^{1,2}	Unadjusted rates among persons not vaccinated (per 100,000) ^{1,2}	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	Unadjusted rates among persons vaccinated with 2 doses (per 100,000) ²	Unadjusted rates among persons not vaccinated (per 100,000) ²
Under 18	531.2	2,301.2	0.0	4.6	0.0	0.1	0.0	0.1
18-29	713.2	805.2	1.4	8.4	0.0	0.3	0.0	0.3
30-39	1,314.9	948.7	4.1	16.9	0.2	0.9	0.2	1.1
40-49	2,043.5	929.5	8.5	31.2	0.7	2.6	0.9	3.2
50-59	1,442.9	689.6	12.4	53.0	1.6	9.8	2.1	11.9
60-69	1,061.1	495.4	20.5	68.0	6.5	27.3	7.8	33.5
70-79	660.9	420.9	37.1	103.0	17.2	60.4	20.3	65.5
≥80	383.2	417.9	58.7	157.9	56.5	140.1	66.6	155.5

COVID-19 vaccine surveillance report - week 46

¹Comparing 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 8 in this report.

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

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 15 of this report and in the further resources below.

Sources of further information

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

The Office of the Statistics Regulator have published a blog.

UKHSA have published a significant amount of <u>research into vaccine effectiveness</u> which is summarised along with other sources on pages 5 to 9 of this report.

The Office for National Statistics have 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 (4) and the <u>risk of death by vaccination status</u>.

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 43 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. 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. Booster doses are given at least 6 months after the second dose.

Please note that this section will be updated monthly. Last update was published 11 November 2021.

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.

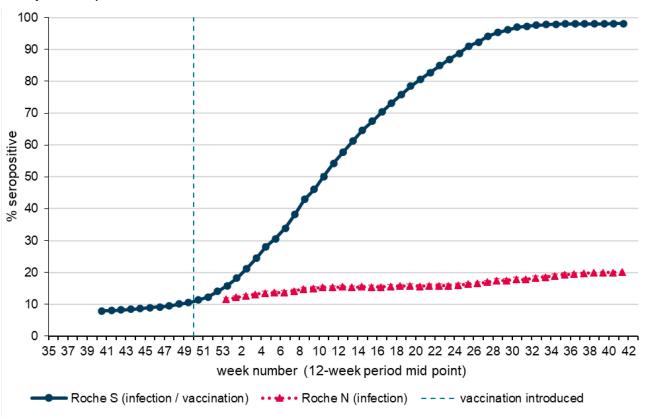
This report presents Roche N and Roche S seropositivity estimates on the same set of samples, using a 12-week rolling prevalence for national, age group and regional estimates. Seropositivity estimates are plotted using the mid-point of a 12-weekly rolling period that reduces to 8 weeks in the most recent 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 20.2% (95% CI 19.5% - 20.9%) using the Roche N assay and 98.1% (95% CI 97.9% - 98.4%) using the Roche S assay for the period 6 September to 29 October (weeks 36 to 43 2021). 2,778 out of 14,275 were Roche N positive and 14,038 out of 14,289 samples were Roche S positive. This compares with 17.5% (95% CI 16.9% - 18.0%) Roche N seropositivity and 96.1% (95% CI 95.8% - 96.4%) Roche S seropositivity for the period of 14 June to 5 September 2021 (weeks 24 to 35 2021).

Seropositivity (weighted by region, age group and sex) varies over time. Figure 6 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 6. 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 7).

Figure 7. 12-weekly rolling SARS-CoV-2 antibody seroprevalence (% seropositive) in blood donors by region, using Roche N test; error bars show 95% confidence intervals.

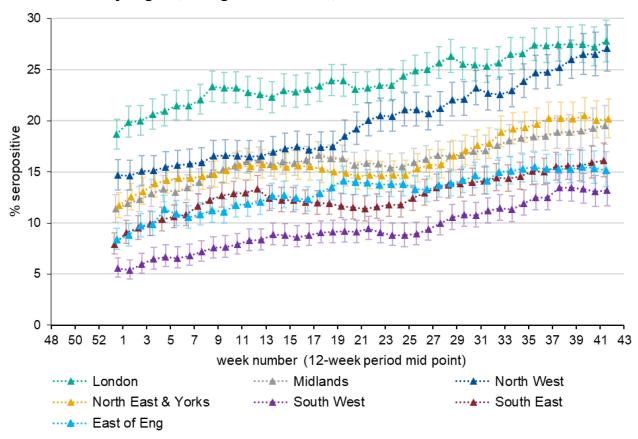


Table 7. Roche N seropositivity (95%CI) estimates by NHS region

NHS region	Weeks 24 - 35	Weeks 36 - 43
East of England	14.2% (13.0% - 15.5%)	15.2% (13.5% - 17.0%)
London	25.6% (24.0% - 27.2%)	27.8% (25.8% - 29.8%)
Midlands	16.6% (15.3% - 18.0%)	19.5% (17.7% - 21.5%)
North East and Yorkshire	17.1% (15.7% - 18.6%)	20.2% (18.3% - 22.2%)
North West	22.1% (20.5% - 23.8%)	27.1% (24.9% - 29.4%)
South East	13.8% (12.5% - 15.2%)	16.1% (14.5% - 17.8%)
South West	10.8% (9.7% - 12.1%)	13.2% (11.7% - 14.8%)

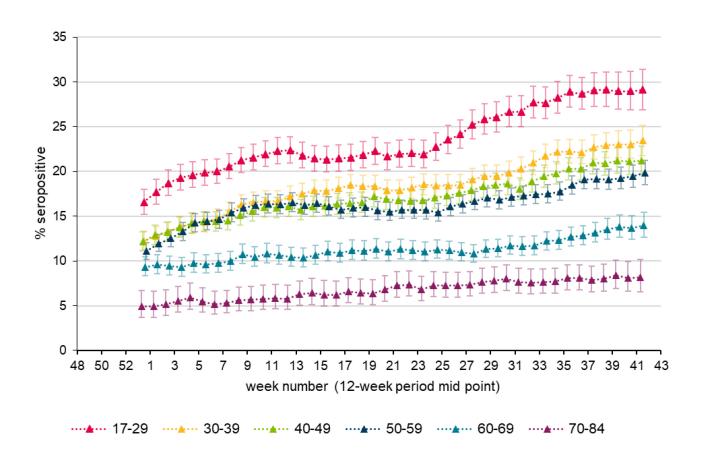
Increases in Roche N seropositivity have recently been observed across all regions (<u>Table 7</u>) compared to the previous 12-week period.

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.

Prevalence by age group

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

Figure 8. 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 8</u>) as a marker of infection, the highest seropositivity has consistently been observed in those aged 17 to 29 and the lowest in those aged 70 to 84.

Table 8. Roche N seropositivity (95%CI) estimates by age group

Age group	Weeks 24-35	Weeks 36-43
17-29	26.1% (24.4% - 27.8%)	29.1% (26.9% - 31.4%)
30-39	19.4% (18.2% - 20.7%)	23.4% (21.8% - 25.1%)
40-49	18.5% (17.3% - 19.8%)	21.2% (19.7% - 22.8%)
50-59	16.8% (15.8% - 17.8%)	19.8% (18.5% - 21.2%)
60-69	11.4% (10.5% - 12.5%)	14.0% (12.6% - 15.4%)
70-84	7.8% (6.5% - 9.3%)	8.2% (6.6% - 10.2%)

Small increases in Roche N seropositivity have recently been observed across all age groups (<u>Table 8</u>) compared to the previous 12-week period. Although COVID-19 case rates in England have plateaued or are falling across most age groups and regions in week 44 (<u>Weekly national Influenza and COVID-19 surveillance report week 44</u>) this is not expected to influence trends in Roche N seropositivity unless low infection rates are maintained for sustained periods of time.

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 UK Health Security Agency (UKHSA) surveillance data that N antibody levels appear to be lower in individuals who acquire infection following 2 doses of vaccination.

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 more recently in younger adults as part of phase 2 of the vaccination programme.

Roche S levels by age group and month

The Roche S assay that the UK Health Security Agency (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.

Figure 9 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 is a small increase in percentage of donors with high antibody levels of 1000+ AU/ml for the 70 to 84 age group only, following the initiation of the booster programme. 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 10</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 1000 AU/ml, after vaccination antibody levels typically exceed 1000 AU/ml. Comparing <u>Figure 9</u> with <u>Figure 10</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 9. Categorised Roche S antibody levels by age group and month in N negative samples, December 2020 to October 2021.

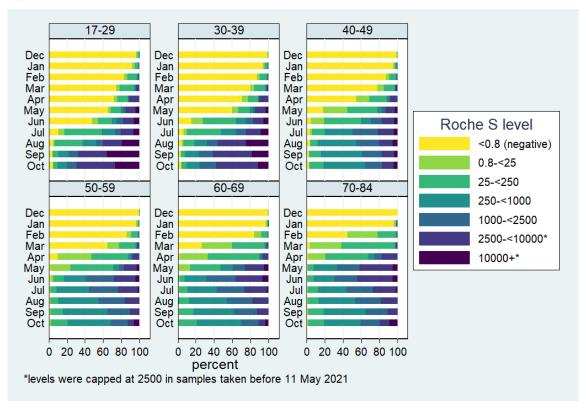
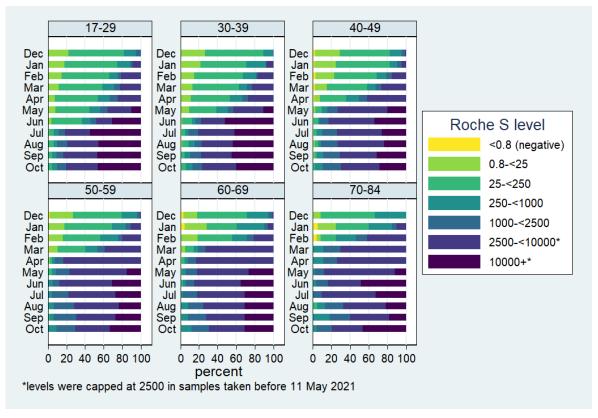


Figure 10. Categorised Roche S antibody levels by age group and month in N positive samples, December 2020 to October 2021.



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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About the UK Health Security Agency

The <u>UK Health Security Agency</u> is an executive agency, sponsored by the <u>Department</u> of Health and Social Care.

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Published: 18 November 2021 Publishing reference: GOV-10461

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