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COVID-19 booster vaccination uptake and infection breakthrough amongst health care workers in Wales: A national prospective cohort study

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ABSTRACT

Background: From September 2021, Health Care Workers (HCWs) in Wales began receiving a COVID-19 booster vaccination. This is the first dose beyond the primary vaccination schedule. Given the emergence of new variants, vaccine waning vaccine, and increasing vaccination hesitancy, there is a need to understand booster vaccine uptake and subsequent breakthrough in this high-risk population.
Methods: We conducted a prospective, national-scale, observational cohort study of HCWs in Wales using anonymised, linked data from the SAIL Databank. We analysed uptake of COVID-19 booster vaccinations from September 2021 to February 2022, with comparisons against uptake of the initial primary vaccination schedule. We also analysed booster breakthrough, in the form of PCR-confirmed SARS-Cov-2 infection, comparing to the second primary dose. Cox proportional hazard models were used to estimate associations for vaccination uptake and breakthrough regarding staff roles, socio-demographics, household composition, and other factors.
Results: We derived a cohort of 73,030 HCWs living in Wales (78% female, 60% 18–49 years old). Uptake was quickest amongst HCWs aged 60 + years old (aHR 2.54, 95%CI 2.45–2.63), compared with those aged 18–29. Asian HCWs had quicker uptake (aHR 1.18, 95%CI 1.14–1.22), whilst Black HCWs had slower uptake (aHR 0.67, 95%CI 0.61–0.74), compared to white HCWs. HCWs residing in the least deprived areas were slightly quicker to have received a booster dose (aHR 1.12, 95%CI 1.09–1.16), compared with those in the most deprived areas. Strongest associations with breakthrough infections were found for those living with children (aHR 1.52, 95%CI 1.41–1.63), compared to two-adult only households. HCWs aged

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60 + years old were less likely to get breakthrough infections, compared to those aged 18–29 (aHR 0.42, 95%CI 0.38–0.47).

Conclusion: Vaccination uptake was consistently lower among black HCWs, as well as those from deprived areas. Whilst breakthrough infections were highest in households with children.

1. Introduction

Several COVID-19 vaccines have been shown to be safe and highly effective against hospitalisation, to a lesser extent at preventing infection, albeit with effectiveness waning over time [1–8]. As we move beyond the primary vaccination schedule and transition to subsequent booster doses, effectiveness of policy becomes determined by the willingness of individuals to receive booster doses and the ability of health systems to deliver them in a timely manner at scale. Engagement with a vaccination programme is complicated by the inequality, both at a structural and individual level. In the global landscape, high-income countries have high availability of vaccines, unlike lower-income countries [1,2]. Additionally, there are also disparities in vaccine uptake across sociodemographic characteristics [3–6]. Health care workers (HCWs) have typically been prioritised to receive a vaccine due to their increased risk of exposure to SARS-CoV-2 and their potential to transmit infection to patients [7]. It has been suggested that ethnicity, sentiment towards the organisation they work for, disability status, flu vaccine uptake, social pressure, and information from trusted sources were associated with first and second dose uptake for HCWs [8,9].

In the UK, HCWs received an early primary course of a COVID-19 vaccination. Following advice from the Joint Committee on Vaccination and Immunisation (JCVI), administration of booster doses began on 16th September 2021 [10]. To be eligible for a booster dose, HCWs had to be at least six months post their previous dose. Given the timing, the majority of HCWs would have met these criteria. From December 2021 onwards, the Omicron variant caused a large wave of SARS-CoV-2 community infection rates in Wales. To respond to this, in line with guidance, NHS Wales increased the availability of booster dose vaccination, reduced the timing from 6 to 3 months, making it possible for all eligible groups to receive a booster dose before the end of 2021, approximately 70% of the adult population [11].

Given the importance of the booster dose, research must attend to questions around vaccine inequality and disparities among HCWs, as well as questions around breakthrough infections (those who were administered a booster dose, who went on to become infected). Therefore, in this study, we aimed to investigate the role of socio-demographics, household composition, prior SARS-CoV-2 infection, and staff role characteristics in relation to uptake of the booster vaccination as well as breakthrough infections for HCWs, with comparisons being to the initial two-dose primary schedule.

2. Material and methods

2.1. Study design and data sources

We constructed a prospective, national-scale, observational cohort study of HCWs in Wales. We used anonymised individual-level, linked electronic health records (EHR) and administrative data sources available within the Secure Anonymised Information Linkage (SAIL) Databank [12,13]. These data sources included NHS Wales workforce records, population demographics, residential history, COVID-19 RT-PCR testing results, COVID-19 vaccinations, General Practitioner (GP) attendances, prescribed and dispensed medications, hospital admissions, and death (Table SM2). We conducted separate analyses of uptake of the two primary doses as well as the 2021 booster dose for this cohort up to 31st January 2022, followed by analyses of breakthrough of the second primary and booster doses over the same time period.

2.2. Definitions of outcomes

For uptake, our outcomes were dates of administration of available COVID-19 vaccinations as part of the primary-two-dose vaccination schedule and the subsequent 2021 booster vaccination. Vaccinations available were Pfizer-BioNTech (BNT162b2), Moderna (mRNA-1273) and Oxford-AstraZeneca (ChAdOx1 nCoV-19).

For vaccine breakthrough infections, our outcomes were dates of COVID-19 infections as determined by a positive COVID-19 RT-PCR test. A new infection was defined at the date of a positive test with at least 90 since the previous positive test.

2.3. Cohort and sample selection

Those initially selected were recorded as being employed as a HCW and living in Wales from 1st January 2020 to 8th December 2020 (Fig. 1). General exclusion criteria were applied to ensure reliable records were being used for analysis: HCWs were included only if they had linked primary care (GP) records, valid vaccination records, and were not recorded as shielding. Sub-samples were then defined for the analyses of uptake and failure separately.

2.4. Characteristics and confounders

Across both sets of uptake and breakthrough analyses, the main characteristics of interest were: HCW staff group, whether working in a patient-facing role, age, sex, ethnic group, body mass index (BMI), number of QCovid co-morbidities [14,15], household composition, and socioeconomic status (SES) at baseline. We considered the following variables as potential confounders: urban/rural classification of the HCW home address, number of previous PCR tests, and health board of residence (geographical NHS administrative area). Staff roles were identified as to whether they were patient-facing, and categorised into nine groups: nursing and midwifery, clinical services, administrative, estates and ancillary (e.g., porter, security, housekeeping, catering), medical and dental, allied health professionals, technical staff, healthcare scientists, and students. To overcome the incompleteness of the recording of ethnicity in any single given data source, ethnicity was identified using multiple data sources and recorded in line with groups defined by the Office for National Statistics: White, Asian, Black, Mixed and Other [16]. Household composition was determined using the number of adults and children living at the same residence at baseline [17]. Socioeconomic status was defined as the Welsh Index of Multiple Deprivation 2019 quintile for the HCWs area of residence [18]. BMI was the only measure with severe missing data (47% missing based on GP records over the previous five years). For computational efficiency, we performed a single imputation of log BMI, using the outcomes and the other covariates. For the uptake

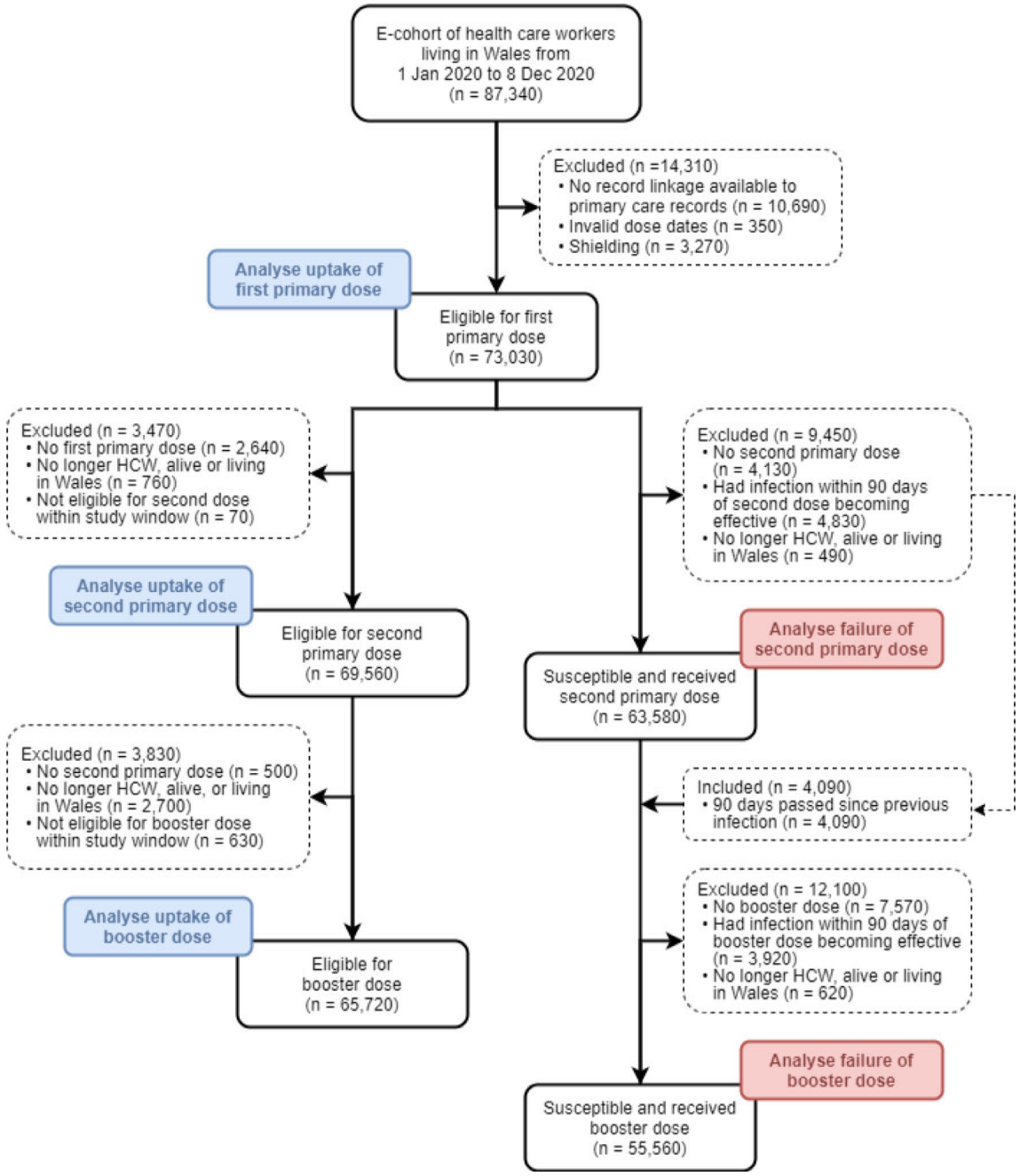

Fig. 1. Flow diagram of sample selection for the separate vaccine uptake and failure analyses from a cohort of 87,340 HCWs living in Wales. Discrepancies between counts are due to rounding.

analyses only, time since previous infection was included, derived from PCR testing.

2.5. Statistical analysis

We used Cox proportional hazard models to analyse the rate of uptake for each dose, separately. We report unadjusted and adjusted hazard ratios (HR) with 95% confidence intervals (CIs) based on robust standard errors, stratifying the baseline by health board. Adjusted hazard ratios (aHR) were estimated by including main effects for all characteristics and confounders. The impact of testing positive for COVID-19 prior to vaccination was captured using a time-varying measure, with post-infection time divided into intervals: 0–3, 4–7, 8–11, 12–25, 26 or more weeks. To check if specific subgroups had different responses to getting vaccinated after testing positive via RT-PCR, we tested for interactions between the post-infection intervals and the other characteristics of interest.

We analysed the rate of vaccine breakthrough also using Cox proportional hazard modelling. Follow-up started from 14 days post second and booster dose. We report unadjusted and adjusted hazard ratios (HR) with 95% confidence intervals (95%CI) based on robust standard errors, stratifying the baseline by health board and by vaccine type. Adjusted hazard ratios (aHR) were estimated by including main effects for all characteristics and confounders. We censored participants if they were no longer employed as a HCW, moved out of Wales, died before becoming infected, or end of follow-up was reached.

Table 1
Descriptive counts and column percentages of the cohort of HCWs in Wales (n = 73,030).

Characteristic	n	Col. %
Staff group		
Nursing and midwifery registered	20,050	27.5
Add prof scientific and technical	2,470	3.4
Additional clinical services	17,470	23.9
Administrative and clerical	15,230	20.9
Allied health professionals	4,600	6.3
Estates and ancillary	6,460	8.8
Healthcare scientists	1,600	2.2
Medical and dental	5,150	7.1
Patient facing status		
Patient facing	49,990	68.5
Non-patient facing	15,960	21.9
Undetermined	7,080	9.7
Sex		
Female	57,170	78.3
Male	15,860	21.7
Age		
18–29	9,260	12.7
30–39	16,610	22.7
40–49	17,950	24.6
50–59	21,180	29.0
60+	8,030	11.0
Ethnicity		
White	67,580	92.5
Asian	3,720	5.1
Mixed	740	1.0
Other	360	0.5
Black	590	0.8
Unknown	50	0.1
Number of co-morbidities		
0	47,300	64.8
1	19,950	27.3
2+	5,770	7.9
BMI		
<18.5	1,350	1.8
18.5–24.9	22,010	30.1
25.0–29.9	23,640	32.4
30.0–34.9	15,670	21.5
35.0–39.9	6,860	9.4
40.0+	3,500	4.8
Household composition		
1 adult	6,580	9.0
2 adults	15,130	20.7
3 + adults	19,700	27.0
1 adult, 1 + children	3,970	5.4
2 adults, 1 + children	17,490	23.9
3 + adults, 1 + children	10,160	13.9
Area of deprivation quintile		
1 - Most deprived	10,990	15.1
2	14,120	19.3
3	13,980	19.1
4	15,170	20.8
5 - Least deprived	18,760	25.7
Urban/rural classification		
Urban city and town	53,950	73.9
Rural town and fringe	11,450	15.7
Rural village and dispersed	7,620	10.4
Weeks since previous infection at 8th Dec 2020		
Uninfected	64,530	71.3
0–3 weeks	6,060	6.7
4–7 weeks	7,500	8.3
8–11 weeks	4,700	5.2
12–25 weeks	2,890	3.2
26 + weeks	4,840	5.3
Number of prior PCR tests		
0	37,090	50.8
1	20,940	28.7
2	8,990	12.3
3	3,310	4.5
4+	2,700	3.7
Residing health board		
Aneurin Bevan	12,180	16.7
Betsi Cadwaladr	14,040	19.2
Cardiff and Vale	13,520	18.5

Table 1 (*continued*)

Characteristic	n	Col. %
Cwm Taf Morgannwg	13,880	19.0
Hywel Dda	7,990	10.9
Powys	740	1.0
Swansea Bay	10,680	14.6

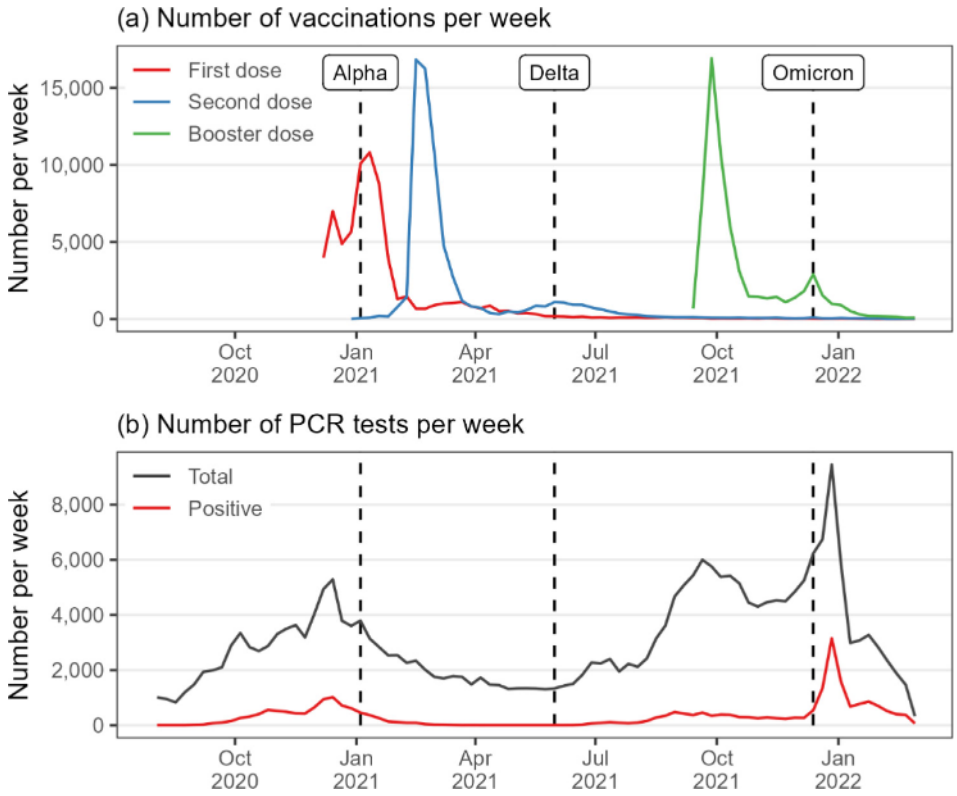

Fig. 2. Weekly frequencies of (a) vaccine uptake and (b) PCR tests for HCWs in Wales up to 28th February 2022, overlaid when each variant became dominant.

For each Cox model, we checked the assumption that hazard ratios were proportional over time by plotting the Schoenfeld residuals for each coefficient. The trend lines for which are included in the Supplementary Material. Analysis was carried out using R v4.1.2 and the survival package [19].

2.6. Ethics and permissions

We conducted this research within the SAIL Databank following permission and approval of the independent Information Governance Review Panel (IGRP) project number 0911.

2.7. Reporting

We used the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist to guide our transparent reporting of our work [20]. Due to disclosure rules imposed by our secure and trusted research environment, counts between 1 and 9 have been suppressed, and counts 10 and above have been rounded to nearest 10.

2.8. Role of funding source

The funding source had no involvement in data collection, study design, data analysis, interpretation of findings or the decision to publish.

3. Results

Across our cohort of 73,030 HCWs (Table 1), nursing and midwifery was the most common staff group (27.5%), and health care scientists being the smallest group (2.2%). The majority of HCWs were patient facing (68.5%). Most HCWs were female (78.3%), aged between 40 and 59 (53.6%), of White ethnicity (92.5%), and have no COVID-specific clinical risks (64.8%). Over a quarter (25.7%) were residing in the least deprived areas of Wales, with HCWs living in households of three or more adults being the most common arrangement (27.0%), next were households of two adults with one or more children (23.9%), and a small proportion living alone with a child (5.4%).

Vaccination of HCWs began in early December (Fig. 2a), with two peaks for the first dose, and sharper and more rapid uptake for the second and booster dose. Meanwhile mass testing became available from September 2020 (Fig. 2b), with both the autumn and winter months in 2020 and 2021 showing greater testing. Subsequently, greater infection followed, with waves of positive tests between September and January 2021.

3.1. Vaccination uptake

Of the 73,030 HCWs in our sample, 69,800 (95.6%) were administered with their first primary dose across the 15-month study

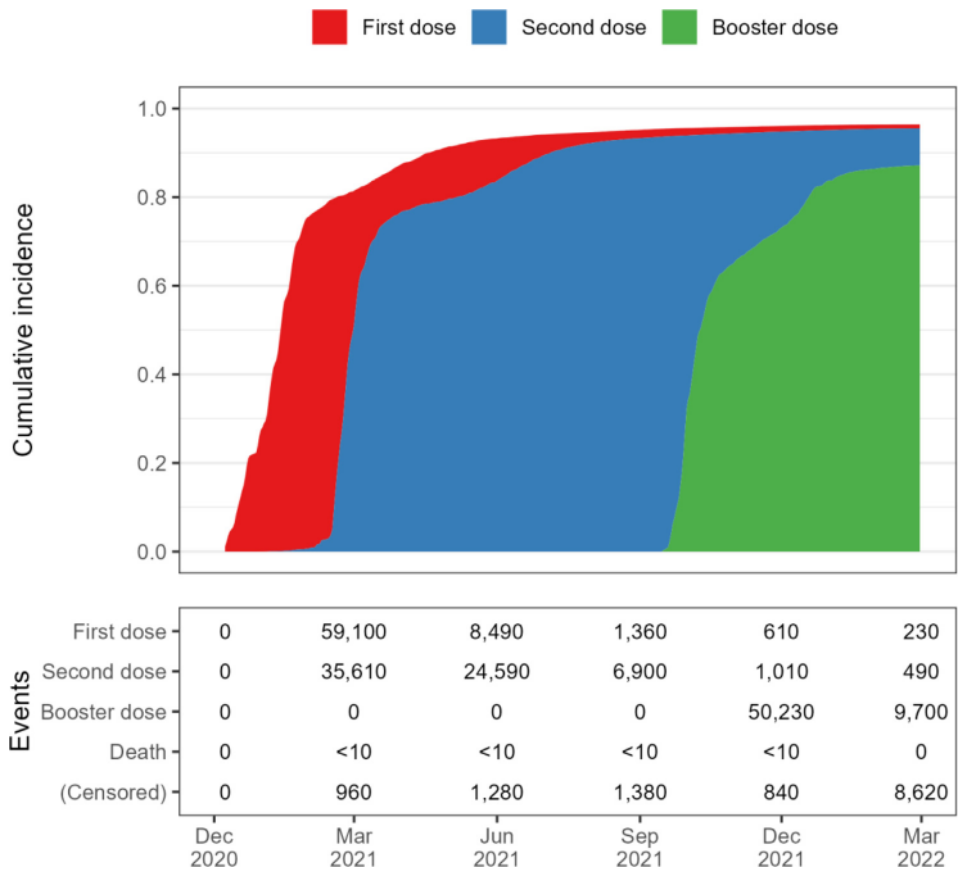

Fig. 3. Cumulative incidence of uptake for HCWs in Wales up to 28th February 2022. Observations were censored upon no longer being a HCW or they had moved out of Wales.

window. Of the 69,560 eligible for their second dose within the study, 68,610 (98.6%) were administered with their second dose. Finally, of the 65,720 eligible, 59,960 (91.2%) were administered with a booster dose,. Cumulative incidences for each dose are shown in Fig. 3.From our analysis of time to vaccination (Fig. 4), we found that staff groups had small variations in their uptake of the first and second primary doses as well as their booster dose, with the first dose showing the largest variations. The staff group with the highest likelihood of booster vaccine uptake was the Medical and Dental group (aHR 1.15, 95%CI 1.11–1.19), with the reference category being Nursing and Midwifery Registered staff. In reverse, Additional Clinical Services were the least likely to be vaccinated with the booster vaccine (aHR 0.84, 95%CI 0.82–0.86). A clear gradient was observed across age, with the steepest gradient being observed for the booster vaccine. Those aged 60 + were 2.54 (95%CI 2.45–2.63) times more likely to be vaccinated for the booster dose compared to those aged 18–29 years. Males and had the same uptake (aHR 1.00, 95%CI 0.98–1.02). HCWs of a Black ethnic background were the least likely to receive a first primary dose as well as a booster dose, compared to White HCWs (Booster aHR 0.67, 95%CI 0.61–0.74). HCWs of a Mixed ethnic background were also less likely to receive their first primary dose and booster dose (Booster aHR 0.89 95%CI 0.82–0.97). Asian HCWs were more likely to be administered with both a primary dose and booster dose (Booster aHR 1.18, 95%CI 1.14–1.22). In addition, we observed a small socioeconomic gradient for the booster dose, whereby those in least deprived areas were more likely to have a first primary dose (aHR 1.25 95%CI 1.22–1.28) as well as a booster dose (aHR 1.12, 95%CI 1.09–1.16). Meanwhile, we found that single parent households were the least likely to receive both a primary dose (aHR 0.77, 95%CI 0.74–0.80) as well as a booster dose (aHR 0.83, 95%CI 0.80–0.87), compared to those living in two-adult households. Of those who had been infected, uptake was rare during the subsequent four weeks following infection (aHR 0.07, 95%CI 0.06–0.08), in line with policy. However, we found a small reduction in uptake for those who it had been at least six months since their previous infection (aHR 0.87, 95%CI 0.85–0.89). Finally, several characteristics were minimally associated with booster uptake, these included; number of co-morbidities, BMI, urban and rural classification, and number of prior PCR tests.

3.2. Vaccine breakthrough

We found that the unadjusted overall crude rate of infection was greater for the booster dose compared to the second dose (Table 2). However, the dominant variant transitioned from Delta to, the more transmissible [21], Omicron during the booster uptake period (Fig. 2b), our survival analysis takes this into account (Fig. 5). Of the 63,580 HCWs who had received a second dose and were considered susceptible 14 days after administration, 5,820 (9.1%) became infected, at a rate of 160 per 1,000 person-years. For the 55,560 HCWs who received a booster dose and were susceptible, 8,500 (15.3%) became infected, a rate of 510 per 1,000 person-years. From our analysis (Fig. 5), characteristics associated with booster vaccine breakthrough were similar to those found for the second primary dose, with a few exceptions. Across both doses, Nursing and Midwifery staff, along with Allied Health Professionals and Additional Clinical Service staff were found to have a slightly higher risk of breakthrough, compared to the other staff groups. Non-patient facing HCWs had a marginally higher risk of break-

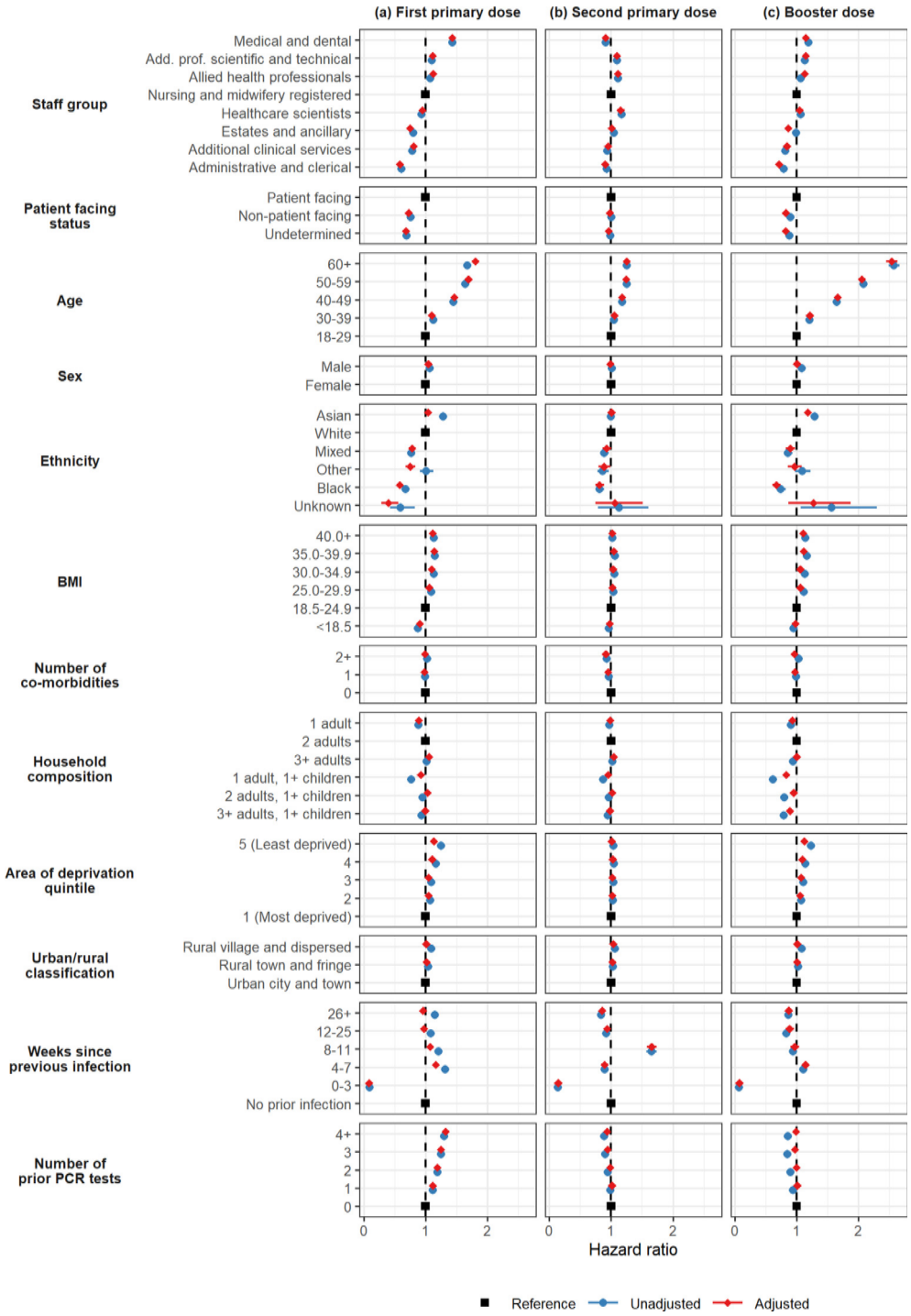

Fig. 4. Hazard ratios (95% confidence interval) of uptake for (a) first and (b) second dose primary dose and (c) booster dose of COVID-19 vaccinations by HCW characteristics.

through at second dose, compared to those in patient facing role (aHR 1.09, 95%CI 1.02–1.17), but the opposite was observed for the booster dose (aHR 0.92, 95%CI 0.87–0.97). Regarding demographics, we found that males were associated with less breakthrough than females (aHR 0.90 (0.83–0.96) and 0.84 (0.79–0.89), for second dose and booster, respectively). Each older age group was at substantially less risk than those aged 18–29, with those aged 60 + having the least risk across their second primary dose (aHR 0.36, 95%CI 0.32–0.41) and their booster dose (aHR 0.43, 95%CI 0.37–0.49). We found few differences among ethnicity groups, except that HCWs with of an Asian ethnicity were at a lower risk of breakthrough infection at second dose (aHR 0.72, 95%CI 0.62–0.83), compared to White HCWs.Household composition showed considerable associations with vaccine breakthrough. Compared to two-adult only households, we found that households with two adults and at least one child were at increased risk of breakthrough infection post second primary dose (aHR 1.80, 95% CI 1.64–1.97), as well as post booster dose (aHR 1.52, 05%CI 1.41–1.63). Similar associations were found for HCWs living with children by themselves or with three or more adults. Meanwhile, we found that HCWs living alone had the same risk as those living with one other adult, and those living in a three-adult household

Table 2
Descriptive counts of HCWs who had received a second dose and booster dose, alongside counts and rates of infection per 1,000 person-years.

	Second dose		Booster dose	
Characteristic	**n (%)**	**Infected (rate)**	**n (%)**	**Infected (rate)**
Total	63,580 (100.0%)	5,820 (160)	55,560 (100.0%)	8,500 (510)
Vaccine name				
PB	55,760 (87.7%)	4,620 (140)	48,910 (88.0%)	8,060 (510)
AZ	7,590 (11.9%)	1,160 (300)	40 (0.1%)	–
MD	240 (0.4%)	40 (430)	6,620 (11.9%)	440 (410)
Staff group				
Nursing and midwifery registered	17,400 (27.4%)	1,650 (160)	15,380 (27.7%)	2,680 (570)
Add prof scientific and technical	2,200 (3.5%)	190 (150)	1,990 (3.6%)	310 (490)
Additional clinical services	14,590 (22.9%)	1,550 (180)	12,300 (22.1%)	2,070 (560)
Administrative and clerical	13,640 (21.5%)	1,290 (170)	11,710 (21.1%)	1,390 (430)
Allied health professionals	4,090 (6.4%)	330 (140)	3,690 (6.6%)	650 (570)
Estates and ancillary	5,560 (8.8%)	400 (120)	4,910 (8.8%)	610 (390)
Healthcare scientists	1,460 (2.3%)	100 (120)	1,310 (2.4%)	190 (460)
Medical and dental	4,650 (7.3%)	290 (100)	4,270 (7.7%)	610 (440)
Patient facing status				
Patient facing	43,070 (67.7%)	3,960 (160)	37,790 (68.0%)	6,220 (530)
Non-patient facing	14,200 (22.3%)	1,270 (160)	12,320 (22.2%)	1,600 (440)
Undetermined	6,320 (9.9%)	590 (170)	5,460 (9.8%)	680 (440)
Sex				
Female	49,700 (78.2%)	4,780 (170)	43,130 (77.6%)	6,920 (530)
Male	13,880 (21.8%)	1,040 (130)	12,440 (22.4%)	1,580 (410)
Age				
18–29	7,560 (11.9%)	1,000 (230)	5,590 (10.1%)	1,160 (780)
30–39	14,130 (22.2%)	1,780 (220)	11,500 (20.7%)	2,110 (650)
40–49	15,750 (24.8%)	1,630 (170)	14,260 (25.7%)	2,430 (560)
50–59	19,000 (29.9%)	1,130 (100)	17,860 (32.2%)	2,250 (390)
60+	7,140 (11.2%)	280 (70)	6,360 (11.4%)	570 (270)
Ethnicity				
White	58,910 (92.6%)	5,500 (160)	51,310 (92.3%)	7,850 (510)
Asian	3,270 (5.1%)	200 (100)	3,090 (5.6%)	490 (500)
Mixed	610 (1.0%)	50 (150)	510 (0.9%)	70 (440)
Other	300 (0.5%)	20 (120)	270 (0.50%)	40 (510)
Black	470 (0.7%)	50 (180)	360 (0.7%)	50 (460)
Unknown	30 (0.0%)	–	20 (0.0%)	–
Number of co-morbidities				
0	41,240 (64.9%)	3,800 (160)	36,050 (64.9%)	5,620 (520)
1	17,290 (27.2%)	1,600 (160)	15,100 (27.2%)	2,280 (500)
2+	5,060 (8.0%)	420 (140)	4,410 (7.9%)	600 (450)
BMI				
<18.5	1,140 (1.8%)	110 (160)	950 (1.7%)	130 (470)
18.5–24.9	19,040 (29.9%)	1,800 (160)	16,120 (29.0%)	2,640 (550)
25.0–29.9	20,610 (32.4%)	1,820 (150)	18,140 (32.7%)	2,740 (500)
30.0–34.9	13,750 (21.6%)	1,240 (150)	12,200 (21.9%)	1,800 (480)
35.0–39.9	5,990 (9.%)	550 (160)	5,430 (9.8%)	770 (460)
40.0+	3,060 (4.8%)	310 (170)	2,730 (4.9%)	420 (510)
Household composition				
1 adult	5,700 (9.0%)	350 (110)	5,030 (9.1%)	540 (350)
2 adults	13,330 (21.0%)	760 (100)	11,960 (21.5%)	1,310 (350)
3 + adults	17,150 (27.0%)	1,240 (120)	15,420 (27.7%)	2,290 (480)
1 adult, 1 + children	3,330 (5.2%)	490 (250)	2,590 (4.7%)	510 (710)
2 adults, 1 + children	15,340 (24.1%)	1,970 (220)	13,130 (23.6%)	2,490 (640)
3 + adults, 1 + children	8,740 (13.7%)	1,010 (200)	7,440 (13.4%)	1,360 (610)
Area of deprivation quintile				
1 - Most deprived	9,290 (14.6%)	1,000 (180)	7,900 (14.2%)	1,210 (510)
2	12,120 (19.1%)	1,230 (170)	10,450 (18.8%)	1,670 (530)
3	12,150 (19.1%)	1,110 (160)	10,500 (18.9%)	1,590 (500)
4	13,310 (20.9%)	1,100 (140)	11,740 (21.1%)	1,760 (490)
5 - Least deprived	16,710 (26.3%)	1,380 (140)	14,970 (26.9%)	2,270 (500)
Urban/rural classification				
Urban city and town	46,800 (73.6%)	4,350 (160)	40,990 (73.8%)	6,450 (520)
Rural town and fringe	10,000 (15.7%)	950 (160)	8,680 (15.6%)	1,300 (490)
Rural village and dispersed	6,780 (10.7%)	520 (130)	5,900 (10.6%)	750 (410)
Number of prior PCR tests				
0	32,960 (51.8%)	2,860 (150)	16,110 (29.0%)	2,030 (410)
1	18,140 (28.5%)	1,710 (160)	14,600 (26.3%)	2,120 (480)
2	7,600 (11.9%)	720 (160)	10,070 (18.1%)	1,620 (530)
3	2,710 (4.3%)	290 (180)	5,920 (10.7%)	1,030 (580)
4+	2,180 (3.4%)	250 (190)	8,860 (15.9%)	1,710 (640)
Residing health board				
Aneurin Bevan	10,550 (16.6%)	1,020 (170)	9,280 (16.7%)	1,460 (530)
Betsi Cadwaladr	12,470 (19.6%)	1,100 (150)	10,570 (19.0%)	1,460 (450)
Cardiff and Vale	12,010 (18.9%)	870 (130)	10,670 (19.2%)	1,680 (500)
Cwm Taf Morgannwg	11,890 (18.7%)	1,170 (170)	10,690 (19.2%)	1,720 (530)

Table 2 (*continued*)

Characteristic	Second dose		Booster dose	
	n (%)	Infected (rate)	n (%)	Infected (rate)
Hywel Dda	6,910 (10.9%)	610 (150)	5,970 (10.7%)	830 (460)
Powys	660 (1.0%)	60 (140)	560 (1.0%)	80 (480)
Swansea Bay	9,090 (14.3%)	1,000 (190)	7,830 (14.1%)	1,280 (570)

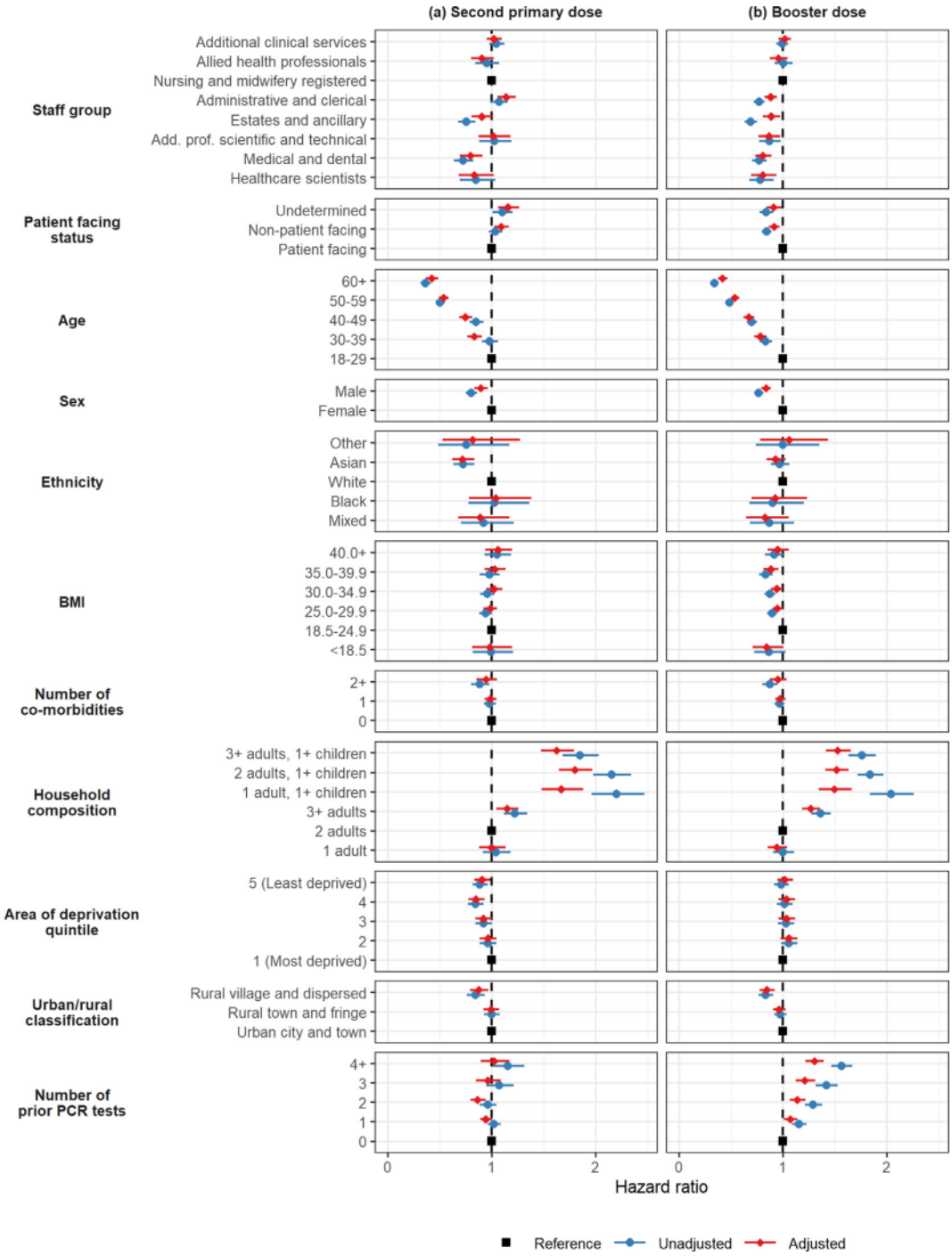

Fig. 5. Hazard ratios (95% confidence interval) of infection for second primary dose and booster dose, separately.

had increased risk (aHR 1.15 (1.05–1.26) and 1.27 (1.18–1.36), for second dose and booster, respectively).

Amongst HCWs, we found no evidence of associations for breakthrough of either the second primary dose or booster dose regarding number of co-morbidities, BMI, socio-economic status,

and urban/rural classification. The estimates in full are available in Table SM4.

4. Discussion

We show that socio-demographics are strongly associated with both uptake of COVID-19 vaccines as well as breakthrough infections in HCWs. HCWs of a younger age and either a Black or Mixed ethnicity were less likely to have a COVID-19 vaccination, as were those residing in a more deprived area or living with children. Relatively fewer associations were found for the second primary dose, as compared to the first primary and booster doses, we attribute this to the primary vaccination schedule being anticipated as two doses and the booster programme being devised later on, as well as requiring people to book their own appointment, at a time when compliance with social restrictions was in decline [22]. Indeed, those who were residing in a household with one or more children were more likely to be infected by SARS-CoV-2 despite being vaccinated with a primary, or booster course. We explore our findings in relation to policy, practice and wider research.

In terms of socio-demographics, younger HCWs had a slower rate of uptake. This is a concern as unvaccinated HCWs may pose a risk to vulnerable patients [23–26]. Building on this, HCWs of a Black or Mixed ethnic group were less likely to receive a booster vaccination, compared with White HCWs. Historical marginalisation of ethnic minorities, alongside previous unethical research and under-representation in clinical trials, may have led to low trust in government bodies, which has further reduced since the pandemic [27]. However, HCWs of an Asian background were more likely to be vaccinated compared to White HCWs, which is in line with other studies in terms of Chinese ethnicity [28,29], however our study is likely to capture other Asian ethnic groups, such as Indian, Pakistani, and Bangladeshi which have been associated with lower vaccine uptake [8,29]. The differences across the ethnic groups highlight the importance of tailored vaccine hesitancy support. Following this, we also found evidence of a small disparity for those residing in more deprived areas, and those living with children.

The inequality in vaccination uptake prompts the question of how public health bodies communicate the benefits of vaccination to the groups with lower uptake identified in this study. Emerging research suggests that the "intention of the majority" along with strong scientific evidence encourages young people to get vaccinated [30]. Moreover, qualitative research has suggested that tackling misinformation may be particularly important for younger HCWs and HCWs from ethnic minority groups [31].

Previous attempts to tackle the disparity in vaccinations have focused on whether to make COVID-19 vaccination mandatory for HCWs [32–35], whilst this has yet to occur in the UK [36], such mandatory vaccination does exist for other diseases. There are challenges with either side of mandatory vaccination, as pressure to receive the vaccine can actually reduce the likelihood of uptake [9], as well as increasing an already pressured National Health Service [37], and would not alleviate concerns around vaccine safety amongst the unvaccinated [38]. Hence, it is likely that building trust, and sharing factual vaccination information on clinical trials which represent a diverse range of patients may encourage at-risk groups to become vaccinated against COVID-19 [39].

In terms of vaccination breakthrough, we found that living in a household with children had the largest association for an infection. Given that most children attend school, even in periods of lockdown for key workers such as HCWs, there is a greater risk of transmission due to the number of close contacts in school settings [40]. Alishaq et al. (2021) also found that those living in family housing or sharing with non-family members had an increased risk of a breakthrough infection, whereas those living alone did not; however, this was only for the primary course and not booster dose [41]. We also found that older age was associated with a lower likelihood of a breakthrough infection for both the second and booster dose. This aligns with Oster et al. (2022) who found a much lower risk of breakthrough infections for those aged 45 and over. Studies have pointed to the benefit of the booster dose, although breakthrough infections occurred, vaccinations still provide important protection against infection [42,43].

Our study benefitted from having a large cohort of HCWs overtime, and due to the SAIL Databank, were able to link to multiple demographic and health data sources. Nevertheless, there were also several limitations: first, we did not have access to information on HCWs not directly employed by NHS Wales, for example, agency staff, for whom exposure could be greater and potentially coming from more disadvantaged parts of society. Second, SES was based on residing area of the HCW as we did not have access to individual measures of SES, such as educational qualifications or household income, these would have enabled a deeper understanding of socioeconomic disadvantage, with potential of identifying different mechanisms within inequality structures. Thirdly, due to the data linkage methods and availability of primary health care in the SAIL Databank, we only had access to data on approximately 84% of HCWs in Wales. Lastly, with the exception of one coefficient, estimated uptake amongst administrative staff, the proportional hazards assumption appeared to be reasonably met across all the Cox models (Figures SM1,2,3 4,5,6). We expect the departure from proportionality is due to the way in which this group was initially deprioritised in favour of the more patient-facing roles.

5. Conclusions

Our study provides national findings that sociodemographic characteristics are associated with lower vaccination uptake in HCWs, along with higher risk of breakthrough infections. HCWs who were younger, residing in a more deprived area, living with children, or of a Black or Mixed ethnicity were less likely to receive a booster vaccination. Likewise, similar characteristics were at a higher risk of a breakthrough infection, particularly after the second dose. We encourage governments and their respective health services to improve communication with the at-risk groups identified in this study, who perhaps have low trust in government, or are vulnerable to misinformation.

Data availability

The authors do not have permission to share data.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This study makes use of anonymised data held in the Secure Anonymised Information Linkage (SAIL) Databank. This work uses data provided by patients and collected by the NHS as part of their care and support. We would also like to acknowledge all data providers who make anonymised data available for research. We wish to acknowledge the collaborative partnership that enabled acquisition and access to the de-identified data, which led to this output. The collaboration was led by the Swansea University Health Data Research UK team under the direction of the Welsh Government

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Availability of data and materials

The data used in this study are available in the SAIL Databank at Swansea University, Swansea, UK, but as restrictions apply they are not publicly available. All proposals to use SAIL data are subject to review by an independent Information Governance Review Panel (IGRP). Before any data can be accessed, approval must be given by the IGRP. The IGRP gives careful consideration to each project to ensure proper and appropriate use of SAIL data. When access has been granted, it is gained through a privacy protecting safe haven and remote access system referred to as the SAIL Gateway. SAIL has established an application process to be followed by anyone who would like to access data via SAIL at https://www.saildatabank.com/application-process

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2023.01.023.

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