# Factors influencing attitudes toward vaccine safety and vaccine effectiveness amongst UK healthcare professionals prior to and at the time of COVID-19 vaccine rollout: Insights from the CoPE-HCP cohort study

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# Factors influencing attitudes toward vaccine safety and vaccine effectiveness amongst UK healthcare professionals prior to and at the time of COVID-19 vaccine rollout: Insights from the CoPE-HCP cohort study

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**ABSTRACT**

Given the potential for nosocomial outbreaks, we must understand factors associated with negative vaccine attitudes amongst healthcare professionals (HCPs) before the rollout of a newly developed vaccine in a pandemic setting. The aim of this prospective cohort study was to study the impact of preexisting and prevailing mental health on United Kingdom HCPs' attitudes towards a newly developed COVID-19 vaccine. Two online surveys were distributed: first during vaccine development (July–September, 2020) and second during nationwide vaccine rollout (December 2020–March 2021). Mental health (PHQ-9 for depression; GAD-7 for anxiety) was assessed in both surveys. Negative attitude regarding vaccine safety and vaccine effectiveness was assessed at vaccine rollout. A series of logistic regression models were developed relating mental health (preexisting during vaccine development, ongoing and new-onset during rollout, and changes in symptom severity) to negative vaccine attitudes. In 634 HCPs, the presence of depression and/or anxiety during vaccine development was associated with elevated negative attitude towards vaccine safety (adj. OR 1.74 [95% CI 1.10–2.75], $p = .02$), but not vaccine effectiveness (1.13 [0.77–1.66], $p = .53$) at rollout. This was independent of other characteristics: age, ethnicity, professional role, and history of contracting COVID-19. Ongoing depression and/or anxiety (1.72 [1.10–2.69], $p = .02$) was associated with elevated negative attitude regarding vaccine effectiveness, but not vaccine safety. Worsened combined symptom scores over time were associated with elevated negative vaccine effectiveness attitudes (1.03 [1.00–1.05], $p < .05$), but not vaccine safety. Overall, adverse mental health can impact on HCPs' attitudes towards a newly developed vaccine. Further work is required to understand how this translates to vaccine uptake.

## Introduction

Vaccination against coronavirus (COVID-19) has proven a success but significant resistance and hesitancy towards vaccination remains. Previous studies have observed rates of 23% for vaccine hesitancy (i.e. considering against receiving the COVID-19 vaccine or unsure whether to take it or not) amongst United Kingdom-based (UK) healthcare professionals (HCPs) during the initial rollout period.[1] This is concerning given that HCPs are often viewed as trusted sources of vaccine information,[2] and because of the potential for nosocomial outbreaks.[3] As such, we must understand the factors associated with negative vaccine attitudes (which likely drives vaccine hesitancy)[4] amongst HCPs, prior to vaccine rollout during an ongoing pandemic. Part of this hesitancy generally relates to a poor perception of vaccine safety and doubts about effectiveness, prompting overall negative attitude towards the vaccine programme.[5,6]

One underexamined factor of COVID-19 vaccine attitudes and hesitancy is mental health. Existing studies examining mental health and vaccine hesitancy in the general population during the COVID-19 pandemic are mixed, likely due to

variations in outcome assessment or inconsistencies in study design.[7–10] Moreover, there are just two quantitative studies examining COVID-19 vaccine hesitancy and attitudes in UK-based HCPs, but neither study included mental health.[11,12] As such, mental health as a potential predictor of vaccine attitudes amongst these HCPs has not been investigated.

The UK began the vaccination programme on 8th December 2020, with frontline healthcare workers being among one of the highest priority groups.[13] The vaccine was produced in record time in response to a current pandemic and, as such, there was considerable skepticism among the general public regarding its safety and effectiveness.[14] The skepticism, in some HCPs, may also be exacerbated by sociocultural and financial aspects.[15] This scenario provided us with the unique opportunity to evaluate the factors associated with negative attitudes (regarding its safety and effectiveness) towards a newly developed COVID-19 vaccine.

The purpose of this study was to examine the impact of mental health status at the time of vaccine development, and prevailing mental health (either new-onset or ongoing by the end of the study period), on the risk of having a negative attitude

regarding vaccine safety and effectiveness at the time of vaccine rollout. We hypothesized that the presence of depression and/or anxiety (at vaccine development and new-onset or ongoing depression and/or anxiety at vaccine rollout) would be associated with elevated negative attitudes regarding vaccine safety and effectiveness, independent of other demographic characteristics. We deemed that this information would be extremely useful for future vaccine rollout programmes.

## Materials and methods

This cohort study is part of the COVID-19 Disease and Physical and Emotional Wellbeing of Healthcare Professionals project (CoPE-HCP; NCT04433260)[16] which involved multiple online surveys distributed to HCPs (in the UK and internationally) and non-HCPs (primarily academic and research staff) during the COVID-19 pandemic.

As part of a wider CoPE-HCP project, HCPs and non-HCPs were contacted by their respective institutions and were sent an e-mail containing a link to the survey. Informed (digital) consent was obtained prior to the baseline survey and participants indicated whether they consent to receiving the follow-up survey. Informed consent was obtained again prior to the follow-up survey. The participants in this study were limited to UK-based HCPs aged 18 or older, and who had answered both surveys (during vaccine development and vaccine rollout).

Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of the research. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the Cambridge East Research Ethics Committee (20/EE/0166).

The baseline survey (July–September 2020), during the vaccine development/trialing phase, collected data on demographic characteristics, current physical health, professional role, smoking status, and mental health. Mental health status was assessed using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7)[17,18] to indicate probable major depressive disorder and generalized anxiety disorder, respectively. The PHQ-9 is a 9-item self-report questionnaire used to provide a provisional diagnosis for major depressive disorder. Each item represents a distinct symptom experienced in the past 2 weeks. Similarly, the GAD-7 is a 7-item self-report questionnaire used to provide a provisional diagnosis for generalized anxiety disorder.

The follow-up survey was distributed during the initial vaccine rollout (December 2020) and assessed vaccine attitudes and vaccine intentions, including the same mental health assessments plus smoking status, physical health morbidities, and an additional item for the history of contracting COVID-19.

In this study, we regard negative attitudes as the negative evaluation of the COVID-19 vaccine, which generally relates to unforeseen future side effects and vaccine ineffectiveness, among other issues.[5,6] Vaccine attitudes were assessed using two items for vaccine safety ("I have doubts about the safety of the COVID vaccine," and "I am concerned about long-term safety and adverse effects related to the COVID vaccine"), and two items

for vaccine effectiveness ("I believe COVID vaccine will end the pandemic" and "I believe COVID vaccine will allow the return to everyday life"). Each item was rated on a 5-point scale (strongly disagree, disagree, neutral, agree, and strongly agree).

Vaccine intentions were assessed using two items: "I will recommend the COVID vaccine to my family, friends and patients" rated on the 5-point scale (strongly disagree to strongly agree), and "if offered, I will have the COVID vaccine" answered by selecting yes, no, or not sure. Data on vaccine intentions were analyzed descriptively.

### Statistical analysis

For formal analysis, the vaccine attitude items were treated as binary: negative attitude regarding vaccine safety was scored if participants responded strongly agree or agree on either vaccine safety item, and negative attitude regarding vaccine effectiveness was scored if participants responded strongly disagree or disagree on either vaccine effectiveness item. The middle ('neutral') response was regarded as absence of negative attitude for each item.

The presence of depression and/or anxiety (combined variable) during vaccine development was indicated if participants scored ≥10 on the PHQ-9 or GAD-7, indicating probable major depressive disorder and generalized anxiety disorder, respectively. The internal reliability of the PHQ-9 (α = 0.89) and GAD-7 (α = 0.92) was high.

Based on the presence of depression and/or anxiety at vaccine development and rollout separately, we categorized participants into three groups to indicate no depression and/or anxiety at rollout, persistent/ongoing depression and/or anxiety (i.e. presence of depression and/or anxiety at both surveys), or new-onset depression or anxiety (i.e. presence of depression and/or anxiety at rollout, but not at vaccine development).

As an indicator of the change in depression and anxiety symptom severity over the study period, we calculated the change in combined PHQ-9 and GAD-7 scores by subtracting the combined baseline score (at vaccine development) from the combined follow-up score (at vaccine rollout).

A series of binary logistic regression models were developed for each outcome: vaccine safety and vaccine effectiveness. Adjusted odds ratios, 95% confidence intervals, and p values were calculated for each model.

Model 1 included the presence of depression and/or anxiety during the vaccine development stage, and adjusted for demographic characteristics (age, self-identified ethnicity, gender identity, education, healthcare professional role), physical health morbidities, and smoking status during the same time period (i.e. during vaccine development).

Model 2 included ongoing and new-onset depression and/or anxiety at vaccine rollout and adjusted for the above demographic characteristics, physical health morbidities (during vaccine rollout), smoking status (during vaccine rollout), and history of contracting COVID-19 assessed at vaccine rollout.

Model 3 included the change in combined PHQ-9 (depression) and GAD-7 (anxiety) scores, adjusted for model 2 variables, and further adjusted for baseline PHQ-9 and GAD-9 scores.

## Results

Figure 1 shows the participant flow for this study. Of the 1,321 UK-based HCPs who completed the baseline survey, 1,033 gave consent to be followed up in another survey, and of them, a total of 634 participants returned valid baseline and follow-up surveys (Figure 1) and comprise the cohort used in this analysis. The follow-up surveys were received between 22 January 2021 to 13 March 2021 and most (62.6%) were received by the end of January.

### Sociodemographic characteristics of the cohort

Most participants (89.0%) were aged 26–60 years, were White (81.1%), female (77.0%), and without a physical health condition (72.4%) (Supplemental Table S1). In the cohort ($n = 634$), the rates of probable major depressive disorder and generalized anxiety disorder increased from 29.8% to 32.3% from vaccine development to vaccine rollout (Supplemental Table S1).

Demographic characteristics between the cohort ($n = 634$) and baseline-only participants ($n = 687$) were similar except a larger proportion of the cohort were White (81.1% vs. 60.1%, $p < .001$) and female (77.0% vs. 71.2%, $p < .05$) and consisted of fewer medical doctors (32.2% vs. 42.2%) and more nurses (28.7% vs. 25.0%) and allied health professionals (AHPs) (23.8% vs. 16.4%, $p < .001$).

### Vaccine intention and attitudes

Intention to be vaccinated was high: 94.6% said they would receive it, while 3.3% and 2.1% were unsure or said they would not receive it, respectively. Most HCPs (90.5%) reported they would recommend the COVID vaccine to their family, friends, and patients (Supplemental Table S2).

Regarding brand preference amongst those willing to receive the vaccine: 40.4% had no preference, 39.0% preferred Pfizer/BioNTech, 18.8% preferred Oxford/AstraZeneca, and 0.8% and 0.2% preferred Moderna and Sputnik, respectively.

Regarding vaccine attitudes: 18.3% ($n = 116$) had a negative attitude regarding vaccine safety and 31.2% ($n = 198$) had a negative attitude regarding vaccine effectiveness (Supplemental Table S2).

As a crude indicator of the relationship between vaccine attitudes and hesitancy, Chi-squared analysis indicated significant differences in the proportions of HCPs with negative vaccine safety ($X^2$ (1) = 89.76, $p < .001$) attitudes who were vaccine hesitant, but no significant differences were observed for vaccine effectiveness ($X^2$ (1) = 2.78, $p = .10$).

### Predictors of negative vaccine attitudes

A series of logistic regression models showed a nuanced relationship between mental health and negative attitudes regarding vaccine safety and vaccine effectiveness. Additionally, the results indicate consistent associations between negative attitude
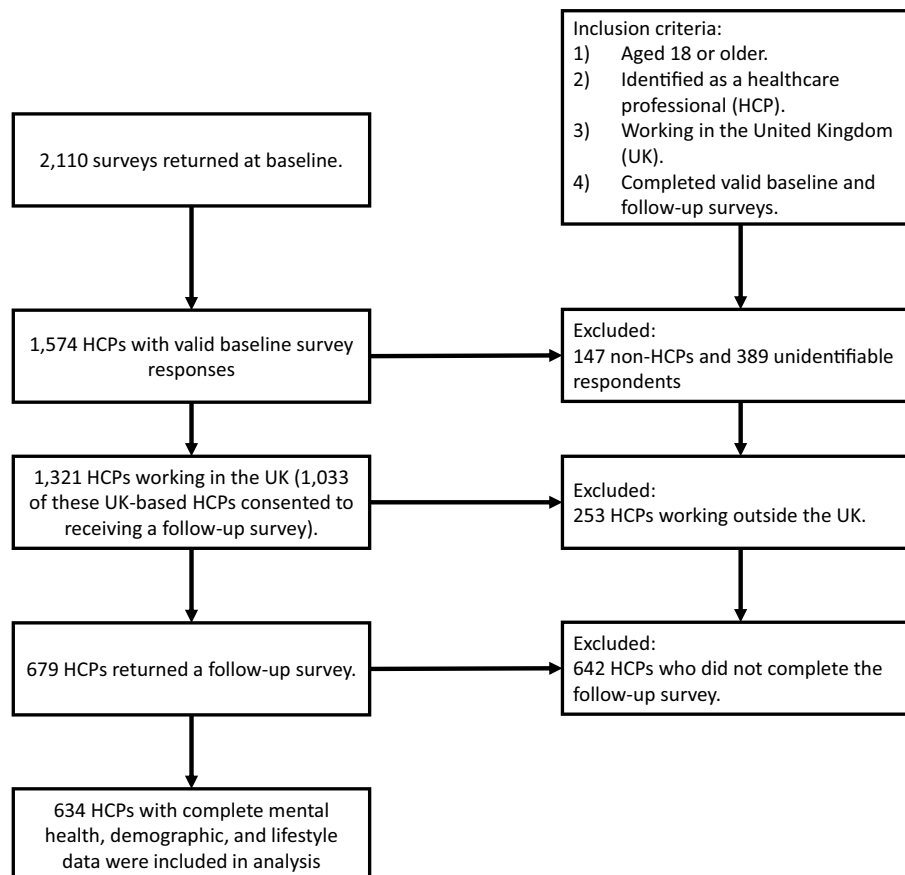


**Figure 1.** Flowchart outlining how the cohort sample were arrived at.

regarding vaccine safety and a profile of sociodemographic characteristics, namely age, ethnicity, and professional role.

### Vaccine safety (right panels)

Table 1 (right panel; $n = 623$) shows the results of model 1 regarding the predictors at the time of vaccine development associated with negative attitudes towards vaccine safety. The presence of depression and/or anxiety during vaccine development (1.74 [1.10–2.75], $p = .02$) was associated with elevated negatives attitudes regarding vaccine safety, compared to HCPs without depression and/or anxiety during vaccine development. This association was independent of other significant predictors: HCPs aged 61 and older had reduced negative attitudes (0.21 [0.05–0.94], $p = .04$) vs. HCPs aged between 18 and 25. Asian (2.10 [1.05–4.22], $p = .04$) or Black ethnicity (7.44 [2.99–18.53], $p < .001$) had elevated negative attitudes vs. White HCPs. Healthcare assistants (3.30 [1.49–7.32], $p < .01$) and nurses or midwives (2.64 [1.39–4.98] $p < .01$) had elevated negative attitudes vs. medical doctors. We observed no association for gender identity, education, physical health condition, or smoking status.

Table 2 (right panel; $n = 623$) shows the results of model 2 regarding the predictors at the time of rollout associated with negative attitudes towards vaccine safety. HCPs with ongoing depression and/or anxiety (1.37 [0.80–2.33], $p = .25$) or new-onset depression or anxiety (0.48 [0.22–1.03], $p = .06$ did not have significantly elevated or reduced negative attitude regarding vaccine safety, compared to those without depression and/or anxiety at rollout. The profile of demographic characteristics remained consistent to model 1, but with further characteristics identified: AHPs or pharmacists (1.98 [1.01–3.88], $p < .05$) were associated with elevated negative attitudes regarding vaccine safety, and HCPs who had previously contracted COVID-19 had reduced negative attitudes regarding vaccine safety (0.51 [0.29–0.90], $p = .02$).

Table 3 (right panel; $n = 623$) shows the results of model 3 regarding the change in depression and anxiety symptom severity as a possible predictor of negative attitudes towards vaccine safety. No significant associations were observed between the change in combined PHQ-9/GAD-7 scores and negative attitude regarding vaccine safety (0.97 [0.94–1.00], $p = .06$). The demographic characteristics were generally consistent to model 1 and model 2.

### Vaccine effectiveness (left panels)

Table 1 (left panel; $n = 632$) shows the results of model 1 regarding the predictors at the time of vaccine development associated with negative attitude towards vaccine effectiveness

**Table 1.** Model 1 including the presence of depression and/or anxiety during vaccine development adjusted for demographic characteristics.

| Predictors | Vaccine effectiveness ($n = 632$) | | | Vaccine safety ($n = 623$) | | |
|---|---|---|---|---|---|---|
| | Adj. OR | 95% CI | p-value | Adj. OR | 95% CI | p-value |
| **Age** | | | | | | |
| 18 to 25 years (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| 26 to 35 years | 1.45 | 0.52–4.01 | .48 | 0.75 | 0.24–2.31 | .62 |
| 36 to 50 years | 1.08 | 0.39–2.95 | .89 | 0.58 | 0.19–1.78 | .34 |
| 51 to 60 years | 0.98 | 0.35–2.76 | .97 | 0.49 | 0.15–1.55 | .22 |
| 61 years + | 1.13 | 0.35–3.62 | .84 | 0.21 | 0.05–0.94 | **.04** |
| **Ethnicity** | | | | | | |
| White (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Asian | 0.67 | 0.35–1.27 | .22 | 2.10 | 1.05–4.22 | **.04** |
| Black | 0.97 | 0.39–2.45 | .95 | 7.44 | 2.99–18.53 | **<.001** |
| Mixed | 1.29 | 0.47–3.53 | .63 | 1.41 | 0.41–4.90 | .59 |
| Other | 2.90 | 0.74–11.43 | .13 | - | - | - |
| Prefer not to say | 2.55 | 0.46–14.17 | .28 | 6.20 | 0.98–39.29 | .05 |
| **Gender identity** | | | | | | |
| Female (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Male | 1.05 | 0.69–1.61 | .81 | 0.69 | 0.38–1.25 | .23 |
| Prefer not to say | 0.39 | 0.04–4.38 | .45 | 10.01 | 0.86–116.93 | .07 |
| **Education** | | | | | | |
| GCSE/A-Levels (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Bachelor's degree/diploma | 1.00 | 0.46–2.16 | 1.00 | 2.16 | 0.84–5.55 | .11 |
| Master's degree or PhD | 0.95 | 0.43–2.09 | .90 | 1.93 | 0.73–5.09 | .19 |
| Other | 0.68 | 0.23–2.04 | .49 | 2.89 | 0.78–10.77 | .11 |
| **Professional role** | | | | | | |
| Medical doctors (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| HCAs or other | 0.59 | 0.30–1.13 | .11 | 3.30 | 1.49–7.32 | **<.01** |
| Nurses or midwives | 0.82 | 0.50–1.32 | .41 | 2.64 | 1.39–4.98 | **<.01** |
| AHPs or pharmacists | 0.88 | 0.55–1.42 | .60 | 1.79 | 0.92–3.48 | .09 |
| **Physical health condition (at vaccine development)** | | | | | | |
| No (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.20 | 0.81–1.79 | .36 | 0.94 | 0.57–1.54 | .80 |
| **Smoking status (at vaccine development)** | | | | | | |
| Current smokers (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Never | 0.56 | 0.32–0.99 | **<.05** | 0.87 | 0.43–1.77 | .71 |
| Already stopped | 1.18 | 0.62–2.25 | .62 | 1.10 | 0.49–2.51 | .81 |
| Prefer not to say | 0.52 | 0.09–2.90 | .46 | 0.66 | 0.07–6.11 | .71 |
| **Depression/anxiety (at vaccine development)** | | | | | | |
| No (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.13 | 0.77–1.66 | .53 | 1.74 | 1.10–2.75 | **.02** |

**Table 2.** Model 2 including prevailing mental health during vaccine rollout adjusted for demographic characteristics, and physical health morbidities, smoking status, and history of positive COVID-19 test assessed at vaccine rollout.

| Predictors | Vaccine effectiveness (n = 632) | | | Vaccine safety (n = 623) | | |
|---|---|---|---|---|---|---|
| | Adj. OR | 95% CI | p-value | Adj. OR | 95% CI | p-value |
| **Age** | | | | | | |
| 18 to 25 (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| 26 to 35 years | 1.48 | 0.54–4.11 | .45 | 0.69 | 0.22–2.15 | .52 |
| 36 to 50 years | 1.22 | 0.45–3.34 | .70 | 0.54 | 0.17–1.65 | .28 |
| 51 to 60 years | 1.14 | 0.40–3.21 | .81 | 0.40 | 0.12–1.30 | .13 |
| 61 years + | 1.31 | 0.41–4.22 | .65 | 0.17 | 0.04–0.78 | **.02** |
| **Ethnicity** | | | | | | |
| White (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Asian | 0.62 | 0.33–1.19 | .16 | 1.98 | 0.98–3.99 | .06 |
| Black | 1.02 | 0.40–2.59 | .96 | 8.39 | 3.27–21.53 | **<.001** |
| Mixed | 1.37 | 0.50–3.74 | .54 | 1.27 | 0.35–4.55 | .72 |
| Other | 2.55 | 0.65–10.05 | .18 | - | - | - |
| Prefer not to say | 2.27 | 0.40–12.80 | .35 | 6.54 | 0.99–43.23 | .05 |
| **Gender identity** | | | | | | |
| Female (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Male | 1.14 | 0.74–1.75 | .56 | 0.77 | 0.42–1.42 | .41 |
| Prefer not to say | 0.42 | 0.04–4.61 | .48 | 11.72 | 1.01–136.02 | **<.05** |
| **Education** | | | | | | |
| GCSE/A-Levels (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Bachelor's degree/diploma | 0.92 | 0.43–2.00 | .84 | 1.91 | 0.74–4.92 | .18 |
| Master's degree or PhD | 0.83 | 0.38–1.84 | .65 | 1.58 | 0.60–4.17 | .35 |
| Other | 0.62 | 0.21–1.87 | .40 | 2.30 | 0.63–8.40 | .21 |
| **Professional role** | | | | | | |
| Medical doctors (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| HCAs or other | 0.60 | 0.31–1.17 | .14 | 3.36 | 1.52–7.43 | **<.01** |
| Nurses or midwives | 0.77 | 0.47–1.26 | .30 | 2.89 | 1.51–5.53 | **.001** |
| AHPs or pharmacists | 0.89 | 0.55–1.43 | .62 | 1.98 | 1.01–3.88 | **<.05** |
| **Physical health condition (at rollout)** | | | | | | |
| No (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 0.89 | 0.47–1.71 | .74 | 1.23 | 0.58–2.59 | .59 |
| **Smoking status (at rollout)** | | | | | | |
| Current (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Never | 0.76 | 0.42–1.38 | .37 | 1.03 | 0.49–2.17 | .94 |
| Already stopped | 1.16 | 0.59–2.31 | .67 | 1.33 | 0.56–3.16 | .52 |
| Prefer not to say | 0.39 | 0.04–3.61 | .41 | 1.00 | 0.10–10.00 | .99 |
| **History of positive COVID-19 test (at rollout)** | | | | | | |
| No (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 0.97 | 0.65–1.46 | .89 | 0.51 | 0.29–0.90 | **.02** |
| **Depression/anxiety (at rollout)** | | | | | | |
| No (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes – Persistent | 1.72 | 1.10–2.69 | **.02** | 1.37 | 0.80–2.33 | .25 |
| Yes – new onset | 1.34 | 0.80–2.25 | .26 | 0.48 | 0.22–1.03 | .06 |

during rollout. Only smoking status was identified as a significant predictor of negative attitude regarding vaccine effectiveness: HCPs who never smoked had reduced negative attitudes towards vaccine effectiveness (0.56 [CI 0.32–0.99], p < .05), compared to current smokers.

Table 2 (left panel; n = 632) shows the results of model 2 regarding the predictors at the time of rollout associated with negative attitudes vaccine effectiveness. Ongoing depression and/or anxiety was associated with increased negative attitude regarding vaccine effectiveness (1.72 [1.10–2.69], p = .02), but no significant increased risk was observed in HCPs with new-onset depression and/or anxiety, compared to HCPs without depression and/or anxiety at rollout. Consistently, no significant associations between demographic variables and negative attitude regarding vaccine effectiveness were observed.

Table 3 (left panel; n = 632) shows the results of model 3 regarding the change in depression and anxiety symptom severity as a possible predictor of negative attitudes towards vaccine effectiveness. A whole unit increase in the change in combined PHQ-9 (depression) and GAD-7 (anxiety) score was associated with 3% increased risk of negative attitude regarding vaccine effectiveness (1.03 [1.00–1.05], p < .05).

## Discussion

To our knowledge, this is the first study to evaluate the impact of mental health status and prevailing mental health on vaccine attitudes in UK-based HCPs. We observed that the presence of probable major depressive disorder and/or generalized anxiety disorder during the vaccine development period was associated with elevated negative attitude towards vaccine safety, but not vaccine effectiveness, at the time of rollout. This observation was independent of demographic characteristics associated with elevated negative attitude towards vaccine safety, namely younger age, Asian and Black ethnicity, and professional role (healthcare assistants, and nurses and midwives). We also observed that HCPs with ongoing (persistent) depression and/or anxiety had elevated levels of negative attitudes regarding vaccine effectiveness, but not vaccine safety. Lastly, we showed that worsened symptoms of depression and anxiety over the study period were associated with elevated negative attitude regarding vaccine effectiveness, but not vaccine safety. Collectively, the findings show that mental health status at different time points can impact on HCPs' attitudes towards the safety and effectiveness of a newly developed

**Table 3.** Model 3 including the change in combined PHQ-9 and GAD-7 scores over time adjusted for demographic characteristics, and baseline PHQ-9 and GAD-7 scores.

| | Vaccine effectiveness (n = 632) | | | Vaccine safety (n = 623) | | |
|---|---|---|---|---|---|---|
| Predictors | Adj. OR | 95% CI | p-value | Adj. OR | 95% CI | P-value |
| **Age** | | | | | | |
| 18 to 25 (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| 26 to 35 years | 1.52 | 0.55–4.25 | .42 | 0.68 | 0.21–2.18 | .52 |
| 36 to 50 years | 1.25 | 0.45–3.44 | .67 | 0.56 | 0.18–1.77 | .32 |
| 51 to 60 years | 1.19 | 0.42–3.40 | .75 | 0.41 | 0.12–1.36 | .14 |
| 61 years + | 1.41 | 0.43–4.57 | .57 | 0.17 | 0.04–0.81 | **.03** |
| **Ethnicity** | | | | | | |
| White (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Asian | 0.61 | 0.32–1.17 | .14 | 2.18 | 1.08–4.42 | **.03** |
| Black | 1.04 | 0.41–2.65 | .93 | 8.90 | 3.43–23.10 | **<.001** |
| Mixed | 1.31 | 0.48–3.58 | .61 | 1.33 | 0.37–4.78 | .67 |
| Other | 2.36 | 0.59–9.38 | .22 | - | - | - |
| Prefer not to say | 1.89 | 0.32–11.10 | .48 | 7.29 | 1.05–50.84 | **<.05** |
| **Gender identity** | | | | | | |
| Female (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Male | 1.14 | 0.74–1.75 | .57 | 0.81 | 0.44–1.49 | .51 |
| Prefer not to say | 0.41 | 0.04–4.50 | .47 | 13.15 | 1.06–162.82 | **<.05** |
| **Education** | | | | | | |
| GCSE/A-Levels (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Bachelor's degree/diploma | 0.92 | 0.43–2.00 | .84 | 1.89 | 0.74–4.84 | .19 |
| Master's degree or PhD | 0.83 | 0.38–1.85 | .65 | 1.64 | 0.62–4.34 | .32 |
| Other | 0.62 | 0.21–1.88 | .40 | 2.44 | 0.66–8.95 | .18 |
| **Professional role** | | | | | | |
| Medical doctors (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| HCAs or other | 0.60 | 0.31–1.17 | .13 | 3.33 | 1.50–7.43 | **<.01** |
| Nurses or midwives | 0.76 | 0.46–1.23 | .26 | 2.94 | 1.53–5.67 | **.001** |
| AHPs or pharmacists | 0.88 | 0.55–1.43 | .61 | 1.94 | 0.98–3.81 | .06 |
| **Physical health condition (at rollout)** | | | | | | |
| No (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 0.85 | 0.44–1.64 | .63 | 1.14 | 0.54–2.40 | .73 |
| **Smoking status (at rollout)** | | | | | | |
| Current (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Never | 0.76 | 0.42–1.37 | .36 | 1.01 | 0.48–2.12 | .98 |
| Already stopped | 1.15 | 0.58–2.28 | .69 | 1.25 | 0.53–2.98 | .61 |
| Prefer not to say | 0.38 | 0.04–3.53 | .40 | 1.11 | 0.11–10.99 | .93 |
| **Positive COVID-19 test (at rollout)** | | | | | | |
| No (reference) | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 0.99 | 0.66–1.48 | .95 | 0.50 | 0.28–0.90 | **.02** |
| **Baseline PHQ-9 score** | | | | | | |
| | 1.04 | 0.99–1.09 | .14 | 1.00 | 0.95–1.06 | .94 |
| **Baseline GAD-7 score** | | | | | | |
| | 1.01 | 0.96–1.06 | .74 | 1.03 | 0.97–1.10 | .38 |
| **Change in combined PHQ-9 and GAD-7 scores** | | | | | | |
| | 1.03 | 1.00–1.05 | **<.05** | 0.97 | 0.94–1.00 | .06 |

vaccine. Since HCPs may be especially susceptible to the mental health impact, these findings reinforce the need to protect the mental health of HCPs over the course of a pandemic. This also has implications for the general population. Firstly, HCPs are often viewed as a source of vaccine information and those HCPs with adverse mental health may verbally and non-verbally influence hesitancy in the general population. Secondly, HCPs are part of the general population but are relative better educated on healthcare or medical-related matters. As such, we expect that our observed findings in HCPs may be attenuated relative to what may occur in the general population.

Willingness to receive a vaccine (and the related attitudes) is not static and fluctuates depending on availability of factual and false information regarding risk,[19] as well as individual-level factors. Naturally, there would be less positive vaccine information demonstrating vaccine safety several months prior to rollout, as compared to during the roll-out period. We suspect that HCPs with probable major depressive disorder and/or generalized anxiety disorder during vaccine development generate negative attitudes regarding vaccine safety because they are more likely to attend to and focus on negative risk information regarding vaccine safety, as per attentional bias and memory bias models.[20–22] Moreover, HCPs with ongoing (persistent) depression and/or anxiety are likely to report more negative attitudes regarding vaccine effectiveness because repetitive negative thoughts regarding past, present, and future events are a predictor and characteristic of depression or anxiety.[23–25] We anticipated that HCPs with ongoing (persistent) depression and/or anxiety would have elevated negative attitudes regarding vaccine safety – a trend was observed in this direction, albeit with large confidence intervals and significance was not met. An explanation for this is that the abundance of positive vaccine safety information during rollout may counter the negative risk information previously attended to, but we are unable to verify this mechanism.

Although scarce, there are studies (primarily cross-sectional) reporting conflicting results regarding mental health and actual vaccine uptake. Such studies[7,26] found no association between mental health status during rollout and vaccine uptake, while other studies found that better mental health or reduced perceived mental health impact was associated with increased vaccine hesitancy.[8,9] One longitudinal study in the general population found that depressive symptom severity prior to rollout was associated with indecisiveness to be vaccinated during rollout.[10] Our findings corroborate with the latter study.

Aside from mental health, we were able to develop a profile associated with vaccine safety attitudes: HCPs aged 18–25 years, Asian and Black ethnicities, and HCAs and nurses or midwives had elevated negative attitudes regarding vaccine safety compared to HCPs aged 61 years+, White ethnicity, and medical doctors, respectively. This generally supports existing studies,[12,27] although we did not observe any impact of gender or education which was unexpected.[27,28] Lastly, HCPs with a history of contracting COVID-19 exhibited more positive attitudes regarding vaccine safety, but we do not anticipate that the association between prior COVID-19 infection and positive attitudes regarding vaccine safety will translate to increased vaccine uptake.[12,29]

There are two key strengths. Firstly, because we serendipitously collected mental health data several months prior to the rollout during an ongoing pandemic, it is unlikely that this study will be repeated in such a setting. Secondly, we gathered complete data from a relatively large cohort at two separate time points (first reflecting the vaccine development stage, and second reflecting the rollout stage) using validated mental health screening tests. Therefore, we provide an in-depth understanding regarding the interplay between mental health status and changes to mental health and attitudes towards a newly developed vaccine.

There are some limitations which must be acknowledged. Firstly, we are limited in generalizability to general populations worldwide, but supplementary analysis (Supplemental Table S3–S5) including a further 57 non-UK-based HCPs and 84 non-HCPs produced consistent results. Related to this, our sample may not be wholly representative, but the proportions of the cohort and the wider CoPE-HCP sample were similar on demographic characteristics, adverse mental health, and negative vaccine attitudes, and the gender and ethnicity of the cohort is similar to that of the wider national health service (NHS) workforce. Secondly and more importantly, while the rates of vaccine intentions were promising, we were unable to robustly test for predictors of hesitancy (just 34 (5.4%) were classed as vaccine hesitant) which leaves one to consider the extent that negative vaccine attitudes are consistent with actual vaccine refusal in HCPs. Further work is required to understand how mental health in HCPs is associated with actual vaccine hesitancy using validated scales[30,31] assessing other attitudes driving hesitancy (e.g. concern for commercial profiteering, preference for natural immunity).[27] Unfortunately, these scales were not available when the CoPE-HCP study was established. Finally, we have examined limited aspects of sociodemographic factors, and there are other factors such as trust in the government[32] and

scientists,[33] and knowledge about COVID-19 vaccines[32,34] and the virus[35] which are associated with vaccine hesitancy amongst healthcare workers. Indeed, there are other mental health domains (not assessed for) which may have nuanced associations with vaccine attitudes (for example, obsessive-compulsive disorder).[36]

Overall, this cohort study of HCPs demonstrates the impact of mental health on attitudes towards a newly developed vaccine during an ongoing pandemic. The key finding is that, in addition to above-mentioned demographic characteristics, the presence of probable major depressive disorder and/or generalized anxiety disorder during vaccine development is prospectively associated with elevated negative attitude regarding vaccine safety several months later during rollout. We also show that persistent adverse mental health (i.e. ongoing presence of probable major depressive disorder and/or generalized anxiety disorder), from vaccine development to vaccine rollout, and worsened symptoms of depression and anxiety, is associated with elevated negative attitude regarding vaccine effectiveness. We hope these findings stimulate future research studies incorporating mental health as a predictor and provide public health officials with useful insights to help tailor vaccination campaigns to those HCPs.

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## Data availability statement

Anonymised data, data dictionary, and survey materials will be made available upon request. Study protocol is available at https://doi.org/10.3389/fpsyg.2021.616280.

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