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Uptake and factors associated with COVID-19 vaccination among healthcare workers: a multicentre cohort study in seven European countries, September 2021–April 2024

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Abstract

Background

Healthcare workers (HCWs) were prioritised for COVID-19 vaccination, leading to high uptake for primary schedule, but decreased for subsequent booster doses. We aimed to describe COVID-19 vaccine uptake over multiple seasons and identify factors associated with vaccination in a cohort of hospital-based HCWs.

Methods

We conducted a prospective multicentre cohort study among HCWs from twelve hospitals in seven countries that collected, besides vaccination, sociodemographic, occupational, and community behaviour data at enrolment and weekly follow-up questionnaires, allowing for time-varying exposures. We analysed vaccine uptake for the first (September 2021–August 2022), second (September 2022–April 2023) and third (September 2023–April 2024) vaccination periods among HCWs eligible for booster doses. We fitted Cox proportional hazards models with vaccination as the outcome, separately by vaccination period, for each sociodemographic, occupational, and community variable. We estimated adjusted hazard ratios (aHRs), adjusting (where applicable) for hospital, age, sex, underlying chronic conditions, and occupational role.

Results

We included a total of 2194 HCWs (997, 1038, and 1055 in the first, second, and third periods, respectively). COVID-19 vaccine uptake during the follow-up was 71%, 32%, and 19% in the first, second, and third vaccination period, respectively. We observed a marked age-sex-interaction, with uptake highest in men over the age of 50 (aHRs 1.5 [1.0, 2.2], 1.4 [0.8, 2.6], 0.9 [0.4, 1.9], compared to women over the age of 50). HCWs in all professional roles presented lower vaccine uptake than medical doctors (aHRs for nurses 0.6 [0.5–0.7], 0.5 [0.4–0.8], and 0.7 [0.4–1.1]). We observed an association between attending gatherings and higher vaccine uptake only during the first vaccination period, and no associations for other infection prevention measures, comorbidities, HCW household size.

Conclusions

COVID-19 vaccine uptake declined substantially over seasons. HCWs other than medical doctors presented a lower uptake during the pandemic compared to medical doctors, though not post-pandemic, indicating they should be targeted in vaccination awareness campaigns in similar pandemic situations. Future vaccination policies designed to respond to emerging health crises should take into account lessons learned from HCWs COVID-19 vaccination dynamics.

1. Background

Healthcare workers (HCWs) were disproportionately affected by the coronavirus disease 2019 (COVID-19) pandemic, facing high risk of infection and severe outcomes (1–3). Early in the pandemic, the global prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among HCWs was estimated at 8–11% (4, 5). Given their increased occupational exposure, elevated risk of healthcare-associated transmission to vulnerable patients, and the need to maintain healthcare workforce capacity, HCWs were prioritised for COVID-19 vaccination (6–9).

The initial vaccination strategy focused on administering a primary series to reduce infection risk and prevent severe disease among HCWs (10–12). However, evidence of waning protection after vaccination, combined with the emergence of SARS-CoV-2 variants with increased immune escape potential, prompted recommendations for booster doses (13–15). In Europe, booster vaccination campaigns were progressively introduced from autumn 2021, with evolving recommendations to account for circulating variants and updated vaccine formulations (16, 17). Although vaccine effectiveness against SARS-CoV-2 infection declined with the advent of viral variants, vaccination remained highly protective against hospitalisation and death (15, 18–20).

Despite the importance of maintaining high vaccination coverage, HCWs' vaccine uptake decreased substantially between the primary series and subsequent booster campaigns (21–23). Although several studies identified factors associated with vaccine uptake (21, 24–27), most focused on a single phase of the vaccination campaign. As a result, little is known about how determinants of vaccination evolved over the course of the pandemic, which drivers of uptake remained stable, and which shifted as epidemiological conditions, perceptions, and public health recommendations changed. Vaccination strategies also evolved, moving from an initial focus on the number of doses received to vaccinating at an optimal interval between vaccine doses and later incorporating vaccines adapted to circulating viral variants happened (32–35).

In this study, we use the longitudinal design of a multicentre perspective cohort of HCWs from seven European countries to describe longitudinal trends in COVID-19 vaccine uptake and assess determinants of (booster) vaccine uptake between September 2021 and April 2024, allowing us to distinguish persistent from time-varying drivers of uptake.

2. Methods

2.1. Study design and population

We conducted a secondary analysis of data from the VEBIS-HCW cohort study, a multicentre study set up to measure the vaccine effectiveness among a population of European HCWs. For this study, we included participants from twelve hospitals (i.e., study sites) in seven European countries (Croatia, Estonia, Ireland, Italy, Latvia, Portugal, and Spain). Detailed methodology and study protocols are available in the VEBIS-HCW protocol (28). Since we conducted a pooled analysis at the European level, we did not describe dynamics and associations at country level.

All HCWs from the participating hospitals were eligible to participate, regardless of their professional role. Enrolment started in May 2021 and ended in April 2024, with site-specific variations in start and end date (Figure S1). To align with COVID-19 booster dose recommendations, we divided the study period into three booster eligibility periods: 1) First vaccination period (1 September, 2021–31 August, 2022), when first booster doses were recommended; 2) Second vaccination period (1 September, 2022–30 April, 2023) when second booster doses were recommended, including the bivalent vaccine; and 3) Third vaccination period (1 September, 2023–30 April, 2024) when the autumn 2023 adapted vaccine was recommended, and which was the only post-pandemic period. HCWs were able to contribute person-time to one or multiple periods. At enrolment, HCWs completed questionnaires about demographic information, medical history, and factors related to occupational and community exposures and behaviours. Throughout follow-up, participants were asked to fill out weekly questionnaires gathering updated information on vaccination status and possible exposures in both healthcare settings and the community. All data collection was managed through the Voozanoo platform (29).

All participants who completed the enrolment questionnaire were included in the analysis, unless they were not eligible for the COVID-19 vaccination, had inconsistent vaccination records (e.g. a second vaccine dose preceding the first), missing age or sex information, an immunocompromising condition (such as an immunodeficiency and/or active cancer), or did not fill out any follow-up questionnaires. Additionally, we removed person-time episodes when participants were not eligible for vaccination: periods within 60 days following a confirmed SARS-CoV-2 infection and periods within 90 days after the receipt of a vaccine dose in a previous vaccination period. Moreover, if no vaccinations were recorded in a hospital during an entire vaccination season, we assumed no HCW vaccination campaigns were carried out, and all HCWs from these hospitals were excluded for the period.

2.2. Variable definitions

The outcome of the study was the receipt of a COVID-19 vaccine dose, analysed separately for each period described above. We considered each administered vaccine dose as an outcome, regardless of whether it aligned with the vaccination period (e.g. if a participant received their first booster dose during the second vaccination period, it was still counted as an outcome). This approach allowed us to examine the key drivers of vaccine uptake within each period. Vaccination status was self-reported by HCWs and verified in nearly all cases (> 90%) by site coordinators, who consulted vaccine registries or vaccination cards.

We categorised potential predictors for vaccine uptake into three main groups: individual, occupational, and community-related factors. Individual factors included sex, age, presence of chronic health conditions, smoking status (non-smoker or current smoker), alcohol use (daily, weekly, or occasionally/never), and prior SARS-CoV-2 infection. Occupational factors encompassed participants'

professional roles, ward, work time (full time, part-time more than 50% or part-time less than 50%), adherence to infection prevention and control (IPC) measures, and workplace contact with COVID-19 cases (patients or coworkers). Community factors included household characteristics, contact with COVID-19 cases at home, and everyday behaviours like taking public transportation and attending gatherings.

Several factors were time-varying and updated during follow-up, including recent SARS-CoV-2 infection, contact with COVID-19 cases, and community behaviours. All other variables were collected at enrolment the start of each vaccination period and assumed to remain constant afterwards.

We applied a complete case approach in our analysis. Participants missing baseline information were excluded from any models requiring those specific variables. For time-dependent variables collected during follow-up, missing values were imputed, carrying the last observation forward.

2.3. Statistical analysis

For descriptive statistics, we calculated the number and percentage of HCWs contributing person-time within each exposure category, stratified by vaccination period and vaccination status at the end of the period. IPC variables were only described among medical doctors and nurses/nurse assistants. To describe cumulative vaccine uptake in each period, we conducted Kaplan-Meier analyses, crude and stratified by HCW age group and sex.

To assess the association between exposures and vaccine uptake, we applied Cox proportional hazards models, using time since the start of the vaccination period as the underlying time scale. Cox proportional hazards models were preferred over logistic regression models due to their capacity to include time-varying variables data and account for participant censoring. Study site was included a priori in all models as a stratification factor to adjust for site-level differences in the baseline hazard function. Participants were censored at loss to follow-up, the end of the study period, or after the receipt of a vaccine dose in each period. We first estimated crude hazard ratios (HRs) and 95% confidence intervals (CIs) for the association of each exposure variable with vaccine uptake separately, using models stratified by study site. Next, we fitted minimally adjusted models (stratified by site and adjusted for age, sex, with an interaction between age and sex) for each exposure of interest, and finally fully adjusted models, with adjustments for age, sex (with an age-sex interaction), underlying conditions, previous SARS-CoV-2 infection, professional role, and stratified by site, separately by period. We included an age-sex interaction term in the Cox proportional hazards models as descriptive analyses suggested effect modification between age and sex in vaccine uptake. All analyses were conducted with Stata version 17.0 (with the coefplot and esttab packages) and R version 4.4.2 (30), using the ‘survival’ package (31).

3. Results

3.1. Descriptive analysis

A total of 2601 HCWs enrolled in the study between September 2021 and April 2024. After applying exclusion criteria, 2194 HCWs were included in the analysis (Fig. 1). Of these, 997, 1038, and 1055 HCWs contributed to the first, second, and third vaccination periods, respectively, with many HCWs being included in multiple periods. In total, 709 (71%), 335 (32%), and 202 (19%) were vaccinated (Table 1). The majority of participants were women (1801, 82.1%) and between 18 and 49 years (1479, 66.7%), with a median age of 44 years. Overall, 640 (28.6%) HCWs reported at least one chronic health condition. Prior infection in the last 3–12 months was reported in 104 (10.4%) HCWs at the start of the first, 454 (34.7%) at the second, and 219 (20.8%) at the third period.

The distribution of HCW roles remained largely stable across the vaccination periods. Overall, 397 (17.8%) HCWs were medical doctors, 943 (42.2%) were nurses or nurse assistants, 315 (14.1%) worked in administrative or reception roles, 125 (5.6%) in laboratories, 17 (0.8%) as catering staff or cleaners, and 319 (14.3%) held other roles (Table 1). Full-time employees accounted for 1534 (64.0%) HCWs. The majority of clinical staff (medical doctors and nurses/ nurse assistants) reported always adhering to IPC measures (ranging from 70.2% to 89.1%, across all IPC variables and periods, disregarding missing data, Table 1 and S1).

Around half of HCWs lived in a household composed of three persons or more, and this proportion was stable over time (ranging from 51.0% to 55.6%). The frequency of public transportation use increased comparing the first period with the other two periods: 228 (22.9%) using public transportation three times or more per week in the first period to 339 (32.7%) and 338 (32.0%) in the

second and third periods, respectively. Likewise, the proportion of HCWs attending gatherings three times or more per week increased from 84 (8.4%) in the first vaccination period to 212 (20.4%) and 257 (24.4%) in the subsequent periods. No other substantial changes between periods could be identified (Table S1).

Table 1: Description of included HCWs, VEBIS-HCW European multi-centre COVID-19 study, factors for vaccination analysis, September 2021–April 2024. The status of each variable as recorded at the start of the respective vaccination period is shown, unless stated otherwise.

Variable	First vaccination period		Second vaccination period		Third vaccination period	
	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated
	N = 288	N = 709	N = 703	N = 335	N = 853	N = 202
Age						
18-49 years	193 (67.0%)	465 (65.6%)	472 (67.1%)	210 (62.7%)	539 (63.2%)	113 (55.9%)
≥50 years	95 (33.0%)	244 (34.4%)	231 (32.9%)	125 (37.3%)	314 (36.8%)	89 (44.1%)
Sex						
Female	243 (84.4%)	547 (77.2%)	615 (87.5%)	265 (79.1%)	699 (81.9%)	168 (83.2%)
Male	45 (15.6%)	162 (22.8%)	88 (12.5%)	70 (20.9%)	154 (18.1%)	34 (16.8%)
Any chronic condition						
No	213 (74.0%)	509 (71.8%)	479 (68.1%)	234 (69.9%)	583 (68.3%)	138 (68.3%)
Yes	74 (25.7%)	199 (28.1%)	221 (31.4%)	99 (29.6%)	244 (28.6%)	63 (31.2%)
Missing	1 (0.3%)	1 (0.1%)	3 (0.4%)	2 (0.6%)	26 (3.0%)	1 (0.5%)
Vaccination status at start of period						
Never vaccinated	4 (1.4%)	2 (0.3%)	5 (0.7%)	0 (0.0%)	15 (1.8%)	0 (0.0%)
1 dose	19 (6.6%)	20 (2.8%)	8 (1.1%)	1 (0.3%)	18 (2.1%)	0 (0.0%)
Primary series	193 (67.0%)	686 (96.8%)	103 (14.7%)	22 (6.6%)	113 (13.2%)	7 (3.5%)
1st booster	72 (25.0%)	1 (0.1%)	491 (69.8%)	310 (92.5%)	429 (50.3%)	48 (23.8%)
2nd booster	0 (0.0%)	0 (0.0%)	96 (13.7%)	2 (0.6%)	205 (24.0%)	146 (72.3%)
3rd booster	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	73 (8.6%)	1 (0.5%)
Recent SARS-CoV-2 infection (in the last 3–12 months)						
No	245 (85.1%)	646 (91.1%)	391 (55.6%)	189 (56.4%)	674 (79.0%)	156 (77.2%)
Yes	42 (14.6%)	62 (8.7%)	310 (44.1%)	144 (43.0%)	173 (20.3%)	46 (22.8%)
Missing	1 (0.3%)	1 (0.1%)	2 (0.3%)	2 (0.6%)	6 (0.7%)	0 (0%)
Professional role						
Administration/ Reception	44 (15.3%)	90 (12.7%)	120 (17.1%)	63 (18.8%)	109 (12.8%)	45 (22.3%)
Medical Doctor	43 (14.9%)	154 (21.7%)	85 (12.1%)	65 (19.4%)	127 (14.9%)	40 (19.8%)
Nurse/nurse assistants	142 (49.3%)	284 (40.1%)	319 (45.4%)	124 (37.0%)	374 (43.8%)	64 (31.7%)
Laboratory	11 (3.8%)	51 (7.2%)	33 (4.7%)	21 (6.3%)	49 (5.7%)	9 (4.5%)
Catering staff/Cleaner	6 (2.1%)	6 (0.8%)	2 (0.3%)	1 (0.3%)	3 (0.4%)	1 (0.5%)
Other	27 (9.4%)	97 (13.7%)	114 (16.2%)	41 (12.2%)	125 (14.7%)	32 (15.8%)
Missing	15 (5.2%)	27 (3.8%)	30 (4.3%)	20 (6.0%)	66 (7.7%)	11 (5.4%)
Following IPC: General hand hygiene rules (clinical staff only)						
Not always	14 (7.6%)	21 (4.8%)	47 (11.8%)	28 (14.8%)	69 (13.8%)	15 (14.6%)
Always	110 (59.5%)	137 (31.4%)	313 (78.6%)	127 (67.2%)	417 (83.4%)	75 (72.8%)
Missing	61 (33.0%)	278 (63.8%)	38 (9.5%)	34 (18.0%)	14 (2.8%)	13 (12.6%)

Following IPC: Standard precautions during patient contact (clinical staff only)						
Not always	9 (4.9%)	15 (3.4%)	48 (12.1%)	25 (13.2%)	72 (14.4%)	18 (17.5%)
Always	105 (56.8%)	132 (30.3%)	305 (76.6%)	128 (67.7%)	415 (83.0%)	72 (69.9%)
Missing	71 (38.4%)	289 (66.3%)	45 (11.3%)	36 (19.0%)	13 (2.6%)	13 (12.6%)
Following IPC: Wearing personal protective equipment (clinical staff only)						
Not always	30 (16.2%)	61 (14.0%)	84 (21.1%)	31 (16.4%)	126 (25.2%)	19 (18.4%)
Always	150 (81.1%)	354 (81.2%)	308 (77.4%)	141 (74.6%)	360 (72.0%)	70 (68.0%)
Missing	5 (2.7%)	21 (4.8%)	6 (1.5%)	17 (9.0%)	14 (2.8%)	14 (13.6%)
Contact with a case in the hospital						
No	172 (59.7%)	408 (57.5%)	455 (64.7%)	185 (55.2%)	559 (65.5%)	139 (68.8%)
Yes	87 (30.2%)	154 (21.7%)	238 (33.9%)	128 (38.2%)	284 (33.3%)	61 (30.2%)
Missing	29 (10.1%)	147 (20.7%)	10 (1.4%)	22 (6.6%)	10 (1.2%)	2 (1.0%)
Contact with SARS-CoV-2 case at home						
No	272 (94.4%)	688 (97.0%)	634 (90.2%)	281 (83.9%)	747 (87.6%)	179 (88.6%)
Yes	13 (4.5%)	9 (1.3%)	42 (6.0%)	27 (8.1%)	72 (8.4%)	15 (7.4%)
Missing	3 (1.0%)	12 (1.7%)	27 (3.8%)	27 (8.1%)	34 (4.0%)	8 (4.0%)
Household size						
1 or 2 members	120 (41.7%)	290 (40.9%)	310 (44.1%)	110 (32.8%)	339 (39.7%)	77 (38.1%)
3 members or more	147 (51.0%)	394 (55.6%)	360 (51.2%)	200 (59.7%)	453 (53.1%)	103 (51.0%)
Missing	21 (7.3%)	25 (3.5%)	33 (4.7%)	25 (7.5%)	61 (7.2%)	22 (10.9%)
Frequency of taking public transportation						
Never	167 (58.0%)	443 (62.5%)	342 (48.6%)	175 (52.2%)	424 (49.7%)	89 (44.1%)
One to two times	43 (14.9%)	104 (14.7%)	104 (14.8%)	51 (15.2%)	152 (17.8%)	46 (22.8%)
Three or more	75 (26.0%)	153 (21.6%)	250 (35.6%)	89 (26.6%)	271 (31.8%)	67 (33.2%)
Missing	3 (1.0%)	9 (1.3%)	7 (1.0%)	20 (6.0%)	6 (0.7%)	0 (0%)
Frequency of attending gatherings						
Never	139 (48.3%)	380 (53.6%)	213 (30.3%)	90 (26.9%)	297 (34.8%)	52 (25.7%)
One to two times	115 (39.9%)	264 (37.2%)	343 (48.8%)	153 (45.7%)	359 (42.1%)	83 (41.1%)
Three or more	30 (10.4%)	54 (7.6%)	140 (19.9%)	72 (21.5%)	191 (22.4%)	66 (32.7%)
Missing	4 (1.4%)	11 (1.6%)	7 (1.0%)	20 (6.0%)	6 (0.7%)	1 (0.5%)

HCW: healthcare worker, IPC: Infection prevention and control

Vaccination uptake in each period increased steeply during the first few months following the start of the vaccination season (September–December) and then plateaued (Fig. 2A overall and Figure S2 by hospital). While vaccination coverage in the first period reached 71%, a vaccine coverage of only 32% and 19% was achieved in the second and third periods, respectively. When stratified by age group and sex, we observed a higher uptake among men over the age of 50 in the first and second periods, but not in the third period (Fig. 2B). Uptake among women was lower than among men but did not vary by age group.

A: overall vaccine uptake. B: vaccine uptake stratified by age and sex categories. Note that the first vaccination period is cut off at the end of April 2022 in the plot because vaccination coverage remained constant afterwards.

3.2. Factors associated with vaccine uptake

Individual factors

Vaccine uptake differed modestly across age–sex strata in the first two vaccination periods (Tables 2–4). Compared to women aged ≥ 50 years as the reference group, men aged ≥ 50 years had a higher hazard of vaccination compared with the reference group in the first and second periods (aHRs 1.46, 95% CI [0.99–2.15] and 1.43 [0.78–2.61], respectively). Although the confidence intervals included the null, the point estimates were consistently above 1 in both periods, suggesting a higher probability of vaccination among older men during these periods. This pattern was not observed in period 3 (aHR 0.87 [0.39–1.91]). In contrast, women aged 18–49 years had comparable rates of vaccination as the reference group across all periods (aHRs ranging from 0.79–0.95). Similarly, men aged 18–49 years did not show a consistent increase or decrease in uptake in any period (aHRs 0.87 [0.63–1.21], 1.06 [0.63–1.76], and 0.73 [0.37–1.44], respectively).Recent SARS-CoV-2 infection in the last 3–12 months was not associated with lower vaccine uptake in any vaccination periods (aHRs 1.01 [0.79–1.31], 1.18 [0.91–1.55], and 0.99 [0.73–1.36], Tables S2–4), nor was having an underlying health condition (aHRs 0.97 [0.80–1.18], 0.98 [0.75–1.30], and 0.86 [0.61–1.22]). Frequent alcohol consumption had HRs below 1 in all three periods, but CIs always included the null (aHRs for daily consumption vs. occasionally/never 0.90 [0.65–1.26], 0.82 [0.50–1.34], and 0.80 [0.45–1.44]).

Table 2

First vaccination period hazard ratios and associated 95% confidence intervals for the association of individual, occupational, and community factors with vaccination uptake among HCWs, VEBIS-HCW European multi-centre COVID-19 study, September 2021–December 2021.

Variable	Levels	participants	person-time	vaccinations	Unadjusted	Minimally adjusted	Fully adjusted
Age	≥ 50	339	31,740	244	1 (ref)		
	18–49	658	57,672	463	0.90 [0.77,1.06]		
Sex	Female	790	72,806	545	1 (ref)		
	Male	207	16,606	162	1.23 [1.02,1.47]		
Age-sex interaction	Female ≥ 50	261	22,409	181	-	1 (ref)	1 (ref)
	Female 18–49	529	40,905	367	-	0.99 [0.81,1.17]	0.95 [0.75,1.2]
	Male ≥ 50	78	5,282	63	-	1.60 [1.14,2.07]	1.46 [0.99,2.15]
	Male 18–49	129	9,401	100	-	1.06 [0.79,1.32]	0.87 [0.63,1.21]
Any chronic condition	No	724	63,832	508	1 (ref)	1 (ref)	1 (ref)
	Yes	273	25,580	199	0.96 [0.81,1.14]	0.91 [0.77,1.09]	0.97 [0.80,1.18]
Smoking status	Non-smoker	798	72,306	558	1 (ref)	1 (ref)	1 (ref)
	Current smoker	167	14,483	123	1.06 [0.87,1.29]	1.06 [0.87,1.30]	1.13 [0.90,1.41]
Alcohol consumption	Occasionally/Never	103	9,221	70	1 (ref)	1 (ref)	1 (ref)
	Weekly	613	58,648	435	0.85 [0.65,1.09]	0.88 [0.68,1.15]	0.94 [0.71,1.24]
	Daily	147	13,576	108	0.80 [0.59,1.08]	0.86 [0.63,1.17]	0.90 [0.65,1.26]
Professional role	Medical Doctor	197	12,521	152	1 (ref)	1 (ref)	1 (ref)
	Administration/ Reception	134	11,725	90	0.76 [0.57,1.01]	0.75 [0.56,1.00]	0.75 [0.55,1.03]
	Nurse/nurse assistants	426	40,715	284	0.57 [0.47,0.70]	0.57 [0.46,0.70]	0.56 [0.45,0.70]
	Laboratory	62	7,464	51	0.51 [0.37,0.70]	0.48 [0.35,0.67]	0.49 [0.35,0.69]
	Catering staff/Cleaner	12	1,082	6	0.31 [0.13,0.70]	0.32 [0.14,0.72]	0.36 [0.14,0.88]
	Other	124	11,252	97	0.69 [0.53,0.90]	0.67 [0.51,0.87]	0.69 [0.52,0.92]
SARS-CoV-2 infection in last 3–12 months	No	799	66,897	534	1 (ref)	1 (ref)	1 (ref)
	Yes	145	14,407	79	1.01 [0.79,1.30]	1.03 [0.80,1.32]	1.01 [0.79,1.31]
Work time	Full-time	422	35,761	244	1 (ref)	1 (ref)	1 (ref)

HCW healthcare worker, IPC infection prevention and control, ref reference

Variable	Levels	participants	person-time	vaccinations	Unadjusted	Minimally adjusted	Fully adjusted
	Part time ≥ 50%	31	2,222	24	1.10 [0.69,1.77]	1.13 [0.71,1.81]	1.17 [0.70,1.95]
	Part time < 50%	523	49,723	422	0.95 [0.60,1.50]	0.95 [0.60,1.51]	1.03 [0.62,1.71]
Contact with SARS-CoV-2: patient	No	531	48,388	349	1 (ref)	1 (ref)	1 (ref)
	Yes	212	16,572	122	1.12 [0.90,1.39]	1.09 [0.88,1.36]	1.13 [0.88,1.45]
Following IPC: General hand hygiene rules	Always	393	35,070	224	1 (ref)	1 (ref)	1 (ref)
	Not always	77	6,590	52	1.11 [0.69,1.79]	1.09 [0.67,1.77]	1.22 [0.73,2.05]
Following IPC: Standard precautions during patient contact	Always	362	30,858	205	1 (ref)	1 (ref)	1 (ref)
	Not always	49	3,830	30	1.24 [0.71,2.17]	1.18 [0.67,2.09]	1.26 [0.67,2.38]
Following IPC: Wearing personal protective equipment	Always	756	64,295	543	1 (ref)	1 (ref)	1 (ref)
	Not always	188	20,851	121	1.01 [0.76,1.35]	1.01 [0.76,1.34]	0.99 [0.74,1.34]
Contact with SARS-CoV-2 at home	No	977	85,261	676	1 (ref)	1 (ref)	1 (ref)
	Yes	178	3,576	19	0.76 [0.47,1.23]	0.77 [0.48,1.24]	0.73 [0.41,1.28]
Frequency of attending gatherings	Never	707	38,000	299	1 (ref)	1 (ref)	1 (ref)
	One to two times per week	724	39,928	306	1.01 [0.86,1.19]	1.03 [0.87,1.21]	1.02 [0.85,1.22]
	Three or more times per week	320	10,794	91	1.58 [1.23,2.02]	1.59 [1.24,2.03]	1.60 [1.22,2.10]
Persons in household	1 or 2 members	410	35,950	290	1 (ref)	1 (ref)	1 (ref)
	3 members or more	541	50,742	392	1.04 [0.89,1.21]	1.05 [0.90,1.23]	1.06 [0.89,1.25]

HCW healthcare worker, IPC infection prevention and control, ref reference

Table 4
Third vaccination period hazard ratios and associated 95% confidence intervals for the association of individual, occupational, and community factors with vaccination uptake among HCWs, VEBIS-HCW European multi-centre COVID-19 study, September 2023–April 2024.

Variable	Levels	participants	person-time	vaccinations	Unadjusted	Minimally adjusted	Fully adjusted
Age	≥ 50	405	47,366	86	1 (ref)		
	18–49	652	76,606	109	0.76 [0.57,1.02]		
Sex	Female	867	99,810	161	1 (ref)		
	Male	188	24,162	34	0.96 [0.66,1.41]		
Age-Sex-interaction	Female ≥ 50	334	33,086	73	-	1 (ref)	1 (ref)
	Female 18–49	535	53,393	95	-	0.76 [0.52,1.00]	0.79 [0.53,1.19]
	Male ≥ 50	71	7,866	17	-	0.96 [0.42,1.49]	0.87 [0.39,1.91]
	Male 18–49	117	13,019	17	-	0.72 [0.33,1.12]	0.73 [0.37,1.44]
Any chronic condition	No	754	89,140	136	1 (ref)	1 (ref)	1 (ref)
	Yes	307	34,832	59	0.93 [0.68,1.28]	0.91 [0.66,1.26]	0.86 [0.61,1.22]
Smoking status	Non-smoker	849	98,928	170	1 (ref)	1 (ref)	1 (ref)
	Current smoker	169	20,698	15	0.68 [0.39,1.15]	0.71 [0.41,1.21]	0.75 [0.43,1.31]
Alcohol consumption	Occasionally/Never	154	17,160	43	1 (ref)	1 (ref)	1 (ref)
	Weekly	688	81,145	111	0.67 [0.46,0.99]	0.69 [0.47,1.03]	0.77 [0.50,1.18]
	Daily	149	17,079	26	0.72 [0.43,1.20]	0.76 [0.45,1.28]	0.80 [0.45,1.44]
Professional role	Medical Doctor	167	18,247	36	1 (ref)	1 (ref)	1 (ref)
	Administration/Reception	155	17,498	45	1.04 [0.66,1.65]	1.01 [0.63,1.61]	1.00 [0.62,1.63]
	Nurse/nurse assistants	438	53,389	63	0.63 [0.41,0.97]	0.62 [0.40,0.96]	0.67 [0.42,1.06]
	Laboratory	58	6,359	8	0.66 [0.30,1.44]	0.67 [0.30,1.49]	0.70 [0.31,1.57]
	Catering staff/Cleaner	4	524	1	DNC	DNC	DNC
	Other	157	17,897	31	0.92 [0.55,1.52]	0.94 [0.56,1.57]	0.97 [0.57,1.66]
SARS-CoV-2 infection in last 3–12 months	No	534	53,931	91	1 (ref)	1 (ref)	1 (ref)
	Yes	545	59,865	91	1.01 [0.75,1.36]	0.99 [0.74,1.34]	0.99 [0.73,1.36]
Work time	Full-time	892	105,156	161	1 (ref)	1 (ref)	1 (ref)
	Part time ≥ 50%	23	2,402	5	1.01 [0.40,2.55]	0.98 [0.39,2.49]	1.00 [0.39,2.57]

DNC did not converge, HCW healthcare worker, IPC infection prevention and control, ref reference

Variable	Levels	participants	person-time	vaccinations	Unadjusted	Minimally adjusted	Fully adjusted
	Part time < 50%	95	8,138	10	0.90 [0.47,1.72]	0.87 [0.45,1.68]	0.81 [0.38,1.69]
Contact with SARS-CoV-2: patient	No	700	76,395	132	1 (ref)	1 (ref)	1 (ref)
	Yes	336	35,104	40	0.97 [0.67,1.40]	0.94 [0.65,1.37]	0.88 [0.57,1.35]
Following IPC: General hand hygiene rules	Always	814	97,979	139	1 (ref)	1 (ref)	1 (ref)
	Not always	160	16,871	38	0.91 [0.50,1.67]	0.96 [0.52,1.76]	0.89 [0.47,1.69]
Following IPC: Standard precautions during patient contact	Always	773	93,348	131	1 (ref)	1 (ref)	1 (ref)
	Not always	166	17,546	38	1.05 [0.57,1.93]	0.99 [0.53,1.84]	1.12 [0.57,2.18]
Following IPC: Wearing personal protective equipment	Always	697	81,801	122	1 (ref)	1 (ref)	1 (ref)
	Not always	284	32,192	53	0.77 [0.43,1.39]	0.77 [0.43,1.39]	0.78 [0.42,1.48]
Contact with SARS-CoV-2 at home	No	992	113,853	173	1 (ref)	1 (ref)	1 (ref)
	Yes	257	6,130	14	1.17 [0.67,2.07]	1.18 [0.67,2.07]	1.05 [0.55,2.00]
Frequency of attending gatherings	Never	606	36,876	51	1 (ref)	1 (ref)	1 (ref)
	One to two times per week	777	54,149	84	1.07 [0.75,1.54]	1.12 [0.78,1.62]	1.15 [0.76,1.73]
	Three or more times per week	535	32,153	59	1.06 [0.71,1.58]	1.14 [0.76,1.71]	1.16 [0.75,1.80]
Persons in household	1 or 2 members	421	49,509	73	1 (ref)	1 (ref)	1 (ref)
	3 members or more	558	65,858	100	0.94 [0.69,1.28]	0.98 [0.72,1.33]	0.94 [0.67,1.32]

DNC did not converge, HCW healthcare worker, IPC infection prevention and control, ref reference

Occupational factors

HCWs in most professional roles showed lower vaccine uptake than medical doctors. Nurses and nurse assistants had aHRs of 0.56 (CI 0.45–0.70) in the first, 0.53 (0.37–0.75) in the second, and 0.67 (0.42–1.06) third period, respectively, compared to medical doctors. Laboratory workers, and HCWs in other roles also had a significantly reduced vaccine uptake in the first and second period, but not in the third, while uptake among administration and reception personnel compared to medical doctors was only reduced significantly in the second period. Catering and cleaning staff had the lowest uptake of all occupational groups in the first period (aHR 0.36 [0.14, 0.88]), while the analysis for this group for the second and third vaccination periods could not be performed due to low sample size. Work status (full-time vs. part-time) did not significantly influence vaccine uptake in any period, nor did contact with SARS-CoV-2-positive patients in the workplace (Tables 2–4) or the work in specific wards (Tables S2–4). Adherence to IPC measures did not show any significant associations with vaccine uptake (Tables 2–4), while results from other hand hygiene variables presented inconsistent and non-significant results (Tables S2–4).

Community factors

HCWs who attended social gatherings three or more times per week during the first period, who had an aHR of 1.60 (1.22–2.10) compared to those who did not attend any gatherings (Table 2). We did not find a significant impact of community-related exposures, like being in contact with SARS-CoV-2 cases at home, household size, or cohabitation with other HCWs. Other variables were considered and no significant associations were found (Additional file 1, Tables S2–4).

Table 2: *First vaccination period hazard ratios and associated 95% confidence intervals for the association of individual, occupational, and community factors with vaccination uptake among HCWs, VEBIS-HCW European multi-centre COVID-19 study, September 2021–December 2021.*

Table 3: *Second vaccination period hazard ratios and associated 95% confidence intervals for the association of individual, occupational, and community factors with vaccination uptake among HCWs, VEBIS-HCW European multi-centre COVID-19 study, December 2021–April 2023.*

Table 3
Second vaccination period hazard ratios and associated 95% confidence intervals for the association of individual, occupational, and community factors with vaccination uptake among HCWs, VEBIS-HCW European multi-centre COVID-19 study, December 2021–April 2023.

Variable	Levels	participants	person-time	vaccinations	Unadjusted	Minimally adjusted	Fully adjusted
Age	≥ 50	356	38,845	125	1 (ref)		
	18–49	682	72,960	210	0.89 [0.71,1.12]		
Sex	Female	880	97,292	265	1 (ref)		
	Male	158	14,513	70	1.54 [1.18,2.03]		
Age-sex interaction	Female ≥ 50	298	29,123	94	-	1 (ref)	1 (ref)
	Female 18–49	582	54,771	171	-	0.95 [0.71,1.20]	0.88 [0.64,1.23]
	Male ≥ 50	58	4,347	31	-	1.87 [1.08,2.67]	1.43 [0.78,2.61]
	Male 18–49	100	8,366	39	-	1.30 [0.80,1.79]	1.06 [0.63,1.76]
Any chronic condition	No	719	75,765	236	1 (ref)	1 (ref)	1 (ref)
	Yes	320	36,040	99	0.96 [0.75,1.23]	0.95 [0.74,1.21]	0.98 [0.75,1.30]
Smoking status	Non-smoker	834	88,079	270	1 (ref)	1 (ref)	1 (ref)
	Current smoker	164	19,442	37	0.77 [0.54,1.09]	0.77 [0.54,1.09]	0.81 [0.56,1.17]
Alcohol consumption	Occasionally/Never	209	20,891	78	1 (ref)	1 (ref)	1 (ref)
	Weekly	681	74,848	198	0.79 [0.59,1.05]	0.84 [0.62,1.12]	0.83 [0.61,1.12]
	Daily	105	11,698	30	0.77 [0.49,1.21]	0.85 [0.54,1.33]	0.82 [0.50,1.34]
Professional role	Medical Doctor	150	13,306	65	1 (ref)	1 (ref)	1 (ref)
	Administration/Reception	183	20,999	63	0.53 [0.36,0.76]	0.56 [0.38,0.81]	0.55 [0.37,0.83]
	Nurse/nurse assistants	443	50,111	124	0.52 [0.37,0.71]	0.56 [0.40,0.78]	0.53 [0.37,0.75]
	Laboratory	54	6,079	21	0.54 [0.32,0.90]	0.57 [0.34,0.95]	0.54 [0.32,0.90]
	Catering staff/Cleaner	3	246	1	DNC	DNC	DNC
	Other	157	15,470	41	0.62 [0.41,0.94]	0.63 [0.42,0.96]	0.62 [0.40,0.95]
SARS-CoV-2 infection in last 3–12 months	No	660	63,092	158	1 (ref)	1 (ref)	1 (ref)
	Yes	415	41,883	149	1.15 [0.89,1.48]	1.18 [0.91,1.53]	1.18 [0.91,1.55]
Work time	Full-time	732	78,037	207	1 (ref)	1 (ref)	1 (ref)
	Part time ≥ 50%	32	3,182	9	1.20 [0.60,2.39]	1.17 [0.59,2.35]	0.88 [0.39,1.99]

DNC did not converge, HCW healthcare worker, IPC infection prevention and control, ref reference

Variable	Levels	participants	person-time	vaccinations	Unadjusted	Minimally adjusted	Fully adjusted
	Part time < 50%	184	20,824	66	1.20 [0.79,1.81]	1.27 [0.83,1.94]	1.22 [0.78,1.90]
Contact with SARS-CoV-2: patient	No	686	67,544	192	1 (ref)	1 (ref)	1 (ref)
	Yes	343	34,084	99	1.27 [0.99,1.64]	1.26 [0.98,1.63]	1.10 [0.82,1.46]
Following IPC: General hand hygiene rules	Always	739	79,293	216	1 (ref)	1 (ref)	1 (ref)
	Not always	146	14,600	48	1.37 [0.88,2.12]	1.25 [0.79,1.96]	1.05 [0.64,1.71]
Following IPC: Standard precautions during patient contact	Always	712	75,354	212	1 (ref)	1 (ref)	1 (ref)
	Not always	133	13,982	38	1.08 [0.69,1.68]	1.08 [0.69,1.69]	1.06 [0.67,1.68]
Following IPC: Wearing personal protective equipment	Always	750	79,950	237	1 (ref)	1 (ref)	1 (ref)
	Not always	241	26,498	68	0.91 [0.61,1.37]	0.90 [0.60,1.34]	0.82 [0.54,1.24]
Contact with SARS-CoV-2 at home	No	964	100,232	283	1 (ref)	1 (ref)	1 (ref)
	Yes	238	5,431	25	1.20 [0.79,1.83]	1.25 [0.82,1.90]	1.29 [0.84,2.00]
Frequency of attending gatherings	Never	584	31,228	79	1 (ref)	1 (ref)	1 (ref)
	One to two times per week	819	50,393	156	1.04 [0.78,1.37]	1.05 [0.80,1.39]	1.09 [0.80,1.49]
	Three or more times per week	564	27,178	80	1.04 [0.75,1.44]	1.03 [0.74,1.43]	0.96 [0.67,1.37]
Persons in household	1 or 2 members	420	46,693	110	1 (ref)	1 (ref)	1 (ref)
	3 members or more	560	59,333	200	1.24 [0.98,1.57]	1.24 [0.98,1.57]	1.24 [0.96,1.60]

DNC did not converge, HCW healthcare worker, IPC infection prevention and control, ref reference

Table 4: *Third vaccination period hazard ratios and associated 95% confidence intervals for the association of individual, occupational, and community factors with vaccination uptake among HCWs, VEBIS-HCW European multi-centre COVID-19 study, September 2023–April 2024.*

4. Discussion

In this prospective multicentre study, we longitudinally analysed vaccine uptake among a cohort of HCWs in 12 hospitals from seven European countries during the later stages of the COVID-19 pandemic and into the post-pandemic period. While the first booster was well accepted among HCWs, we observed substantially lower uptake of subsequent doses. Males over the age of 50 presented higher uptake during the first and second periods, while uptake was very low in general in the third period (i.e., post-pandemic). This dynamic in HCWs was similar to the general population, where vaccine uptake greatly decreased over time (36, 37). Several factors may explain this trend, such as the known short duration of protection (38) as well as low perceived risk of consequences of infection (27, 39, 40). Additionally, pandemic fatigue and shifting public health messaging may have contributed to lower motivation for continued vaccination, particularly as natural infection became more common and hybrid immunity was widely recognised (41).

Our study identified several key factors associated with vaccine uptake across vaccination periods. In addition to the combination of older age and male sex, occupational role emerged as a strong determinant of vaccine uptake: compared to medical doctors, all other professional groups demonstrated lower uptake, with nurses, nurse assistants (aHR 0.56, 95% CI [0.45,0.70], and particularly catering and cleaning staff (aHR 0.36 [0.14,0.88]) showing the lowest rates of vaccination in the first period. Interestingly, the minimally adjusted hazard ratios for the age-sex-interaction attenuated once adjusting for role, underlying conditions, previous SARS-CoV-2 infection. The effects of behavioural and health-related factors, such as previous SARS-CoV-2 infection, underlying health conditions, and smoking status, on vaccine uptake were low to null (aHRs 0.75 to 1.13) in our analysis. However, frequent participation in social gatherings was linked to increased vaccine uptake in the first period (aHR 1.60 [1.22,2.10]), likely due to vaccine passport requirements during this time in many countries. Adherence to IPC recommendations was not significantly associated with lower vaccine uptake in any vaccination period. In the third period, i.e., post-pandemic, we did not observe any significant associations in fully adjusted models, likely due to the limited number of vaccinations and the resulting low statistical power rather than the absence of true effects.

Similar patterns have been observed in other studies, where older age, higher educational attainment and male sex were consistently associated with higher vaccine uptake (21, 23, 42–44). Our results also align with previous findings that medical doctors were consistently more likely to get vaccinated than HCWs in other roles (21, 22, 27, 43, 45). In an American study, race and household income were significant predictors of vaccine uptake (43, 44), but we did not collect these sociodemographic variables. In our study, previous infection was not associated with COVID-19 vaccine uptake (aHRs ranging from 0.99 to 1.18), but it was found to be an important negative factor in other studies (23, 42). The absence of an association in our study may be explained by our study design, which allowed us to take into account time-varying eligibility and exclude person-time within 60 days after an infection when vaccination was not recommended. In contrast, studies relying on logistic regression models were generally unable to account for this dynamic aspect of vaccination eligibility (23, 45).

Our study presents several limitations: First, as HCWs were a priority group for booster recommendations, some HCWs, particularly those with underlying conditions, might have received a booster earlier than the general start of the vaccination season, which could have influenced overall uptake trends. Second, participating HCW were representative of the source population of all HCWs in participating sites in terms of age and sex. However, HCWs with underlying conditions may have been slightly overrepresented in the cohort compared to the source population, which could have led to an overestimation of vaccine uptake, even in the periods with low vaccine coverage. Third, vaccination information was not cross-checked in registries or vaccination cards for all HCWs, but remained self-reported for 8.1%, 4.8% and 6.5% of participants in the first, second, and third study periods, respectively. However, any resulting misclassification is likely to be minimal because HCWs completed weekly follow-up questionnaires that reduced inaccurate recall. Moreover, previous studies have shown high validity of self-reported vaccination status for the current season (46, 47), and we observed high agreement between self-reported and registry-based vaccination data in a study conducted in the same cohort (unpublished data). Fourth, other factors not collected in this study, such as educational attainment or household income, may have influenced the uptake of vaccinations among HCWs and could be targeted for further efforts to improve vaccine uptake. Lastly, the reduced sample size of participating HCWs limited a more in-depth analysis by strata. The lower number of vaccinations during the third period (post-pandemic) led to lower power and a general trend towards non-significant associations during this period.

5. Conclusions

Our study highlights the decrease in booster vaccine uptake over time and identifies factors associated to COVID-19 vaccination in a cohort of HCWs from twelve hospitals in seven European countries. A novelty of our study is the interaction between age and sex in vaccine uptake. Professional role was consistently and independently associated with vaccine uptake over multiple vaccination periods, therefore HCWs other than medical doctors emerged as key groups for targeted vaccination awareness campaigns. Better understanding the change in behaviour and drivers of vaccination in HCWs during emerging health crises is essential for designing more effective vaccination policies in response to future health threats, taking into account lessons learned from COVID-19 vaccination dynamics over time among HCWs.

Abbreviations

COVID-19	Coronavirus disease 2019

ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
HCW	Healthcare worker
HR	Hazard ratio
IPC	Infection prevention and control
PCR	Polymerase chain reaction
PPE	Personal protective equipment
RR	Rate ratio
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
VEBIS	Vaccine Effectiveness, Burden and Impact Studies

Declarations

Ethics approval

The study was approved by the Ethical review committees of each participating hospital: Etičko Povjerenstvo Hrvatskog zavoda za javno zdravstvo (HZJZ) Croatia, Zagrefigb: 381-15-21-3; Tartu Ülikooli inimuuringute eetika komitee, Estonia: 382/M-7; Clinical research ethics committee, Galway University Hospital, Ireland: C.A. 2693; SJH/TUH Joint Research Ethics Committee, Ireland: 0513; Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Dipartimento di Sicurezza e Bioetica, Rome, Italy: 00372/23; Università degli Studi di Milano-Bicocca presented same approval as Policlinico Gemelli, Università Cattolica del Sacro Cuore, Rome, Italy; Ethics Committee for Clinical Research at Pauls Stradins Clinical University Hospital, Latvia: 241023-3L; Ethics Committee for Clinical Research at Pauls Stradins Clinical University Hospital, extended to Children Clinical University Hospital, Latvia: 241023-10L; Comité de Ética de la Investigación de la Comunidad Autónoma de Aragón (CEICA), HU Miguel Servet, Zaragoza, Spain: PI21-176 and PI22/483; Comité De Ética De La Investigación Con Medicamentos, Sant Joan de Déu, Fundacio de Recerca, Barcelona, Spain: 17/2023; Comissão de Ética para a Saúde, INSA Doutor Ricardo Jorge, Approval Code: INSA-IM60_05 / 2021-03-05, Approval Date: 16/03/2021; Comissão de Ética para a Saúde, Centro Hospidalar Tondela-Viseu, Approval Code: 06/16//06/202, Approval Date: 16/04/2021.

Consent for publication

Not applicable

Availability of data and materials

The data used in this study are available at each study site.

Competing interests

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Author’s contributions

I.G wrote to the statistical plan of analysis, contributed to the analysis, interpreted and reviewed results, and wrote the manuscript. A.P.U led the analysis, interpreted and reviewed results, and reviewed the manuscript. K.B and S.B were involved in the study design, interpretation of results, and reviewing the manuscript. A.N supported the coordination of the VEBIS HCWs network, was involved in the study's original methodological design (generic protocol), reviewed and interpreted results, and reviewed the manuscript. C.S coordinated the VEBIS HCWs network, was involved in the study's original methodological design (generic protocol), supported the statistical plan of analysis, reviewed and interpreted results, and reviewed the manuscript. Z.L.M, A.U, C.B, C.F, P.B, R.M, V.Z, D.Z, V.G, M.C.P, M.L.M, G.P, L.L, J.M, L.T, A.S, K.G.D, I.A, D.G, A.M, P.S.C, L.C, G.S, J.S, C.K, S.L, D.K, E.B, R.G, A.M, C.M.A and the VEBIS HCW study group were responsible for the coordination of the study at the national/regional/hospital level, contributed to developing the study site-specific protocols, were in charge of the collection, management and validation of the clinical and laboratory data. They interpreted the results, reviewed and contributed to all manuscript versions. All authors read and approved the final manuscript.

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Figures

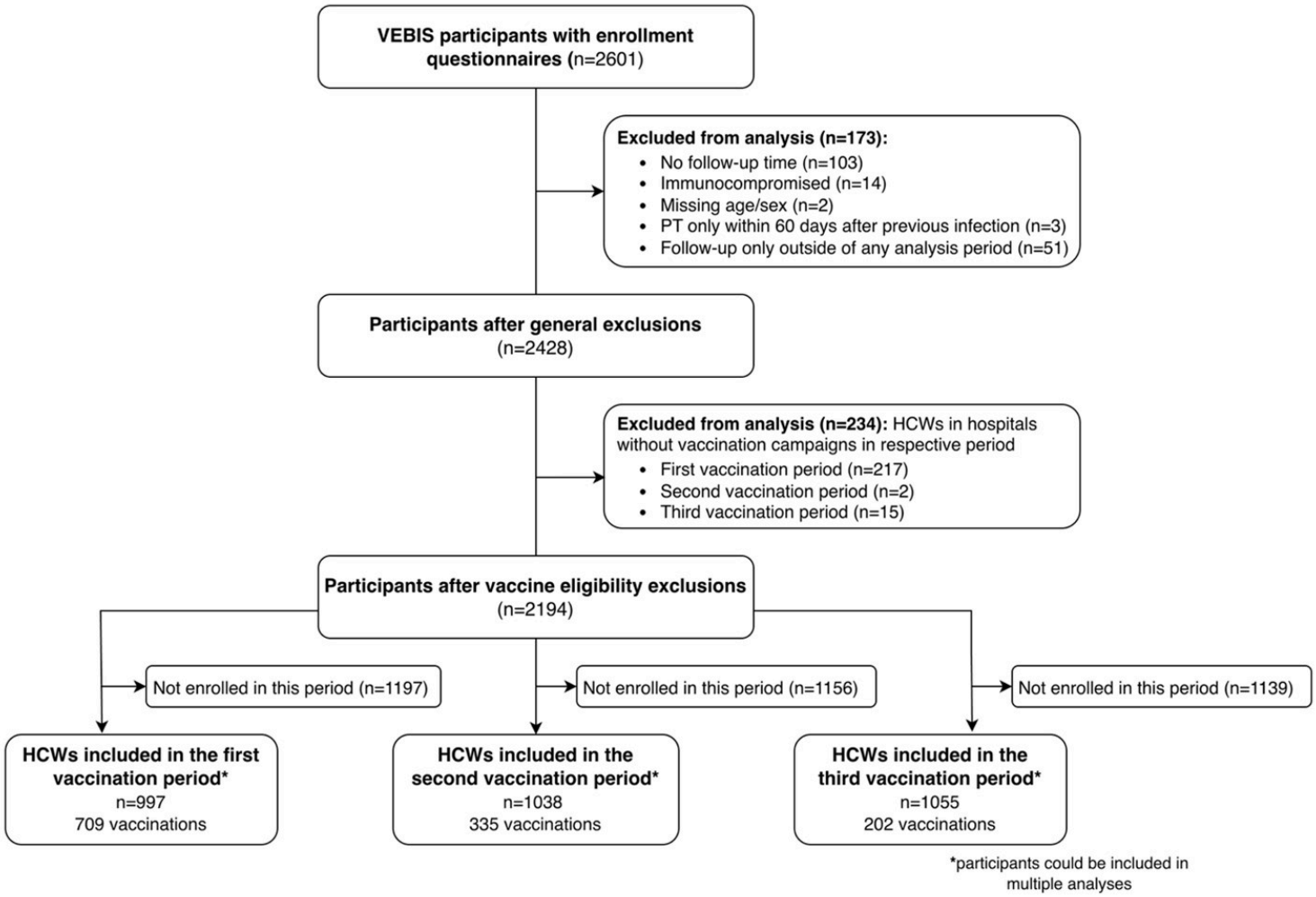


Figure 1

Participant flowchart, VEBIS-HCW European multi-centre COVID-19 study, September 2021-April 2024. Participants could be included in multiple periods. HCWs in hospitals in which no vaccinations were reported within a vaccination period were deemed not eligible for vaccine doses and excluded from the analysis of respective period.

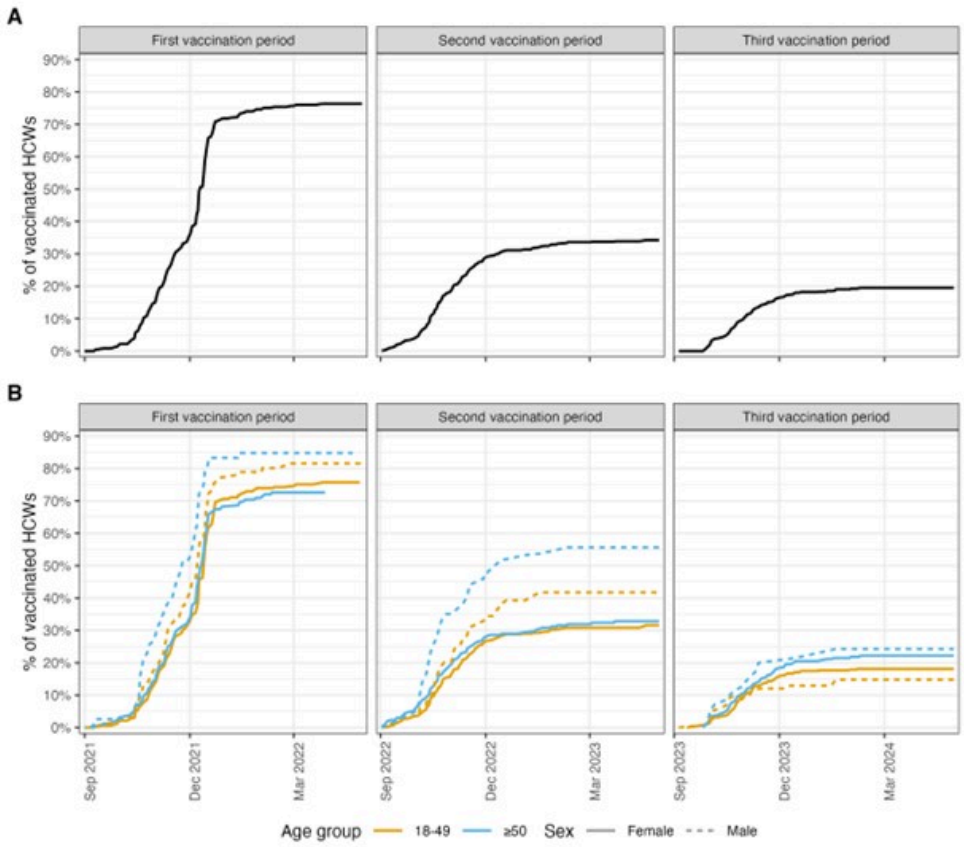


Figure 2

Vaccine uptake in the HCW cohort throughout the three vaccination periods, VEBIS-HCW European multi-centre COVID-19 study, September 2021-April 2024. Note that the final vaccine coverage displayed in the vaccine uptake curves overestimates the real uptake due to loss-to-follow-up of HCWs during the vaccination periods.

A: overall vaccine uptake. B: vaccine uptake stratified by age and sex categories. Note that the first vaccination period is cut off at the end of April 2022 in the plot because vaccination coverage remained constant afterwards.

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