Hospitalised vaccinated patients during the second wave in the ISARIC4C CO-CIN cohort

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Summary

This report investigates hospitalised vaccinated patients during the second wave of the UK COVID-19 outbreak using the ISARIC4C / CO-CIN data set.

For patients enrolled to ISARIC4C / CO-CIN:

- 1 in 25 patients admitted to hospital since December 8th 2020 have received at least the first dose of a COVID-19 vaccination.
- The median time between vaccination and symptom onset for these patients was 5 days.
- The median time between vaccination and hospital admission for these patients was 10 days.
- Most vaccinated hospitalised patients were infected shortly before or around the time of vaccination, and others after vaccination but before immunity had developed (immunization).

Admission trends

The period of the second wave of COVID-19 is defined as from September 1st 2020 to present. There have been 74,405 hospital admissions enrolled to ISARIC/CO-CIN in the second wave. There were 1,802 hospitalised vaccinated patients enrolled as of March 5th 2021. This accounts for 4.2% (1,802/42,788) of enrolled hospital admissions since December 8th 2020, the date when the first people in the UK were vaccinated. Of these patients we have information on date of first vaccination for 1,685 of them and information on date of second vaccination for 27 of them. (Figure 1, Figure 2).
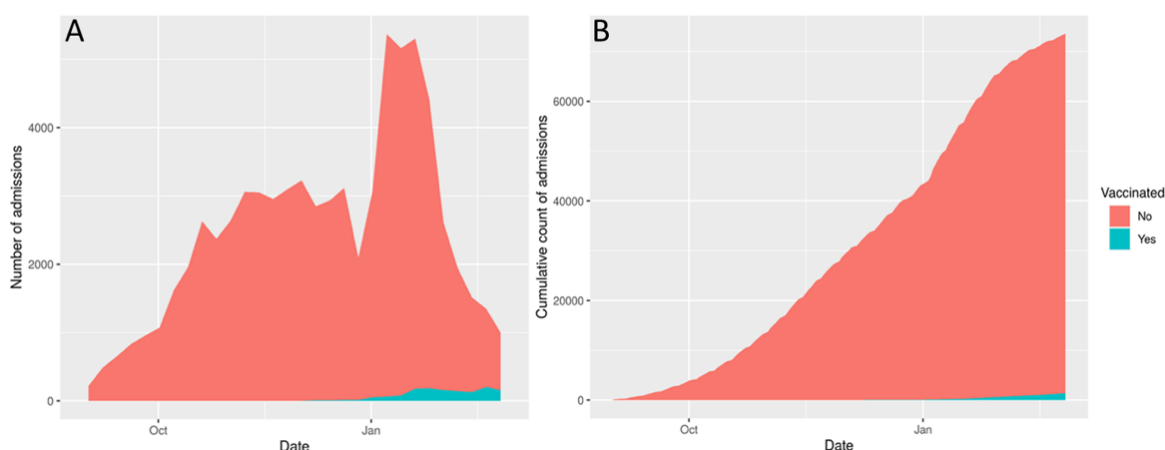

Figure 1: Number of second wave hospital admissions stratified by vaccinated vs non-vaccinated. A: Absolute counts, B: cumulative counts

Time to symptom onset for vaccinated patients

There was information on difference in date of symptom onset and date of vaccination for 1,027 patients (57% of vaccinated population, Figure 2). The difference in date of symptom onset and date of vaccination was filtered to include patients that experienced symptoms 7 days prior to vaccination onwards. The median time between vaccination and symptom onset was 5 days (IQR = [0,10]). Given that the median incubation period is 5 days, the distribution indicates that most vaccinated hospitalised patients were infected shortly before or around the time of vaccination, and the remainder after vaccination but before immunity had developed (immunization).

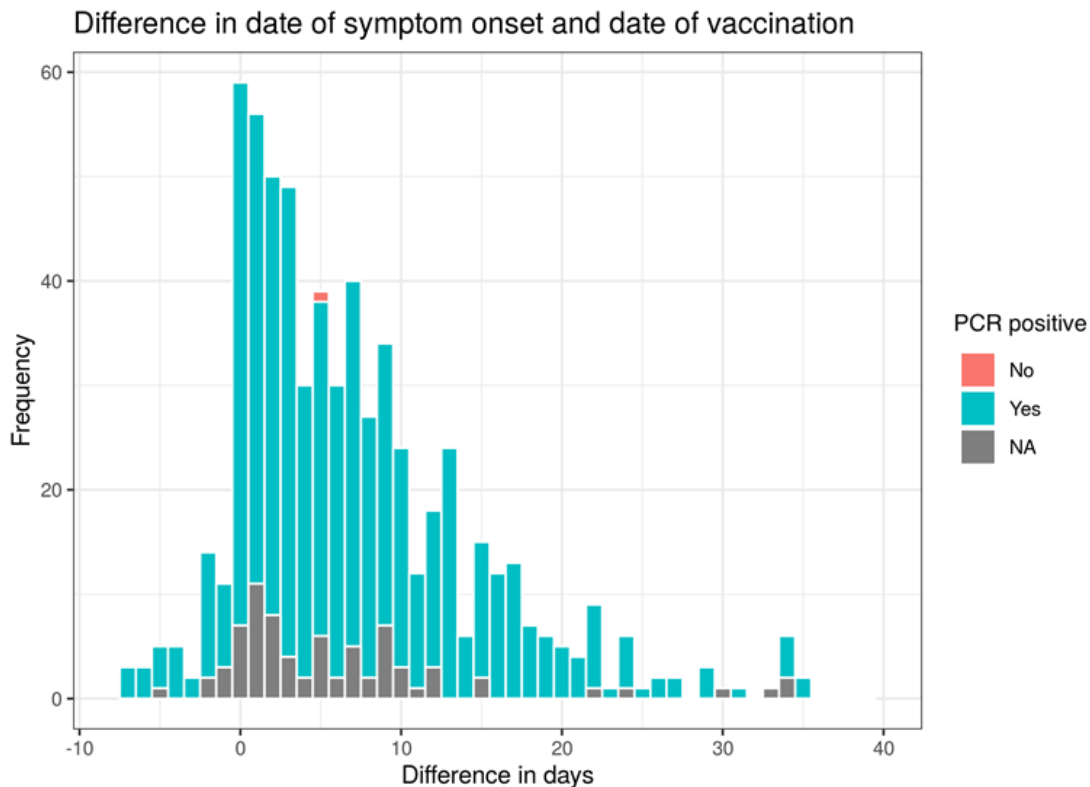Difference in date of symptom onset and date of vaccination

Figure 2: Histogram of count of difference of date in vaccination and symptom onset in hospitalised patients (PCR Positive No, Yes and NA= Not Available).

Time to admission for vaccinated patients

There was information on difference in date of vaccination and date of admission for 1,257 patients (70% of vaccinated population, Figure 3). The difference in date of admission and date of vaccination is filtered to include only patients admitted after vaccination i.e. only positive values. The median time between vaccination and admission to hospital was 10 days (IQR = [5,15]). The data is heavily skewed right. This distribution is expected to shift over time as more patients in the community are vaccinated.
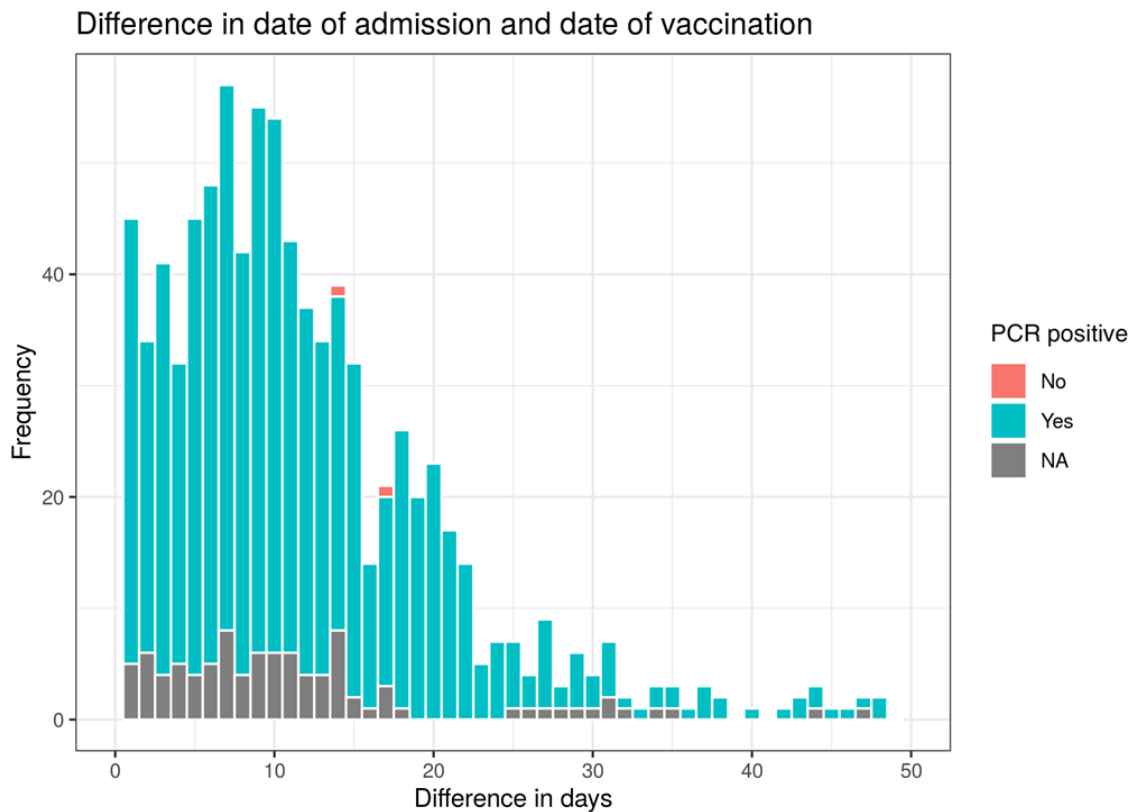

Figure 3: Histogram of count of difference in date of vaccination and date of admission to hospital (PCR Positive No, Yes and NA= Not Available).

Early admissions post-vaccination

We observed an abundance of patients admitted to hospital within 7 days of vaccination (Figure 3). Discussed below are potential reasons for this trend in admissions:

- Most vaccinated hospitalised patients were infected shortly before or around the time of vaccination, and the remainder after vaccination but before immunity had developed (immunization).
- Elderly and vulnerable people who had been shielding, may have inadvertently been exposed and infected either through the end-to-end process of vaccination, or shortly after vaccination through behavioural changes where they wrongly assume they are immune.
- An additional hypothesis, that we cannot exclude in this analysis, is that some people had recent asymptomatic COVID-19 and vaccination precipitated admission. Previously asymptomatic or paucisymptomatic PCR positive patients may experience symptoms likened to COVID-19 symptoms including fever due to vaccination. This happens within 48 hours of the vaccination and usually resolves within 48 hours [1].

We have recognised that some vaccinated patients were admitted for non-COVID-19 reasons and were asymptomatic but later identified as PCR positive. Of the 1,802 vaccinated patients admitted to hospital, 1,560 tested PCR positive (87% of vaccinated admissions). Of these patients 342 were asymptomatic (22% of PCR positive vaccinated admissions). Of these asymptomatic patients 164 (48% of asymptomatic PCR positive vaccinated admissions) were admitted within 7 days of vaccination, indicating infection before immunity had opportunity to develop.

Patients with previous COVID-19 infection may test PCR positive for up to 17 days post infection and rarely up to 90 days post-infection. This is because fragments of virus genes can be persist in the upper respiratory tract following infection [2].

Sub-populations based on vaccination efficacy

We have stratified our population of vaccinated hospitalised cases based on difference in date of vaccination and date of symptom onset (Figure 4, Table 1):

- 0-7 days (red): Admissions in this population do not correlate with vaccinations. This is too little time for the vaccination to work (immunity to develop) for most people and infection will have occurred before vaccination in many.
- 8-14 days (blue): Admissions in this population remain unlikely due to vaccination failure, as immunity is not expected to have fully developed.
- 14+ days (yellow): We have defined admissions in this population as vaccination failure only for the purpose of this analysis, as some immunity would be expected to have developed.

Regardless of stratification, visual inspection gives appreciation of decay of frequency of vaccinated hospitalisation of time, or evidence of vaccine immunization (success) developing over time.
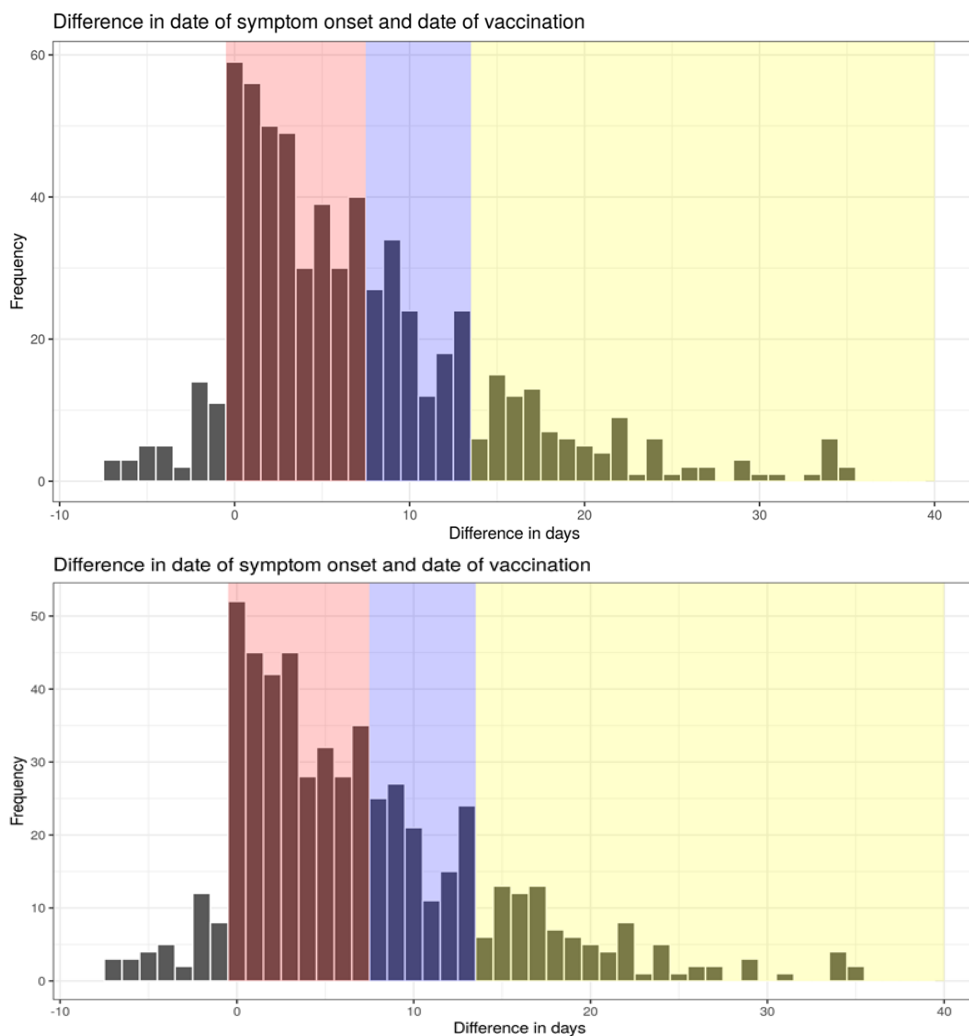

Figure 4: Histogram of count of difference of date in vaccination and symptom onset in hospitalised patients stratified by efficacy of vaccination. Plot A: all patients, Plot B: PCR +ve patients only

While the majority of "vaccine failures defined as Difference in symptom onset and vaccination >= 14 days" occur in people age >80yr (highlighted in yellow in table 1) it must be remembered that at the time of analysis this group also made up the majority of people vaccinated.

As such we recommend that this analysis be repeated at monthly intervals.

Table 1: Baseline characteristics of the vaccinated population stratified by time from vaccine to symptom onset (n=1408).
Stratified unlikely to be caused by vaccine (<14 days) and possibly due to vaccine failure (>=14 days). We are unable to identify Tier 1 care home residents from our data – these people are likely to be predominantly in Tier 2. Vaccination tier 10 is comprised of patients aged 16-50 not in a higher vaccination tier [3]. Column three is patients who were asymptomatic (and therefore unable to assign to <14 or >14 days).

	Difference in symptom onset and vaccination < 14 days (N=881)	Difference in symptom onset and vaccination >= 14 days (N=146)	No symptoms (N=381)	Overall (N=1408)
Sex				
Female	423 (48.0%)	70 (47.9%)	193 (50.7%)	686 (48.7%)
Male	457 (51.9%)	76 (52.1%)	188 (49.3%)	721 (51.2%)
Missing	1 (0.1%)	0 (0%)	0 (0%)	1 (0.1%)
Age				
< 50	54 (6.1%)	3 (2.1%)	22 (5.8%)	79 (5.6%)
50-69	166 (18.8%)	4 (2.7%)	23 (6.0%)	193 (13.7%)
70-79	217 (24.6%)	12 (8.2%)	78 (20.5%)	307 (21.8%)
80+	444 (50.4%)	127 (87.0%)	258 (67.7%)	829 (58.9%)
Ethnicity				
Black	14 (1.6%)	1 (0.7%)	5 (1.3%)	20 (1.4%)
Other	45 (5.1%)	4 (2.7%)	20 (5.2%)	69 (4.9%)
White	689 (78.2%)	129 (88.4%)	303 (79.5%)	1121 (79.6%)
Asian	51 (5.8%)	4 (2.7%)	10 (2.6%)	65 (4.6%)
Missing	82 (9.3%)	8 (5.5%)	43 (11.3%)	133 (9.4%)
Vaccination Tier				
2	461 (52.3%)	127 (87.0%)	260 (68.2%)	848 (60.2%)
3	131 (14.9%)	7 (4.8%)	48 (12.6%)	186 (13.2%)
4	87 (9.9%)	5 (3.4%)	30 (7.9%)	122 (8.7%)
5	37 (4.2%)	1 (0.7%)	11 (2.9%)	49 (3.5%)
6	19 (2.2%)	3 (2.1%)	12 (3.1%)	34 (2.4%)
7	42 (4.8%)	1 (0.7%)	7 (1.8%)	50 (3.6%)
8	52 (5.9%)	2 (1.4%)	3 (0.8%)	57 (4.0%)

	Difference in symptom onset and vaccination < 14 days (N=881)	Difference in symptom onset and vaccination >= 14 days (N=146)	No symptoms (N=381)	Overall (N=1408)
9	36 (4.1%)	0 (0%)	2 (0.5%)	38 (2.7%)
10	16 (1.8%)	0 (0%)	8 (2.1%)	24 (1.7%)
IMD quintile				
1 most deprived	205 (23.3%)	22 (15.1%)	74 (19.4%)	301 (21.4%)
2	209 (23.7%)	26 (17.8%)	71 (18.6%)	306 (21.7%)
3	185 (21.0%)	40 (27.4%)	83 (21.8%)	308 (21.9%)
4	155 (17.6%)	36 (24.7%)	88 (23.1%)	279 (19.8%)
5 least deprived	126 (14.3%)	22 (15.1%)	64 (16.8%)	212 (15.1%)
Missing	1 (0.1%)	0 (0%)	1 (0.3%)	2 (0.1%)
Fever				
YES	439 (49.8%)	58 (39.7%)	17 (4.5%)	514 (36.5%)
NO	331 (37.6%)	67 (45.9%)	313 (82.2%)	711 (50.5%)
Unknown	64 (7.3%)	16 (11.0%)	22 (5.8%)	102 (7.2%)
Missing	47 (5.3%)	5 (3.4%)	29 (7.6%)	81 (5.8%)
Cough				
YES	506 (57.4%)	66 (45.2%)	20 (5.2%)	592 (42.0%)
NO	277 (31.4%)	56 (38.4%)	303 (79.5%)	636 (45.2%)
Unknown	52 (5.9%)	19 (13.0%)	28 (7.3%)	99 (7.0%)
Missing	46 (5.2%)	5 (3.4%)	30 (7.9%)	81 (5.8%)
Shortness of breath				
YES	606 (68.8%)	85 (58.2%)	24 (6.3%)	715 (50.8%)
NO	200 (22.7%)	43 (29.5%)	297 (78.0%)	540 (38.4%)
Unknown	31 (3.5%)	13 (8.9%)	31 (8.1%)	75 (5.3%)
Missing	44 (5.0%)	5 (3.4%)	29 (7.6%)	78 (5.5%)

Table 2: Baseline characteristics stratified by time from vaccine to hospital admission (n=1802)

	Difference in admission and vaccination < 14 days (N=964)	Difference in admission and vaccination >= 14 days (N=293)	Missing (N=545)	Overall (N=1802)
Sex				
Female	464 (48.1%)	166 (56.7%)	252 (46.2%)	882 (48.9%)
Male	499 (51.8%)	127 (43.3%)	285 (52.3%)	911 (50.6%)
Missing	1 (0.1%)	0 (0%)	8 (1.5%)	9 (0.5%)
Age				
< 50	58 (6.0%)	12 (4.1%)	34 (6.2%)	104 (5.8%)
50-69	153 (15.9%)	20 (6.8%)	112 (20.6%)	285 (15.8%)
70-79	227 (23.5%)	37 (12.6%)	136 (25.0%)	400 (22.2%)
80+	526 (54.6%)	224 (76.5%)	255 (46.8%)	1005 (55.8%)
Missing	0 (0%)	0 (0%)	8 (1.5%)	8 (0.4%)
Asymptomatic				
Asymptomatic	208 (21.6%)	72 (24.6%)	101 (18.5%)	381 (21.1%)
Symptomatic	756 (78.4%)	221 (75.4%)	444 (81.5%)	1421 (78.9%)
Ethnicity				
Black	17 (1.8%)	2 (0.7%)	5 (0.9%)	24 (1.3%)
Other	50 (5.2%)	15 (5.1%)	25 (4.6%)	90 (5.0%)
White	760 (78.8%)	240 (81.9%)	417 (76.5%)	1417 (78.6%)
Asian	47 (4.9%)	12 (4.1%)	28 (5.1%)	87 (4.8%)
Missing	90 (9.3%)	24 (8.2%)	70 (12.8%)	184 (10.2%)
Vaccination Tier				
2	542 (56.2%)	227 (77.5%)	258 (47.3%)	1027 (57.0%)
3	138 (14.3%)	30 (10.2%)	73 (13.4%)	241 (13.4%)
4	89 (9.2%)	8 (2.7%)	63 (11.6%)	160 (8.9%)
5	32 (3.3%)	6 (2.0%)	52 (9.5%)	90 (5.0%)
6	22 (2.3%)	5 (1.7%)	18 (3.3%)	45 (2.5%)
7	43 (4.5%)	3 (1.0%)	33 (6.1%)	79 (4.4%)
8	51 (5.3%)	5 (1.7%)	17 (3.1%)	73 (4.1%)
9	28 (2.9%)	6 (2.0%)	10 (1.8%)	44 (2.4%)

	Difference in admission and vaccination < 14 days (N=964)	Difference in admission and vaccination >= 14 days (N=293)	Missing (N=545)	Overall (N=1802)
10	19 (2.0%)	3 (1.0%)	13 (2.4%)	35 (1.9%)
Missing	0 (0%)	0 (0%)	8 (1.5%)	8 (0.4%)
IMD quantile				
1 most deprived	219 (22.7%)	58 (19.8%)	117 (21.5%)	394 (21.9%)
2	219 (22.7%)	58 (19.8%)	114 (20.9%)	391 (21.7%)
3	203 (21.1%)	66 (22.5%)	128 (23.5%)	397 (22.0%)
4	179 (18.6%)	61 (20.8%)	105 (19.3%)	345 (19.1%)
5	144 (14.9%)	49 (16.7%)	80 (14.7%)	273 (15.1%)
Missing	0 (0%)	1 (0.3%)	1 (0.2%)	2 (0.1%)
Fever				
YES	381 (39.5%)	93 (31.7%)	187 (34.3%)	661 (36.7%)
NO	467 (48.4%)	154 (52.6%)	218 (40.0%)	839 (46.6%)
Unknown	64 (6.6%)	18 (6.1%)	48 (8.8%)	130 (7.2%)
Missing	52 (5.4%)	28 (9.6%)	92 (16.9%)	172 (9.5%)
Cough				
YES	428 (44.4%)	115 (39.2%)	221 (40.6%)	764 (42.4%)
NO	425 (44.1%)	130 (44.4%)	187 (34.3%)	742 (41.2%)
Unknown	59 (6.1%)	21 (7.2%)	46 (8.4%)	126 (7.0%)
Missing	52 (5.4%)	27 (9.2%)	91 (16.7%)	170 (9.4%)
Shortness of breath				
YES	511 (53.0%)	147 (50.2%)	264 (48.4%)	922 (51.2%)
NO	360 (37.3%)	104 (35.5%)	156 (28.6%)	620 (34.4%)
Unknown	44 (4.6%)	15 (5.1%)	35 (6.4%)	94 (5.2%)
Missing	49 (5.1%)	27 (9.2%)	90 (16.5%)	166 (9.2%)

References

1. *Side effects of the coronavirus vaccines.* Available at: https://www.nhsinform.scot/covid-19-vaccine/the-vaccines/side-effects-of-the-coronavirus-vaccines (Accessed: 10 March 2021).
2. *COVID-19: management of staff and exposed patients or residents in health and social care settings.* Available at: https://www.gov.uk/government/publications/covid-19-management-of-exposed-healthcare-workers-and-patients-in-hospital-settings/covid-19-management-of-exposed-healthcare-workers-and-patients-in-hospital-

settings#:~:text=If%20a%20person%20is%20re,contacts%20should%20be%20traced. (Accessed: 10 March 2021).

3. *Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination, 30 December 2020.* Available at: https://www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-30-december-2020/joint-committee-on-vaccination-and-immunisation-advice-on-priority-groups-for-covid-19-vaccination-30-december-2020 (Accessed: 10 March 2021).