Early effectiveness of COVID-19 vaccination on symptomatic SARS-CoV-2 infection in the UK

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Early effectiveness of COVID-19 vaccination on symptomatic SARS-CoV-2 infection in the UK

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Abstract

Objectives

To estimate the real-world effectiveness of one and two doses of COVID-19 vaccination against Confirmed COVID-19 and on the new UK variant of concern

Design

Test negative case control design

Settings

Community COVID-19 PCR testing in England and Scotland

Participants

All adults in England aged 80 years and older and healthcare workers aged 65 years and under tested for COVID-19 in the community and reporting symptoms between 8th December 2020 and 17th January 2021. All adults in Scotland aged 65 years and under tested for COVID-19 in the community and reporting symptoms between 8th December 2020 and 17th January 2021.

Main outcome measures

Symptomatic PCR confirmed SARS-CoV-2 infection

Results

In England, 209,180 individuals were included in the analysis. Vaccinated individuals had a higher odds of testing positive in the first 9 days after vaccination, suggesting a higher background risk. In the >=80 years age group there is a notably reduced odds of testing positive from 21 days after the first dose of vaccination (OR 0.57; 95% CI 0.39-0.84), in those aged <65 years, the reduced odds is observed from 14 days after vaccination (OR 0.59; 95%CI 0.52-0.66). From 7 days after the second dose of vaccination the odds ratios were 0.32 (95%CI 0.11-0.96) in the >=80 years age group and 0.26 (95%CI: 0.14-0.52) in those aged <65 years. Results were similar when the analysis was restricted to those with S-gene target failure on PCR (a proxy for the UK variant of concern). Results for Scotland followed a similar pattern to those in England

Conclusion

This early analysis suggests that vaccination with a both a single dose and two doses of Pfizer/BioNTech COVID-19 vaccination is associated with a significant reduction in symptomatic SARS-CoV2 positive cases in both older and younger adults. There is a notable effect from 14 days after the first dose in younger adults, and around 21 days after the first dose in older adults. The vaccine also appears to be effective against the UK variant of concern.

Introduction

On the 8th December 2020 the UK became the first country to implement a COVID-19 vaccination programme following the approval of the Pfizer-BioNtech messenger RNA (mRNA) vaccine BNT162b2 for emergency use.(1) The programme has since expanded to include the AstraZeneca adenovirus-vector vaccine and over 6.5 million individuals have now been vaccinated. The burden of COVID-19 in the UK is at its highest since the start of the pandemic and early evidence on the effectiveness of the vaccine is essential for informing policy decisions on the ongoing rollout of the programme and the use of other non-pharmaceutical interventions.(2)

During these first few weeks of the programme, the priority groups for vaccination included: (i) residents in a care home for older adults and their carers; and (ii) all those 80 years of age and over and frontline health and social care workers.(3) Delivery was initially through hospital trusts and care homes, where possible, subsequently also through primary care providers and mass vaccination centres. Interim results from phase 3 clinical trials have found the Pfizer-BioNtech and AstraZeneca vaccines to be highly effective using a two-dose schedule with a target interval of 3 weeks and 4 weeks respectively between doses.(4, 5) Data from the AstraZeneca trial suggests that protection may be greater with a longer dosing interval.(5) A reanalysis of the Pfizer trial data suggests that a single dose of this vaccine has an efficacy of 89% in the early post-vaccination period.(6) Furthermore, with other vaccines an extended interval between the prime and booster doses typically provides a better immune response to the booster dose.(7, 8) Based on this evidence, the increasing incidence of COVID-19 in the UK and the need to rapidly vaccinate as many vulnerable people as possible, on the 20th December 2020, the Joint Committee on Vaccination and Immunisation (JCVI) advised that the dose interval for both vaccines could be extended to up to 12 weeks. A policy decision was subsequently made to prioritise vaccinating as many people as possible with the first dose.

Also in December 2020, a new COVID-19 variant of concern (labelled VOC 202012/01) was found to be associated with increasing case numbers in Kent in South East England.(9) Recent analyses suggest that this variant has increased transmissibility and it has since become the dominant strain in large parts of the UK.(10, 11) The variant is characterised by 23 mutations, including mutations to genes encoding the spike protein, the target in the two vaccines currently in use, as well as the majority of vaccine candidates.(9) Concerns have been raised on the possible impact of the new variant on vaccine effectiveness.(12)

Public Health England and Public Health Scotland have undertaken their first analysis of the early effect of COVID-19 vaccination using routine testing and vaccination data. The aims of this analysis were to estimate the effect of vaccination on confirmed COVID-19 with one and two doses and on the new variant of concern, VOC 202012/01.

Methods

Data sources

Testing for COVID-19 in the UK is conducted through hospital and public health laboratories for those with a clinical need as well as some healthcare workers (referred to as Pillar 1) and through community testing (referred to as Pillar 2).(13) Anybody can access a Pillar 2 test if they have coronavirus symptoms (high temperature, new continuous cough, loss or change in sense of smell or taste), or if they are part of a local or national mass testing programme. For this analysis, PCR testing data from Pillar 2 in individuals who reported having symptoms were included, data were extracted for all tests between 26th of October 2020 and the 17th of January 2021.

The mutations to the Spike (S) gene in VOC 202012/01 cause a reproducible S gene target failure (SGTF) in laboratories using a three target from Thermo Fisher (TaqPath) PCR assay.(9) Between 1st of December 2020 and 3rd of January 2021, VOC 202012/01 accounted for between 91 and 100% of SGTF in England. SGTF therefore provides a good proxy for identification of VOC 202012/01 without relying on sequencing.(11) An analysis of the vaccine effects against COVID-19 detections with SGTF was undertaken restricted to data from laboratories using the TaqPath assay.

Testing data for England and Scotland were linked to individual vaccination histories from national vaccination registers (the National Immunisation Management System, NIMS, in England and the Vaccine Management Tool in Scotland) using NHS number and date of birth in England and Community Health Index number in Scotland.

For England. data were restricted to those aged over 80 (defined as those turning 80 on or after 31st of March 2021) and to individuals aged under 65 who were identified as likely health and social care workers. Likely health and social care workers were identified using the occupation fields in the test request form, if they were indicated as staff in pillar 2 testing conducted within care homes, if they were a member of the SIREN study, a large-scale cohort study in health care workers, or if they were identified as a health and social care worker according to cohorts identified for influenza vaccination in the vaccination register.(14) In Scotland most individuals over 80 are tested in the NHS laboratories and so are not included in this analysis. All symptomatic individuals aged 18-64 who were tested were included.

Statistical methods

A test negative case control design was used to estimate the odds of vaccination in PCR confirmed cases compared to those testing negative.

England:

Analysis was by logistic regression with adjustment for five-year age group (at 31 March 2021), gender, NHS region and week of symptom onset.

Only individuals swabbed within 0-10 days of onset were included in the analysis. Individuals only contribute their first positive from 8th December and if they were not tested positive in the previous 6 weeks. If individuals had more than one negative result then they contributed a maximum of two negative results separated by >=21 days. Negatives within three weeks of a positive result or at any time after a positive result are also excluded.

For the primary analysis those with a history of a previous positive PCR or antibody test at any time prior to 8th December were excluded.

This analysis only includes the Pfizer/BioNTech vaccine. Individuals who had received AZ vaccine at the time of symptom onset were excluded from positive and negative results.

The following time periods between vaccination and symptom onset are considered: post dose 1: 0-3,4-7,8-10,11-13,14-20,21-27, 28-35; and post dose 2: 0-7, 8-14. Analyses were also stratified by age group (>=80 and ≤65 years), SGTF, and history of prior infection. Comparison was to unvaccinated as the baseline group, however, a post-hoc analysis comparing to days 7-9 post-vaccination was also conducted to help account for the likely higher underlying risk of COVID-19 among those groups targeted for vaccination first.

A sensitivity analysis was also conducted using the screening method, whereby vaccine uptake in the cases is compared to uptake in the general population (rather than the test negative controls).(15) This analysis is included in the supplementary appendix.

Scotland:

PCR testing data from Pillar 2 in individuals who reported having symptoms were included, data were extracted for all tests between 8th December 2020 and the 20th of January 2021.

Analysis was by generalised additive logistic regression with spline terms for age, day the swab sample was taken and number of PCR tests prior to vaccination. Further adjustment was made for gender and deprivation.

Some individuals have repeated tests during the post vaccination period. One of these tests was selected at random with sensitivity analyses using the first test and last test. Similar results were obtained from all three methods as there was little repeated symptomatic testing.

The same stratifications as for England were used, however, symptom onset date was not available therefore test date was used.

Ethics

Surveillance of COVID-19 testing and vaccination is undertaken under Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002 to collect confidential patient information (http://www.legislation.gov.uk/uksi/2002/1438/regulation/3/made) under Sections 3(i) (a) to (c), 3(i)(d) (i) and (ii) and 3(3). The study protocol was subject to an internal review by the PHE Research Ethics and Governance Group and was found to be fully compliant with all regulatory requirements. As no regulatory issues were identified, and ethical review is not a requirement for this type of work, it was decided that a full ethical review would not be necessary.

Surveillance of COVID-19 testing and vaccination in undertaken by the NHS Scotland organisation Public Health Scotland. This study used data-linkage from the MREC approved EAVE-II* study (12/SS/0201/SA 1) **(*Early estimation of pandemic Antiviral, therapy and Vaccine Effectiveness and enhanced surveillance (EAVE) - use of a unique community and laboratory national linked dataset).**

Results

74% of individuals tested in pillar 2 successfully linked to vaccination data in the NIMS. This resulted in 22,832 individuals aged 80 years or older and 186,348 likely health and social care workers aged 65 years or younger included in the analysis. Vaccine coverage by any vaccine at January 17th 2021 and the number of cases and controls in each age band are shown in table 1.

Table 1: vaccine coverage at January 17th and numbers of cases and controls by age group, England

Age	Vaccinated	%	Cases	Controls	Total
<35	13,423	19.1%	21,372	48,864	70,236
35-39	5,468	23.6%	7,006	16,134	23,140
40-44	5,086	24.1%	6,719	14,350	21,069
45-49	5,166	24.9%	7,007	13,725	20,732
50-54	5,546	25.5%	7,393	14,369	21,762
55-59	5,013	26.9%	6,396	12,257	18,653
60-64	2,889	26.9%	3,843	6,913	10,756
80-84	5,571	44.5%	4,280	8,234	12,514
85-89	2,840	43.8%	2,422	4,066	6,488
>=90	1,370	35.8%	1,573	2,257	3,830
Total	52,372	25.0%	68,011	141169	209,180

Figure 1 shows the number of cases and controls by intervals around dose 1 and dose 2 of vaccination. The number of individuals tested beyond 28 days after vaccination is very small with the maximum follow up being 37 days after dose 1. In the 7 days prior to vaccination the numbers of tests dropped and were mainly negative tests due to the requirement for vaccine deferral for COVID-19 cases. There was a notable increase in testing in those aged <65 years in the two days after each dose. A small increase in testing was also seen in the over 80s immediately after dose 2.

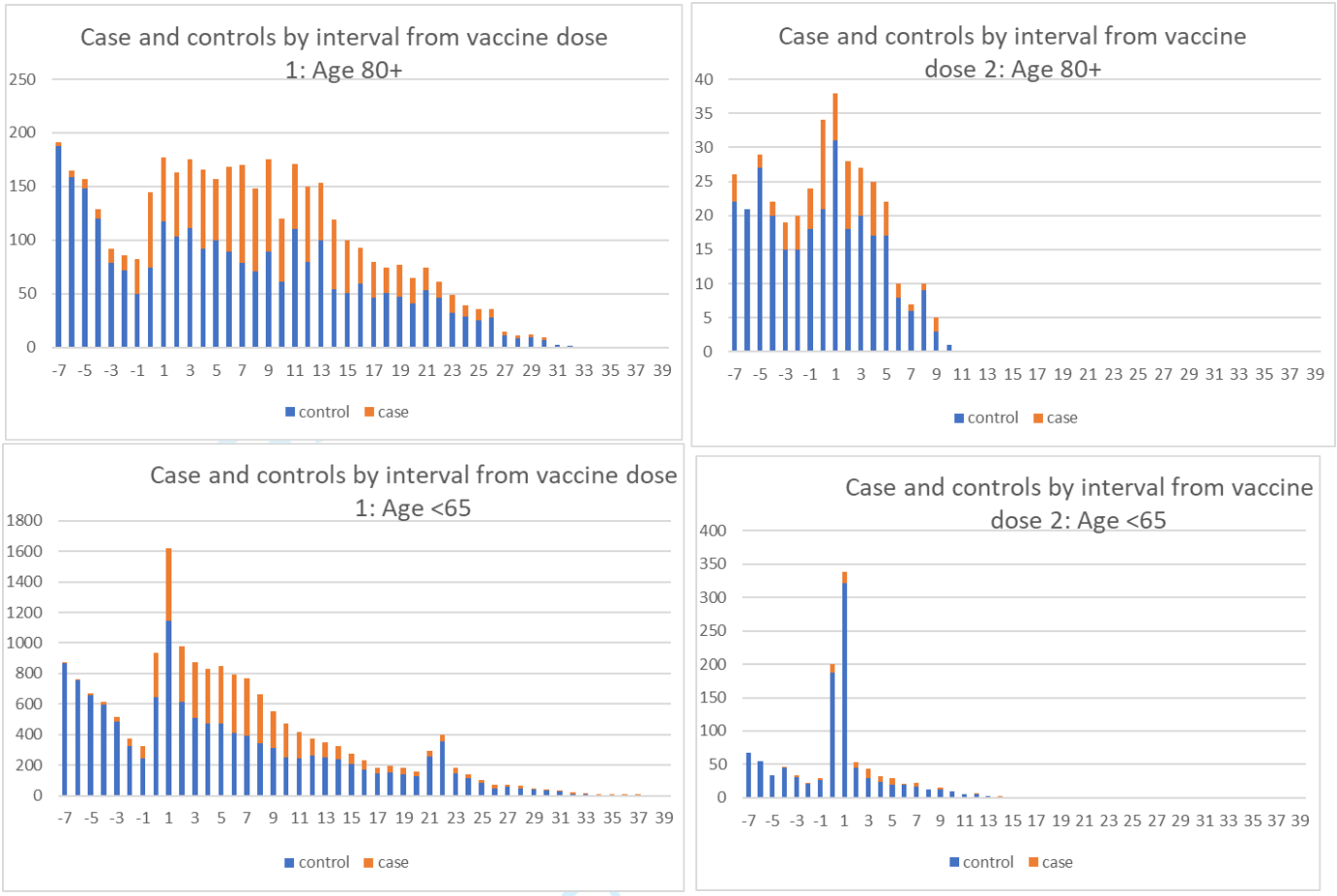


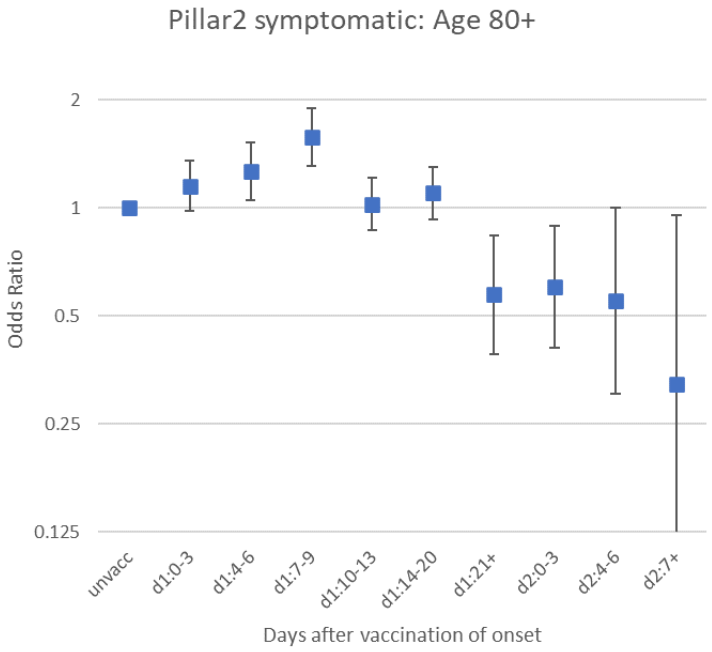
Figure 1: Cases and controls by interval from vaccination in >=80 years and <65 years by dose, England

Table 2 and Figure 2 show the odds of testing positive by interval after vaccination compared to those unvaccinated. In both age groups the odds of testing positive increases up to 7-9 days after vaccination, then begins to decline. In the >=80 years age group there is a notably reduced odds of testing positive from 21 days after vaccination (OR 0.57; 95% CI 0.39-0.84), in those aged <65 years, the reduced odds is observed from 14 days after vaccination (OR 0.59; 95%CI 0.52-0.66). Relative to the peak at days 7-9 the odds ratios are 0.36 (95%CI: 0.24-0.55) and 0.35 (95%CI: 0.29-0.42) from 21 days after the first dose in the >=80 years and <65 years age groups respectively.

Table 2: Adjusted odds ratios for confirmed case by interval after vaccination for >= 80 years and <65 likely healthcare workers, England

Age 80+	Interval	controls	cases	case:con	OR (95% CI)	OR vs day 7-9
	unvacc	12,674	6,958	0.55	base	
	d1:0-3	405	255	0.63	1.15 (0.98-1.36)	
	d1:4-6	281	210	0.75	1.27 (1.05-1.52)	
	d1:7-9	239	254	1.06	1.57 (1.31-1.89)	
	d1:10-13	351	243	0.69	1.02 (0.87-1.21)	
	d1:14-20	349	259	0.74	1.1 (0.93-1.3)	0.7 (0.55-0.89)
	d1:21+	100	38	0.38	0.57 (0.39-0.84)	0.36 (0.24-0.55)
	d2:0-3	90	37	0.41	0.6 (0.41-0.89)	
	d2:4-6	42	15	0.36	0.55 (0.3-1)	0.35 (0.19-0.65)
	d2:7+	19	4	0.21	0.32 (0.11-0.96)	0.21 (0.07-0.62)
Age <65	Interval	controls	cases	case:con	OR (95% CI)	OR vs day 7-9
	unvacc	117,857	54,960	0.47	base	
	d1:0-3	2911	1496	0.51	1 (0.94-1.07)	
	d1:4-6	1354	1119	0.83	1.59 (1.47-1.73)	
	d1:7-9	1047	933	0.89	1.67 (1.53-1.83)	
	d1:10-13	1001	609	0.61	1.14 (1.03-1.26)	
	d1:14-20	1180	370	0.31	0.59 (0.52-0.66)	0.35 (0.3-0.41)
	d1:21+	548	169	0.31	0.58 (0.49-0.69)	0.35 (0.28-0.42)
	d2:0-3	585	50	0.09	0.16 (0.12-0.22)	
	d2:4-6	62	20	0.32	0.64 (0.39-1.06)	0.38 (0.23-0.64)
	d2:7+	67	10	0.15	0.26 (0.14-0.52)	0.16 (0.08-0.31)

(a)



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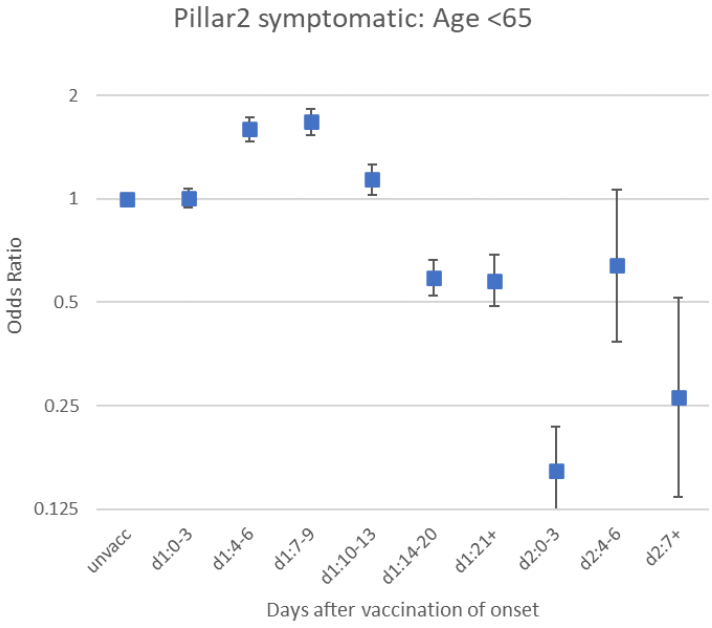
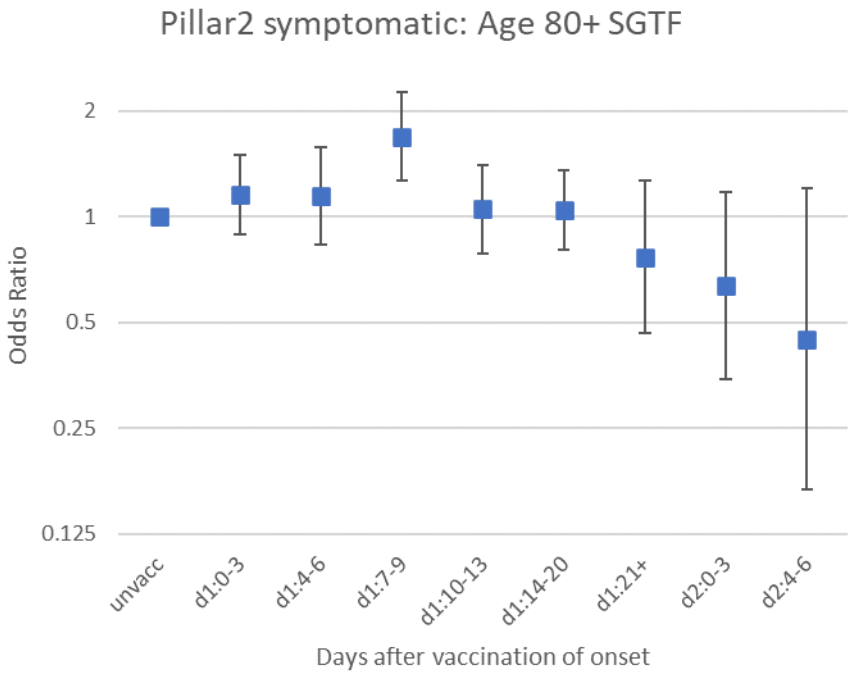


Figure 2: Adjusted odds ratios for confirmed case by interval after vaccination for >= 80 years and <65 likely healthcare workers, England

Table 3 and Figure 3 show the odds ratios for testing positive by interval after vaccination for those with SGTF. The effects are very similar to the overall results for all cases.

Table 3: Adjusted odds ratios for confirmed case by interval after vaccination for >= 80 years and <65 likely healthcare workers with SGTF, England

80+_SGTF	Interval	controls	cases	case:con	OR (95% CI)	OR vs day 7-9
	unvacc	6,445	2,001	0.31	base	
	d1:0-3	215	92	0.43	1.15 (0.89-1.5)	
	d1:4-6	147	59	0.40	1.14 (0.83-1.57)	
	d1:7-9	127	89	0.70	1.69 (1.27-2.26)	
	d1:10-13	162	75	0.46	1.05 (0.79-1.4)	
	d1:14-20	202	90	0.45	1.05 (0.81-1.36)	0.62 (0.42-0.91)
	d1:21+	60	23	0.38	0.77 (0.47-1.27)	0.45 (0.26-0.81)
	d2:0-3	49	14	0.29	0.64 (0.35-1.18)	
	d2:4-6	23	5	0.22	0.45 (0.17-1.2)	0.27 (0.1-0.74)
	d2:7+	12	0	0.00	NA	NA
<65 SGTF	Interval	controls	cases	case:con	OR (95% CI)	OR vs day 7-9
	unvacc	65,710	19,965	0.30	base	
	d1:0-3	1740	598	0.34	0.88 (0.8-0.97)	
	d1:4-6	758	474	0.63	1.61 (1.43-1.82)	
	d1:7-9	619	401	0.65	1.62 (1.42-1.85)	
	d1:10-13	577	253	0.44	1.12 (0.96-1.31)	
	d1:14-20	730	171	0.23	0.6 (0.5-0.71)	0.37 (0.3-0.46)
	d1:21+	347	81	0.23	0.57 (0.45-0.74)	0.35 (0.27-0.47)
	d2:0-3	332	26	0.08	0.2 (0.14-0.3)	
	d2:4-6	43	7	0.16	0.45 (0.2-1)	0.27 (0.12-0.62)
	d2:7+	41	6	0.15	0.36 (0.15-0.86)	0.22 (0.09-0.54)



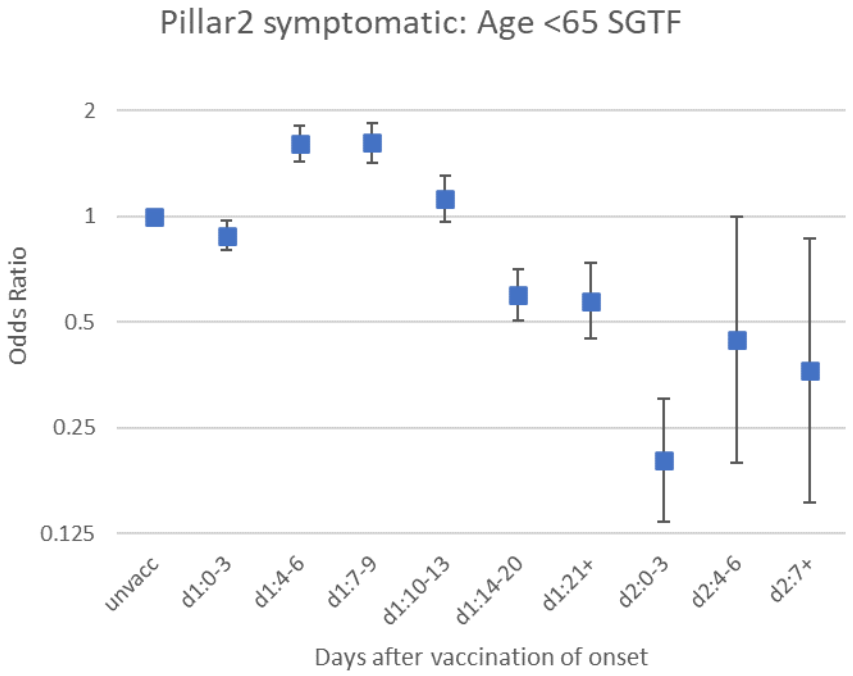


Figure 3: Adjusted odds ratios for confirmed case by interval after vaccination for >= 80 years and <65 likely healthcare workers with SGTF, England

Table 4 and Figure 4 show the odds of testing positive by interval after vaccination compared to those unvaccinated in those aged <65 years in Scotland. The pattern by timing after vaccination is similar to England, though OR are generally higher.

Table 4: Adjusted odds ratios for confirmed case by interval after vaccination for <65 years, Scotland

Interval	controls	cases	case:con	OR (95% CI)
unvacc	197,536	36,796	0.19	base
d1:0-3	446	110	0.25	1.53 (1.22-1.91)
d1:4-6	577	131	0.23	1.27 (1.04-1.55)
d1:7-9	521	179	0.34	2.11 (1.74-2.54)
d1:10-13	537	153	0.28	1.39 (1.14-1.69)
d1:14-20	705	135	0.19	0.78 (0.64-0.95)
d1:21+	763	138	0.18	0.79 (0.65-0.95)
d2:0-6	37	3	0.08	0.35 (0.11-1.15)
d2:7+	8	1	0.13	0.63 (0.08-5.16)

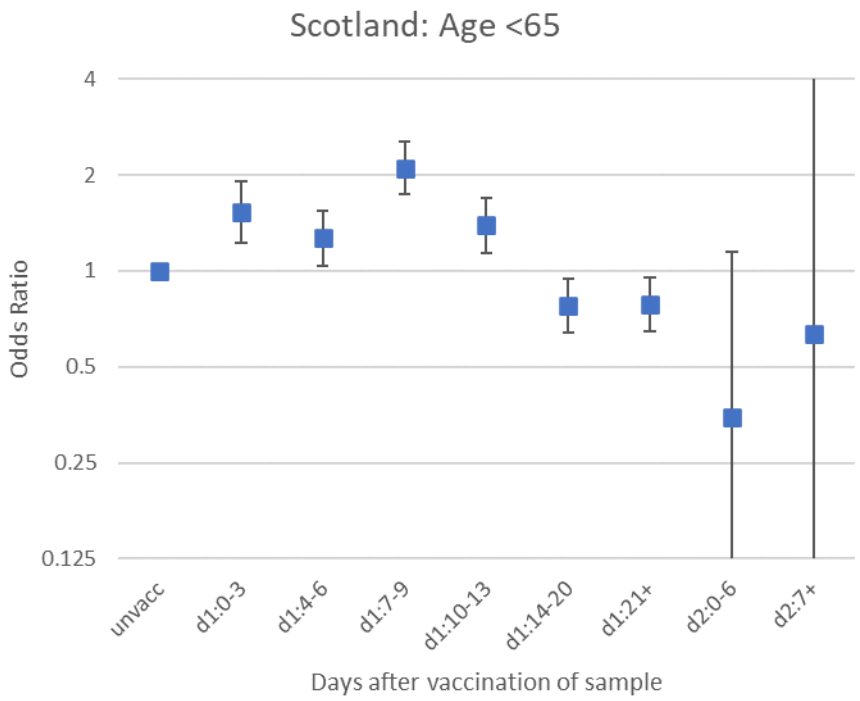


Figure 4: Adjusted odds ratios for confirmed case by interval after vaccination for <65 years, Scotland

Results of the analysis for England using the screening method are shown in the supplementary appendix. The effects are similar to those seen using the test negative case control design though odds ratios are slightly lower .

Discussion

This study provides the first real world evidence of COVID-19 vaccine effectiveness. While there are now two vaccines in use in the UK, delivery of the AstraZenca vaccine only began in January therefore follow-up data is very limited, and this analysis focusses only on the Pfizer/BioNTech vaccine. This early analysis suggests that vaccination is associated with a reduction in symptomatic SARS-CoV2 positive cases. This effect is evident from the first dose in both adults aged over 80 years and health and social care workers aged under 65 years in England. There is a notable effect from 14 days after the first dose in younger adults, and around 21 days after the first dose in older adults. The vaccine appears to have a similar effect against VOC 202012/01 when analysis is restricted to cases with SGTF. Similar results are found for adults receiving their first dose in Scotland.

These data are observational and there are range of factors that influence the odds of testing positive which may also be associated with vaccination, thereby acting as confounders when examining vaccine effectiveness through routine testing, in particular in the early stages of the vaccination programme. A key factor that is likely to increase the odds of testing positive in vaccinees (therefore underestimating vaccine effectiveness) is that individuals initially targeted for vaccination are likely to be at increased risk of exposure to COVID-19. For example, delivery started in hospitals, and frontline healthcare workers caring for COVID-19 patients in hospital are likely to have been offered the vaccine ahead of those working in the community. Similarly, care home residents and those aged over 80 accessing hospital may have been vaccinated earlier and may also be at higher risk of COVID-19. This may explain the higher odds of testing positive in vaccinees in the first 4-9 days after vaccination (before they would have been expected to develop an immune response to the vaccine).(4, 16) This effect is likely to lessen as roll-out vaccination programme progresses and it is less focussed on those at higher risk. In the opposite direction, vaccinees may have a lower odds of testing positive in the first few days after vaccination because individuals are asked to defer vaccination if they are acutely unwell or have had a recent coronavirus test.(17) This explains the lower odds of testing positive in the week prior to vaccination but may also persist for some time after vaccination. Vaccination can also cause systemic reactions including fever and fatigue, in particular in younger adults.(16, 17) This may prompt testing for COVID-19 in the first few days after vaccination, which, if due to a vaccine reaction, will be negative. This is likely to explain the increased testing immediately after each dose seen in Figure 1 and the reduced odds ratios after each dose, in particular in the <65 years age group and after the second dose in the >=80 years age group. Together, these different factors may explain the pattern seen in the first 10 days after vaccination – that is, the underlying risk in vaccinees is higher than in the unvaccinated, however, this is suppressed for the 3-6 days due to the deferral and reactogenicity effects. As the vaccine starts to have an effect, from 10 days onwards, the odds ratios start to decline, this continues up to >=21 days after the first dose. These effects may also mean that we might expect the odds ratios in the later periods after vaccination (>= 21 days after vaccination) to come down over time, as these will currently reflect the very earliest groups vaccinated who may have highest risk.

The odds ratios in <65 years in Scotland are generally higher than in England, this is likely because the analysis in Scotland was not restricted to likely healthcare workers, therefore the unvaccinated group will primarily be non healthcare workers who are likely at lower risk of infection relative to the vaccinated group who will be health and social care workers. Also, because the Scottish analysis uses

test date rather than onset date, the effects by period after vaccination will have a lag. Relative to the peak, results in Scotland are similar to England.

The results are similar when the screening method is used though odds ratios are generally slightly lower (greater vaccine effects). This could reflect the fact that those seeking testing are also more likely to access vaccination which could reduce apparent vaccine effects when using test negative controls and also the fact that there may be misclassification due to sensitivity of PCR testing which would attenuate the effects.

There are similarities between our results and those seen in the phase 3 clinical trial of the Pfizer/BioNTech vaccine.(4) As in the trial, we begin to see a decline in the odds of testing positive among vaccinees from 10-14 days after the first dose. The trial found an overall efficacy of 95% (95%CI: 90.3-97.6) from 7 days after the second dose (median follow-up of 2 months). We have limited data beyond 7 days after a second dose, however, if unvaccinated are considered the baseline, we estimate a vaccine effectiveness of 69% in the over 80s and 74% in the under 65s. If we consider days 7-9 post vaccination as the baseline, to help account for the likely increased underlying risk in those vaccinated early in the programme the vaccine effectiveness is 79% and 84% in >=80 years and <65 years respectively. In the trial the reported vaccine effectiveness after dose 1 to before dose 2 was 52.4% (95% CI: 29.5-68.4%). However, this included cases from the first 2 weeks after vaccination when we wouldn't expect any effect. Reanalysing the trial data using only cases observed between days 15 and 21 after the first dose, efficacy against symptomatic COVID-19 is estimated at 89% (95% CI: 52-95%).(6) Our analysis using the observational data suggests vaccine effectiveness of 45% in those aged >=80 years and 43% in <65 years, or 63% and 65% respectively when compared to the 7-9 days post-vaccination period. The delay before a clear effect is seen in >=80 years relative to <65 years in our data may reflect the reduced immunogenicity seen in older adults in the phase 1 study.(16) Delayed immune response in older adults is also seen with other vaccines.(18)

We see evidence that the vaccine is effective against VOC 202012/01. This supports recent evidence that sera from vaccinated individuals elicits equivalent neutralising titres to VOC 202012/01 and similar variants.(19, 20) The OR at each time interval are similar in those with SGTF to the overall results for all cases.

This study has number of strengths: we have a large sample size, including all community COVID-19 testing in England and Scotland since the start of the vaccination programme, data on symptoms and onset date, detailed vaccine history and data on all prior testing. We provide the first evidence of effectiveness without restricting to defined populations and storage, maintenance and cold chains that can be well controlled in trial conditions are more challenging in the real world. The large sample size allows us to look at very fine intervals after vaccination which helps to understand some of the biases that need to be accounted for in this early phase of the programme. The observational nature of this analysis means that there are limitations and the results should be interpreted with caution. Some of the key confounding issues have been outlined above but there are others. Factors that could increase the risk of COVID-19 in vaccinees (and therefore result in underestimation of

vaccine effects) include: individuals may have more risky behaviours after vaccination if they believe they are protected; also, presenting for vaccination may be a risk factor in itself (for example travelling to a vaccination centre with a friend or relative). Conversely, individuals who have been self-isolating may defer vaccination and may also be at lower risk of infection, this could underestimate vaccine effectiveness in the short period after vaccination. Misclassification is also likely to be a factor in this study. For example, individuals may falsely report symptoms in order to be tested – which will both include asymptomatic individuals in the symptomatic analysis and meant that onset dates are incorrect. Low sensitivity or specificity of PCR testing may also mean that cases and controls are misclassified. Failure to exclude those with past infection because of low testing rates in wave 1 is another possibility although most health and social care staff have been tested for antibody over the summer. Any misclassification could attenuate vaccine effects. Furthermore, at this stage in the vaccination programme, the length of follow-up in this analysis is very limited. Further estimates in the coming weeks will include larger sample sizes and longer follow-up.

Despite the limitations, this study provides early evidence that the vaccine is having a significant effect on COVID-19 cases in England and Scotland. We see a clear effect of the first dose of vaccine, supporting the decision to maximise the number of individuals vaccinated with a single dose, though we have limited evidence on the duration of this effect. There are still significant numbers of vaccinated individuals who go on to develop COVID-19 and our study indicates that vaccinated individuals must maintain other precautions, in particular during the first two to three weeks after vaccination. Further evidence is needed on the duration of any effect, the effect against severe disease, asymptomatic infection and transmission and the four UK nations will continue to work closely to develop and share evidence on this as it becomes available. Nevertheless, the fact that the vaccine appears to be preventing symptomatic disease, including with the new variant of concern, is encouraging and we would anticipate an impact on case detections at a population level in the coming weeks and months.

All authors have completed the ICMJE uniform disclosure form and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research

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Screening method assessment of vaccine effects on Pillar 2 Symptomatic data in England

1. Methods

This report uses the same over 80s data as the test negative case-control method analysis but only uses the COVDI-19 PCR positive cases (no controls). The comparator is NIMS vaccine uptake matched individually to each case based on age, sex , region and by day of onset. Coverage is matched according to various intervals after the first and second dose and by vaccine.

The odds of vaccination in the cases is divided by the odds of vaccination in the population to give the vaccine effect, for which 1-OR is the vaccine effect (effectiveness).

To estimate the odds in any interval after vaccination it is necessary to only include cases within that interval or unvaccinated and do the same with the population coverage. For example if 10% of the population are vaccinated 14-20 days after PF and 60% are totally unvaccinated then adjusted coverage for the calculation is adjusted PPV = (10/(10+60)) =14.3%. If within the cases 5500 were unvaccinated and 500 vaccinated in this interval the adjusted PCV = 500/(500+5500) = 8.3%. Odds ratio is then 0.083/ 0.143 = 0.58.

The matching by period region, sex and age effectively adjusts for these three variables.

In this first report age 80+ are not split further by age. Region is 7 NHS regions. Period is per day.

The vaccine intervals considered were 0-3,4-6,7-9,10-13,14-20,21-27,28+ after dose1 and 0-3,4-6 and 7+ after dose2. At this stage AZ is only considered in terms of those vaccinated with AZ are excluded from the PF analyses but there is not enough time after the first dose to evaluate.

2. Results

Figure1 shows an example of coverage data in Females aged 80+ in East of England by day. The interval shown are broader than those used in the analysis but illustrate the population transitioning between intervals. A case with the same characteristics has a coverage matched at the date of their onset using proportion in each interval on that date.

Figure 1

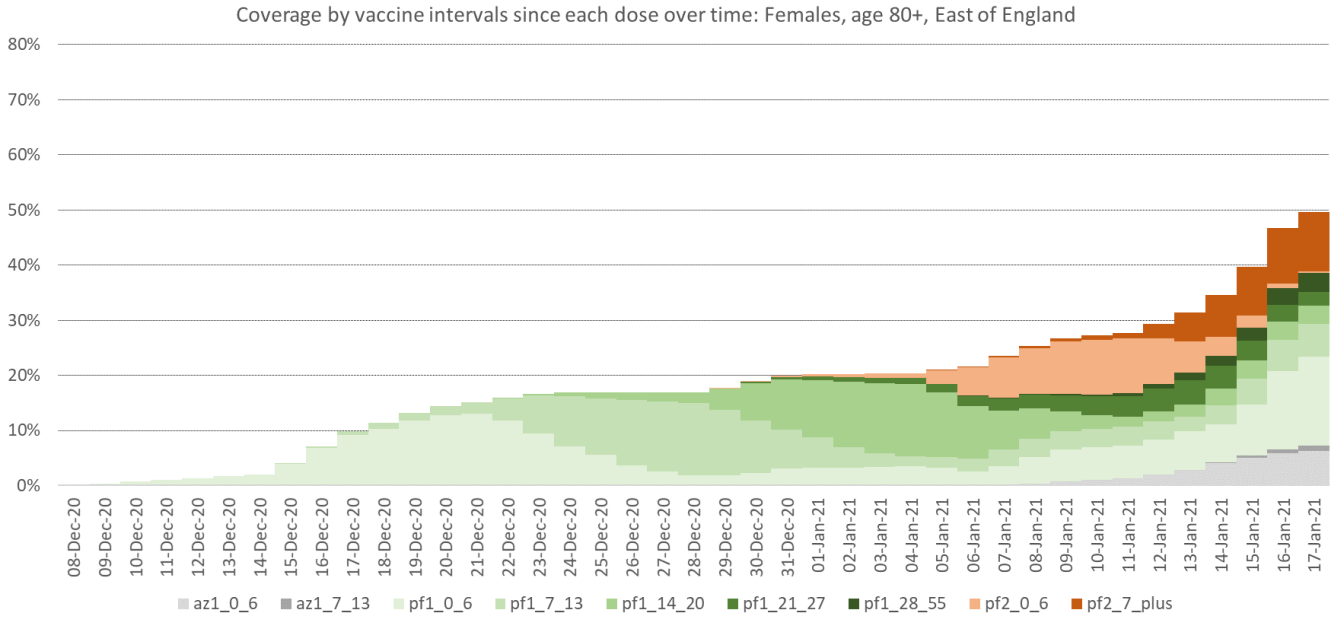

Table 1 gives the number of cases in each interval along with expected cases if the vaccine has no effect and the adjusted odds ratios for each interval

Table 1: Odds of vaccination in cases compared to controls showing vaccine effects

Interval	cases	expected_based on PPV if no effect	OR (95% CI)
unvacc	7122	6744	1.00 (baseline)
pf1_0_3	265	340	0.76 (0.67-0.86)
pf1_4_6	213	227	0.93 (0.81-1.07)
pf1_7_9	261	211	1.25 (1.11-1.42)
pf1_10_13	248	289	0.85 (0.74-0.96)
pf1_14_20	260	406	0.61 (0.54-0.69)
pf1_21_27	35	79	0.43 (0.31-0.6)
pf1_28_55	3	6	0.5 (0.16-1.57)
pf2_0_3	37	114	0.31 (0.22-0.42)
pf2_4_6	15	56	0.26 (0.15-0.43)
pf2_7_plu	4	21	0.18 (0.07-0.48)

A reduced odds is seen in the first few days and then a slightly increased odds as seen in the TNCC method. This then falls to significantly lower than 1 by days 14-20 and to a 57% reduction by days 21-27. Odds are also low in the post second dose period. Results have similarities to the TNCC but show slightly greater reductions and an earlier reduction.