**Pre-pandemic mental and physical health as predictors of COVID-19 vaccine hesitancy: evidence from a UK cohort study**

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**Abstract**

*Background*: Although several predictors of COVID-19 vaccine hesitancy have been identified, the role of physical health and, particularly, mental health is unclear.

*Objective*: To test the association of mental and physical health with self-reported vaccine hesitancy after the announcement of the successful testing of the Oxford University/AstraZeneca vaccine.

*Design, Setting, and Participants*: We used individual-level data from a pandemic-focused investigation (COVID Survey), a prospective cohort study nested within Understanding Society (Main Survey). In the week immediately following the announcement of successful testing of the first efficacious inoculation (November/December 2020), data on vaccine intentionality were collected in 11740 individuals (6702 women) aged 16-95. Pre-pandemic, study members responded to enquiries about prior diagnoses of mental and physical health, and also completed the general health questionnaire (version 12) for symptoms of psychological distress (anxiety and depression). (XXXXXX wave of the Main Survey).

*Measurements*: Self-reported intention to take up a vaccination for COVID-19. To summarise our results, we computed odds ratios with accompanying 95% confidence intervals for indices of mental health adjusted for selected covariates.

*Results*: Of the study sample, XXXXXX indicated they were hesitant about having the vaccine. After adjustment for age, sex, and ethnicity, study members with a lower baseline XXXX were markedly more likely to be vaccine hesitant (odds ratio per standard deviation lower score in cognition; 95% confidence interval: XXXXXX). Adjustment for XXXXX had no impact on these results, whereas controlling for educational attainment led to partial attenuation but the probability of hesitancy was still elevated (XXXXX). There was a linear association for vaccine hesitancy across the full range of cognition scores (p for trend: XXXXXX).

*Limitations:* Our outcome was based on intention rather than behaviour.

*Conclusions*: XXXXXX.

**Introduction**

There is growing evidence from cohort studies[ref] that people with a serious mental illness and those with a higher prevalence of distress symptoms (anxiety and depression) experience an elevated burden of infection with SARS-CoV-2,[ref] in addition to hospitalisation for, and death from, the disease caused by it, coronavirus 2019 (COVID-19). Vaccination against COVID-19, central to attaining herd immunity,1 has therefore been prioritised for people with mental health problems, although this is not as universal as for individuals with existing somatic disorders.[ref]

There are several reasons to anticipate vaccine hesitancy in people with mental health problems. First, people with severe mental illness tend to perform less well educationally, and have lower levels of health literacy and cognitive function,[ https://www.psychiatrist.com/jcp/covid-19/perspectives-on-covid-and-individuals-with-serious-mental-illness/] itself link to greater hesitancy.[ref] Such characteristics may mean that people with mental health problems are less able to source and synthesis information about vaccination. Second, although this is not a universal finding,[] individuals with psychological health problems have lower rates of compliance with medication as evidenced by treatment for somatic comorbidities.[] Third, individuals with psychiatric morbidity tend to have a lower prevalence of health-protecting behaviours. Relative to their unaffected counterparts, for instance, they are more likely to smoke, take less exercise, have an imprudent diet, and be obese.[ref] Fourth, people with mental health issues also appear to be less likely to take up the offer of cancer screening.[ref]. Lastly, of most relevance, in a study of uptake of the influenza inoculations, users of an outpatient psychiatry clinic had markedly lower take up than the general population.[ https://journals.sagepub.com/doi/pdf/10.2190/PM.46.1.a]

Collectively, these observations provide a *prima facie* case that people with mental health problems may be less willing to take up the offer of a vaccination against COVID-19. In an absence of any empirical data, there have been recent calls for an examination of this relationship.[ref] Accordingly, in a large, general-population based UK sample we examine the predictive capacity, if any, of mental health problems, for vaccine hesitancy. In doing so, we draw direct comparison with somatic illness which gas recently been shown to be consistently associated with lower levels of hesitancy.[ Nguyen; Ruiz] Importantly, data collection on vaccine intention took place following the announcement of successful testing of the Oxford University/AstraZeneca vaccine, rendering as no longer theoretical the future offer of a vaccination.

**Methods**

Understanding Society, also known as the UK Household Longitudinal Study, is a nationally-representative, on-going, open, cohort study (hereinafter, the ‘Main Survey’). Based on a clustered-stratified probability sample of households, participants have been interviewed annually since 2009.2 Households who had participated in at least one of the two most recent waves of data collection (wave 8, 2016-18; wave 9, 2017-19) comprised the target sample for a pandemic-focused study initiated in April 2020 (hereinafter, the ‘COVID Survey’).3,4 The derivation of the present analytical sample from the Main and COVID surveys, including the whereabouts of relevant data, is depicted in figure 1. The University of Essex Ethics Committee gave approval for data collection in the COVID-orientated surveys (ETH1920-1271); no further ethical permissions were required for the present analyses of anonymised data.

The COVID Surveys took place monthly/bimonthly between April (wave 1) and November 2020 (wave 6), with questions on vaccine intention first administered in the November wave when study members were aged 16-95 (mean 53).4 Data collection in wave 6 (starting 24th November) commenced the day immediately following the announcement of the efficacy of the Oxford University/AstraZeneca vaccine5 and continued for one week, comprising a total of 12,035 individuals of 19,294 invitations issued (response proportion, 62%).4

*Assessment of mental and physical health*

Study members indicated if a doctor or other health professional ever told them that they had an emotional, nervous, or psychiatric problem, which included anxiety, depression, psychosis or schizophrenia, bipolar disorder or manic depression, an eating disorder, post-traumatic stress disorder, or any other mental illness (wave 10, Main Survey). Self-reported psychiatric history, in particular depression, show reasonable agreement with a structured clinical interview.[ 24467941] With a low prevalence hesitancy for selected conditions, the latter five mental health groups were aggregated.

Psychological distress (wave 6, COVID Survey) was ascertained using administration of the 12-item version of the General Health Questionnaire. Validated against standardised psychiatric interviews,6,7 this is a widely used measure of distress in population-based studies. Consistent with published analyses, we used the following classifications: asymptomatic (score 0), sub-clinically symptomatic (score 1-3), symptomatic (score 4-6), and highly symptomatic (score 7-12).8-10 A history of physical morbidities was also captured (wave 10, Main Survey) and based on whether a doctor or other health professional told the participant that they had a cardiometabolic condition (congestive heart failure, coronary heart disease, angina, heart attack or infarction, stroke, diabetes, and/or hypertension); respiratory disease (respiratory disease comprised bronchitis, emphysema, chronic obstructive pulmonary disease, and/or asthma); or cancer of any type. Self-reports of these physical conditions reveal moderate to high agreement with clinical records.[ref] Related, during the pandemic, based on their physical medical history, people judged as clinically extremely vulnerable and therefore at high risk from COVID-19 were contacted by the UK National Health Service or general practitioner and recommended to stay at home. Conditions that met the criteria for shielding included selected cancers, severe respiratory disorders such as cystic fibrosis, severe asthma, organ transplant recipients, and people with a disability such as Down’s syndrome. Study members were therefore asked about the shielding status for themselves or a household member (waves 1-5, COVID Surveys; denoted by yes/no).

*Assessment of covariates*

Covariates were self-reported and included age; sex (both wave 10, Main Survey); ethnicity (wave 10, Main Survey; denoted as white or non-white); and highest education level (wave 10, Main Survey; categorised as degree & other higher degree, A’ level or equivalent [Advanced Placement in the US], GCSE or equivalent [Grade 10 in the USA], other qualification, and none). In the third wave of data collection in the Main Survey (2011-2013), six cognitive function tests were administered: immediate word recall and delayed word recall tasks; semantic verbal fluency; cognitive impairment; numerical reasoning skills; and fluid reasoning. Representing a range of cognitive skills, these tests have been repeatedly deployed in large-scale, population-based studies.11-15 Using scores from the six tests of cognitive function we generated a single general cognitive function variable (*g*).

*Assessment of vaccine intentionality*

At wave 6 in the COVID Survey, study members were asked “Imagine that a vaccine against COVID-19 was available for anyone who wanted it. How likely or unlikely would you be to take the vaccine?”. Possible responses were “Very likely”, “Likely”, “Unlikely” and “Very unlikely”. The latter two categories were combined to denote vaccine hesitancy.

*Statistical analyses*

To summarise the relation between the mental health indicators and vaccine hesitancy, we used logistic regression to compute odds ratios with accompanying 95% confidence intervals. The most basic analyses were adjusted for age, sex, and ethnicity. Retaining these covariates, we then explored the impact of controlling for somatic medical conditions, education, cognition, and shielding status.

**Results**

In table 1 we show study member characteristics according to vaccine intention in unadjusted analyses. In a sample of 11,955 individuals (6741 women) who responded in full to the enquiry regarding COVID-19 vaccine intentionality, 15.4% indicated that they were hesitant (table 1). Relative to the group who indicated a willingness to have the vaccine, those who were hesitant were more likely to be younger, female, from an ethnic minority background, be less well educated, and have a lower general cognitive function score. The hesitant were also less likely to have an existing somatic morbidity, as indexed by cardiometabolic disease and cancer. Related, there was also a lower prevalence of shielding in the hesitant category (correlation between any physical morbidity and shielding: *ρ*=0.12, p<0.0001, N=10916). There was little evidence of a difference in prevalence of specific mental health condition across the hesitant groups; only ‘other’ conditions was more common in study members expressing hesitancy but the difference was marginal. People who declared themselves reticent in taking the vaccine when offered had slightly higher levels of distress, however.

In table 2 we used multiple regression analyses to explore the independent role, if any, of a pre-pandemic diagnosis of a physical or psychological morbidity as predictors of vaccine hesitancy. After adjustment for age-, sex- and ethnicity-adjusted, relative to people without a physical condition, those with a diagnosis of cardiometabolic disease (odds ratio; 95% confidence interval: 0.82; 0.67, 0.99) or respiratory disease (0.71; 0.57, 0.88) were less like to decline an offer of vaccination. There was no relationship with cancer, however. Adjusting for a range of covariates – individually (appendix X) and collectively (table 2 and figure 2) – had little impact on these relationships.

In analyses in which mental illness diagnosis was the exposure of interest, none of the individual psychiatric conditions were related to vaccine hesitancy. In categorising the scores on psychological distress, there was a suggestion of a quadratic (‘U’-shaped) effect such that people who had either low or high scores on the distress scale were marginally more likely to be vaccine hesitant, and those with moderate symptoms had the lowest risk. We further explored this association by using raw scores in the 12 item distress scale (range 0-12). Based on this disaggregation, there was no support for an association, linear or quadratic (figure 3).

**Discussion**

**Our main finding was that, in data collected immediately XXXXXX, selected pre-existing physical but not psychiatric morbidities were related to a higher likelihood of vaccine hesitancy. While the results for physical disease have empirical support elsewhere, those for mental health – hitherto untested – run counter to our expectations given that people with such morbidity are less likely to engage in health-protecting behaviours such as a healthy lifestyle and screening for somatic disorder.[ref].**

***Comparison with existing studies***

**The notion people with a long-standing physical condition are less likely to be hesitant has been reported elsewhere.16[ref] That we also recapitulated known associations with hesitancy such as being female,17-19 being younger,17,19 and from an ethnic minority group,4,19,20 gives us some confidence in our novel results for mental health. To the best of our knowledge, there has been one prior examination of the relationship between mental health and vaccine hestinacy.**21 **Comprising two small cross-sectional studies where data collection took place prior to the announcement of the successful testing of the first efficacious vaccination, study members were administered a very brief and unvalidated enquiry as to whether they had experience of mental health problem. In that study, there was no clear evidence of a link.**21 **Data from other vaccination programmes offer limited insights. In patients with schizophrenia which took place during the 2009 H1N1 influenza pandemic in Australia, three-quarters indicated that they were willing to be vaccinated;[** **PMC7906686] however, in keeping with similar studies,[ref] the absence of a general population comparison group renders interpretation problematic. In a small cohort of socioeconomically disadvantaged mothers, those with mental health problems were seemingly less likely to have children with up-to-date vaccine coverage, although the association was weak and the sample size small.[** **PMID: 33489723]**

***Study strengths and weaknesses***

**While the present study has its strengths, including its size, national representativeness, and timing, there are also some weaknesses. First, we used vaccine intentionality as an indicator vaccine uptake but the correlation is imperfect. In a small scale longitudinal study conducted during the period of the 2009 H1N1 pandemic in Hong Kong, less than 10% of people who expressed a commitment to being inoculated reported that they had received a vaccination two months later.22 Elsewhere, in a US adult population at high risk of seasonal influenza, around half of those intending to be vaccinated had received the inoculation within the following 5 months.23 Second, there was inevitably some loss to follow-up (figure 1). While this attrition may have impacted upon the estimation of the prevalence vaccine hesitancy which is likely to be lower in our select sample relative to the general population,24 it is unlikely to have influenced our estimation of its relationship with mental and physical health. Thus, in other contexts, we have shown that highly select cohorts reveal very similar risk factor–outcome associations to those seen in studies with conventionally high response.25**

**In conclusion,** **we found that some somatic medical conditions but not mental health problems were related to a lower likelihood of being vaccine hesitant.**

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**Figure 1. Flow of cohort members into the analytical sample:**

**Main Survey and COVID Survey in Understanding Society**

(Drew: This is taken from the cognition paper. Please update.)

50,994 participants in Wave 1 of Main Survey (2009-11)

N=7361 with full data on mental and physical health, intention, and covariates

N=11,955 with full data on vaccine intentionality

Wave 6 (N=12,035) of COVID Survey

(Nov 2020)

*(vaccine hesitancy, psychological distress)*

Wave 1 (N=17,761) COVID Survey

(April 2020)

34,318 participants in Wave 10 of Main Survey

(*educational level, ethnicity, history of comorbidity*)

40,730 participants in Wave 3 of Main Survey (2011-13)

(*cognitive function*)

42,330 participants in Waves 8 (2016-18) and 9 (2017-19) of Main Survey

**Figure 2. Odds ratios (95% CI) for the relation of mental and physical health with later COVID-19 vaccine hesitancy in Understanding Society (N=7361)**

(Drew: in keeping with figure 3, can we add the numerical values for each point estimate [95%CI]). If it’s complicated to show ORs from both models for each exposure, then let’s just have the multiply-adjusted effects. It’s also optimal to have the same style of figure presentation throughout. Lastly, note ‘heath’ typing error)

**Chart

Description automatically generated**

Numbers of study members in this sample corresponds to those with complete data on all variables in the analyses (N=7361). \*for physical comorbidities, adjustment is for psychological morbidities, and vice versa; \*\*comparator group is those study members without the condition

**Figure 3. Odds ratios (95% CI) for the relation of psychological distress with later COVID-19 vaccine hesitancy in Understanding Society (N=7361)**

(Drew: please confirm these are effects estimates after adjustment for all covariates; that would be optimal here)

|  |
| --- |
|  |
|  |
| All covariates are: age, sex, ethnicity, education, somatic comorbidity, shielding, and cognitive function.  (Drew: here and throughout, can you confirm we do not adjust psychological distress based on the GHQ for self-reported psychiatric diagnosis and, in analyses featuring psychiatric diagnosis as our independent variable, the reverse us also true? This would be overadjustment because anxiety and depression feature twice – as diagnosis and in the GHQ) |

**Table 1. Study member characteristics according to**

**COVID-19 vaccine hesitancy in Understanding Society**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Vaccine hesitant** | | **P value** |
|  | **Yes** | **No** |  |
| Numbers of people | 1842 (15.4) | 10113 (84.6) |  |
| **Demographic factors** |  |  |  |
| Age, yr, mean (SD) | 45.0 (14.5) | 54.6 (15.6) | < 0.0001 |
| Female | 1162 (63.1) | 5530 (54.7) | < 0.0001 |
| Non-white ethnicity | 406 (22.7) | 698 (7.0) | < 0.0001 |
| **Socioeconomic factors** |  |  |  |
| No university education | 939 (22.0) | 4298 (6.9) | < 0.0001 |
| **Physical comorbidities** |  |  |  |
| Cardiometabolic disease | 268 (15.0) | 2513 (25.2) | < 0.0001 |
| Respiratory disease | 219 (12.3) | 1372 (13.8) | 0.144 |
| Any cancer | 45 (2.5) | 525 (5.3) | < 0.0001 |
| Shielding in the household | 196 (10.6) | 1187 (11.7) | < 0.0001 |
| **Psychiatric morbidities** |  |  |  |
| Anxiety | 85 (4.0) | 404 (4.6) | 0.153 |
| Depression | 92 (5.0) | 466 (4.6) | 0.352 |
| ‘Other’ mental disorder | 36 (1.9) | 121 (1.2) | 0.007 |
| Psychological distress symptoms, mean (SD) | 2.82 (3.9) | 2.34 (3.4) | < 0.0001 |
| **Cognitive function** |  |  |  |
| *g* factor, mean (SD) | 96.6 (15.7) | 100.5 (14.8) | < 0.0001 |
|  |  |  |  |

Numbers of study members corresponds to those with complete data

on vaccine intentionality only. Results are N (%) unless otherwise indicated.

**Table 2. Odds ratios (95% CI) for the relation of mental and physical health with later**

**COVID-19 vaccine hesitancy in Understanding Society (N=7361)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Number hesitant / Total at risk** | **Age, sex, & ethnicity** | **All covariates** |
| **Physician diagnosis** |  |  |  |
| Anxiety | 50/324 | 1.00 (0.72, 1.36) | 1.11 (0.79, 1.52) |
| Depression | 54/368 | 0.99 (0.72, 1.33) | 1.12 (0.81, 1.53) |
| Other mental health condition(s) | 20/111 | 1.08 (0.64, 1.75) | 1.21 (0.71, 1.97) |
| Any mental health condition | 71/491 | 0.99 (0.75, 1.29) | 1.14 (0.86, 1.49) |
|  |  |  |  |
| **Psychological distress** |  |  |  |
| Asymptomatic (score 0) | 443/3339 | 1.0 (ref) | 1.0 (ref) |
| Subclinically symptomatic (1-3) | 247/2256 | 0.77 (0.64, 0.91) | 0.81 (0.68, 0.96) |
| Symptomatic (4-6) | 90/750 | 0.77 (0.59, 0.98) | 0.82 (0.63, 1.05) |
| Highly symptomatic (7-12) | 173/1016 | 1.05 (0.85, 1.28) | 1.12 (0.91, 1.38) |
| P for quadratic |  | < 0.0001 | 0.003 |
| P for linear trend |  | 0.251 | 0.075 |
| Per SD (3.5 points) decrease | XXX/XXXX | 0.93 (0.81, 1.06) | 0.88 (0.77, 1.01) |
|  |  |  |  |
| **Physical comorbidities** |  |  |  |
| Cardiometabolic disease | 147/1905 | 0.82 (0.67, 0.99) | 0.78 (0.64, 0.95) |
| Respiratory disease | 107/1034 | 0.71 (0.57, 0.88) | 0.74 (0.59, 0.93) |
| Any cancer | 29/389 | 0.87 (0.58, 1.28) | 0.95 (0.62, 1.39) |
| Any physical health condition | 225/2389 | 0.72 (0.61, 0.85) | 0.72 (0.60, 0.85) |
|  |  |  |  |

All covariates are: age, sex, ethnicity, education, shielding, and cognitive function. Depending on

the predictor variable there was mutual adjustment for somatic comorbidity or psychiatric

morbidity/psychological distress

***Appendix***

*Batty GD, Deary IJ, Altschul D. Pre-pandemic mental and physical Health as predictors of*

*COVID-19 vaccine hesitancy: evidence from a UK cohort study*

**Table a1. Odds ratios (95% CI) for the relation of mental and physical health with later**

**COVID-19 vaccine hesitancy in Understanding Society – with models featuring individual covariates (N=7361)**

Drew: please update this table as per Table 2 categorisations

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Age, sex, ethnicity, & comorbidity\*** | **Age, sex, ethnicity, & shielding** | **Age, sex, ethnicity, & education** | **Age, sex, ethnicity, & cognition** | **All covariates** |
| **Physician diagnosis\*\*** |  |  |  |  |  |
| Anxiety | 1.04 (0.75, 1.43) | 0.98 (0.70, 1.34) | 1.02 (0.73, 1.40) | 1.00 (0.72, 1.38) |  |
| Depression | 1.04 (0.76, 1.41) | 0.98 (0.71, 1.32) | 1.01 (0.73, 1.36) | 1.02 (0.74, 1.38) |  |
| Psychosis or schizophrenia | 1.70 (0.24, 7.75) | 1.57 (0.22, 7.09) | 1.45 (0.20, 6.66) | 1.62 (0.23, 7.32) |  |
| Bipolar disorder or manic depression | 0.95 (0.27, 2.62) | 0.89 (0.25, 2.45) | 0.80 (0.22, 2.23) | 0.93 (0.27, 2.56) |  |
| An eating disorder | 0.24 (0.01, 1.23) | 0.22 (0.01, 1.11) | 0.22 (0.01, 1.16) | 0.23 (0.01, 1.17) |  |
| Post-traumatic stress disorder | 2.16 (1.02, 4.22) | 1.86 (0.88, 3.62) | 1.82 (0.86, 3.55) | 1.93 (0.91, 3.78) |  |
| ‘Other’ | 0.62 (0.15, 1.84) | 0.61 (0.14, 1.78) | 0.60 (0.14, 1.79) | 0.67 (0.16, 1.99) |  |
| Any of the above | 1.05 (0.79, 1.37) | 0.99 (0.75, 1.29) | 1.03 (0.78, 1.34) | 1.04 (0.79, 1.36) |  |
| **Psychological distress** |  |  |  |  |  |
| Asymptomatic (score 0) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |  |
| Subclinically symptomatic (1-3) | 0.76 (0.64, 0.91) | 0.77 (0.64, 0.91) | 0.79 (0.66, 0.94) | 0.79 (0.66, 0.94) |  |
| Symptomatic (4-6) | 0.80 (0.62, 1.03) | 0.79 (0.61, 1.02) | 0.80 (0.62, 1.03) | 0.81 (0.62, 1.04) |  |
| Highly symptomatic (7-12) | 1.09 (0.89, 1.34) | 1.07 (0.88, 1.31) | 1.09 (0.88, 1.33) | 1.08 (0.88, 1.33) |  |
| P for trend | p = 0.099 | p = 0.148 | p = 0.147 | p = 0.145 |  |
| Per SD (XX points) decrease | 1.12 (0.98, 1.28) | 1.10 (0.96, 1.26) | 1.10 (0.96, 1.26) | 1.10 (0.97, 1.26) |  |
| **Physical comorbidities\*\*** |  |  |  |  |  |
| Cardiometabolic disease | 0.81 (0.66, 0.99) | 0.82 (0.67, 1.00) | 0.80 (0.65, 0.97) | 0.77 (0.63, 0.94) |  |
| Respiratory disease | 0.70 (0.56, 0.88) | 0.72 (0.57, 0.89) | 0.72 (0.58, 0.90) | 0.71 (0.57, 0.89) |  |
| Any cancer | 0.86 (0.56, 1.26) | 0.88 (0.57, 1.29) | 0.89 (0.58, 1.31) | 0.90 (0.59, 1.33) |  |
| Any of the above | 0.71 (0.60, 0.84) | 0.72 (0.60, 0.85) | 0.71 (0.60, 0.84) | 0.70 (0.59, 0.82) |  |

\*All covariates are: age, sex, ethnicity, education, shielding, and cognitive function. Depending on the predictor variable there was also adjustment for somatic comorbidity or psychiatric

morbidity/psychological distress