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**Pre-pandemic Cognitive Function and COVID-19 Vaccine Intentionality: Prospective Cohort Study**

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Access to data: Data from Understanding Society (XXXXXX) are available to *bona fide* researchers upon application.

**Abstract**

*Importance*: While several predictors of COVID-19 vaccine intentionality have been examined, the role of cognitive function following the announcement of successful trial results is unknown.

*Objective*: To relate pre-pandemic scores on an array of cognitive function tests to vaccine hesitancy.

*Design, Setting, and Participants*: We used individual-level data from a pandemic-focused study (the COVID Survey), a prospective cohort study nested within Understanding Society (Main Survey). Data on vaccine intentionality were collected in 11740 individuals (6702 women), in November/December 2020 when study members were aged 16-95 (mean 53). General cognitive function, ascertained from a battery of six tests, was captured in 2011/12 in the Main Survey.

*Main Outcomes and Measures*: Self-reported intention to take up a vaccination. To summarise our results, we computed odds ratios with accompany 95% confidence intervals for tertiles of general cognitive function adjusted for selected covariates.

*Results*: Of the study sample, 17.2% (N=1842), indicated they were hesitant in having the vaccine. After adjustment for age, sex, and ethnicity, study members with a lower baseline cognition score were markedly more likely to be vaccine hesitant (odds ratio per standard deviation decrease in cognition; 95% confidence interval: 1.76; 1.62, 1.90). Adjustment for mental and physical health plus shielding status had no impact on these results, while controlling for educational attainment led to partial attenuation but the probability of hesitancy was still elevated (1.52; 1.37, 1.67). There was also clear linear relationship across the full range of cognition scores (p for trend: p<0.0001).

*Conclusions and Relevance*: Erroneous messaging around the roll-out of the vaccine programme may have complicated decision-making, leading to people with lower scores on standard tests of cognitive function being less willing to take up the future offer of vaccination for COVID-19. With this group also experiencing higher rates of the disease, these new findings may represent a dual burden.

**Introduction**

Cognitive function – also known as mental ability or intelligence – refers to psychological functions that involve the storage, selection, manipulation, and organisation of information, and the planning of actions.1[Ian/Catharine – best refs please.] Assessed using standard tests, there is marked inter-person variation in how rapidly and precisely people carry out these mental tasks.2[Ian/Catharine – best refs please.] Health protection and health care can be regarded as a complex set of tasks that similarly require assimilation of knowledge, decision-making, and planning. It has posited that people with higher cognitive function manage preventative behaviours and treatment more effectively,3 and there is growing evidence that this is the case.

In well-characterised cohort studies, relative to their lower-performing counterparts, people with higher ability are more likely to have a healthy diet,4 choose dietary supplements,5 be physically activity,4 and have superior oral hygiene.6 People who score better on cognitive tests are also less likely to smoke cigarettes,7,8 and drink harmful levels of alcohol.9,10 Cessation rates are also elevated in smokers with higher mental ability.11 Further, in individuals with a greater risk of a first cardiovascular disease event,12 in those at increased risk of re-infarction,13 and patients with respiratory disease,14 improved compliance with known efficacious drug therapies is apparent in people with a higher cognition score.

These observations provide circumstantial evidence for a link between cognitive ability and another health-protecting behaviour, vaccine uptake. Vaccination is central to controlling the pandemic, with success reliant on a sufficiently high uptake to achieve herd immunity.15 In the only empirical investigation of which we are aware, investigators administered a measure of analytical reasoning to samples in two small cross-sectional from the UK (N = 2025) and Ireland (N = 1041).16 Relative to the group who indicated they would be likely to accept a COVID-19 inoculation if one became available, somewhat lower cognition scores were apparent in study members indicating vaccine reticence.16 These data were collected in March/April 2020 when no vaccine was available. Around 8 months later, the development of the first efficacious vaccine for COVID-19 was announced,17 progress that may have impacted upon individual intentionality. Accordingly, in the present study, we investigated the link between cognitive function and COVID-19 vaccine intentionality in a large general population-based sample in which data collection took place immediately following the announcement of vaccine discovery.

**Methods**

Understanding Society, also known as the UK Household Longitudinal Study, is a nationally-representative, on-going, open, longitudinal study (hereafter, the ‘Main Survey’). Based a clustered-stratified probability sample of UK households, participants have been interviewed annually since 2009.18 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 (hereafter, the ‘COVID Survey’).19,20 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 or bimonthly between April (wave 1) and November 2020 (wave 6) when study members were aged 16-95 (mean 53), with questions on vaccine intention first administered in the latest round of data collection.20 Data collection in wave 6 (24th November) commenced the day immediately following the announcement of the Oxford University/AstraZeneca vaccine17 and continued for one week, finally comprising a total of 12,035 individuals of 19,294 invitations issued (response proportion, 62%).20

*Assessment of cognitive function*

In the third wave of data collection in the Main Survey (2011-2013), six cognitive function tests were administered following piloting.21,22 Representing a range of cognitive skills, these tests have been previously used in large-scale, population-based studies.23-27 *Verbal declarative memory* was assessed using both immediate and delayed word recall tasks. Respondents were asked to listen to a list of ten words delivered by a computer to ensure standardised delivery, then asked to recall the words immediately after the reading and, again, at a later stage in the interview without interviewer repetition. The number of correct responses was recorded each time. For *semantic verbal fluency*, respondents named as many animals as they could in one minute; the final score was based on the number of unique correct responses. Using components of screening instruments for *cognitive impairment* including the Mini Mental State Examination28 and the Cambridge Cognitive Examination (CAMCOG),29 respondents were asked to subtract 7 from 100 and then to subtract 7 from their answer on four more occasions. The number of correct responses of a maximum of five was recorded.

*Fluid reasoning* was assessed using a number sequence in which the respondent is asked to populate the gap(s) in a logical series. Respondents were initially presented with simple examples to test their understanding; those who seemed confused or unable to understand test requirements after two examples relayed were not asked to complete the test. Remaining study members were administered two sets of three number sequences, with the difficulty of the second set determined by their performance on the first. A score was derived which accounts for the difficulty of the items. For *numerical reasoning skills*, individuals were given three numerical problems to solve and, depending on their responses, were then administered a further one (simpler) or two (more difficult) problems. The total number of correct responses was recorded.

*Assessment of covariates ~~(Drew: can you ensure the months used to denote data collection in the covid survey match those given on-line:~~* [*~~https://www.understandingsociety.ac.uk/documentation/covid-19/questionnaires~~*](https://www.understandingsociety.ac.uk/documentation/covid-19/questionnaires) *~~- april, oct, dec do not feature. I suppose there might be overlap but let’s denote the survey by month of commencement of data collection as I think is used in the above link)~~*

Covariates were self-reported and included age (wave 10, summarising data from 2009 to 2019, Main Survey), sex(wave 10, Main Survey) ethnicity (wave 10, Main Survey; denoted as White British, White non-British, Mixed, Asian, Black, Other); highest education level (wave 10, Main Survey; denoted by Degree & Other Higher Degree, A-Level or equivalent, GCSE or equivalent, other qualification and none); NHS Shielding category (waves 1-5, COVID Surveys April, May, June, July and September 2020; denoted by yes/no). A history of physical morbidities was also captured during wave 10 of the Main Survey and based on cardiometabolic disease (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); and/or cancer of any type. Current psychological distress (wave 6, November 2020, COVID Survey) was ascertained using the administration of the 12-item version of the General Health Questionnaire. Validated against standardised psychiatric interviews,30,31 this is a widely used measure of distress in population-based studies. Consistent with published analyses,32-34 we used a score of ≥3 to denote psychological distress.

*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*

It is well-replicated that performance on tests of cognitive abilities tend to be positively inter-related, whereby people who perform well on a test of one cognitive ability tend to score well on another.[Ian/Catharine – best refs please.] This had led to the use of the term ‘general cognitive ability’, usually known as ‘g’. Accordingly, using scores from the six tests of cognitive function we generated a single general cognitive function variable. Computed using principal components analysis, the first unrotated component of the six cognitive tests was used as a single measure of cognitive function. To summarise the relation between cognition and vaccine hesitancy, we used logistic regression to compute odds ratios with accompanying 95% confidence intervals. In these analyses we calculated effect estimates for tertiles of cognitive function scores and those for a unit (standard deviation) disadvantage in score. The most basic analyses were adjusted for age, sex, and ethnicity. Retaining these covariates, we then explored the impact of separately controlling for existing medical conditions, education, and shielding status.

**Results**

In the sample of 11740 individuals (6702 women), 1842 individuals (1162 women), representing 17.2% of study members, indicated that they were hesitant in having the vaccine for COVID-19. In table 1 we show study member characteristics according to vaccine intention. Relative to the group who indicated a willingness to have the vaccine, those who were hesitant were more likely to be younger, female, and from an ethnic minority background. The hesitant were also better educated and less likely to have an array of existing somatic morbidities and be shielding at home, although the prevalence of psychological distress was somewhat higher.

There were marked differences in cognitive function between the vaccine groups, such that the vaccine hesitant study members had lower general ability scores (p-value for difference: <0.0001). We investigated these differentials in table 2 where we present the results of regression analyses incorporating potential explanatory variables. In age- and sex-adjusted analyses, relative to people in the highest-scoring cognition tertile, those in the lowest were twice as likely to be vaccine hesitant (odds ratio; 95% confidence interval: 1.99; 1.66, 2.40). Separate adjustment for comorbidity – whether physical or psychological – and shielding status had no impact on these effect estimates. Only controlling for educational achievement led to any attenuation in risk (lowest scoring cognition tertile vs. highest: 1.64; 1.35, 1.99) – the Kendall rank correlation between cognition and educational attainment was 0.27 (p<0.0001). Simultaneous adjustment for all covariates had no additional impact on effects estimates relative to those apparent in the statistical model featuring education.

In these analyses there was evidence of a linear relationship between cognition and vaccine intention, such that the lowest scoring ability group had the highest prevalence of hesitancy, and the intermediate group had intermediate risk (p-value for trend: <0.0001). To scrutinise the shape of the cognition–hesitancy association, we utilised deciles of cognition, and there was again evidence of a clear trend although this was not perfectly stepwise across all categories (figure 2).

**Discussion**

**Our main finding was that, net of several covariates, people with poorer scores on tests of cognitive function were less minded to take up an offer of vaccination for COVID-19 if it was made. Of note, these data were collected immediately following the announcement in the UK of an efficacious vaccination produced by Oxford-AstroZeneca.17 That we were able to replicate know predictors of COVID-19 vaccine hesitancy – being female,35-37 younger,35,37 non-white ethnicity,37,38 and having a lower morbid load39 gives us some confidence in our novel results for cognitive function.** Although education correlates positively with cognition in the present cohort and other studies,40 ours is not the first to suggest that better educated people report being less likely to take up a COVID-19 vaccination (table 1).For other inoculations, including those developed during past pandemics, results are inconsistent across studies **with both ‘U’-shaped[ref] and inverse relationships reported41 with hesitancy.**

We have recently shown that, of a range of baseline psychosocial factors which included socioeconomic status, education, personality type, and mental health, cognitive function was the most strongly associated with severe COVID-19, whereby a doubling of the risk of hospitalisation was apparent in the lowest scoring group.42 This supports other data that individuals with higher cognitive function experience a lower risk of death from other respiratory diseases, including influenza and pneumonia.43 The notion that people with lower cognitive ability may have greater rates of severe COVID-1942,44 and are simultaneously less likely to take up the offer of vaccination, may represent a dual burden, as may also be the case for people from ethnic minority groups and the socioeconomically disadvantaged.

***Plausible explanations***

Various explanations may be germane to the cognition–vaccine intention link, including the observation that people with higher cognitive ability are better equipped to obtain, process, and respond to disease prevention advice, as well as having healthier behaviours which include a lower prevalence of cigarette smoking,8 itself a risk factor for pneumonia.45 There has been a deluge of health advice in the current pandemic during an era when news outlets and social media platforms have never been more ubiquitous. Preventative information has ranged from the simple and practical to the complex, contradictory, false, and fraudulent. In order to diminish their risk of the infection, the population has to acquire, synthesise, and deploy this information but the ability to do so seems to vary by levels of health literacy46 just as it may for its close correlate, cognitive function.

***Study strengths and weaknesses***

**While the present study has its strengths, including its size, national representativeness, and timing relative to the announcement of a successfully-tested vaccine for COVID-19, there are also some weaknesses. We used vaccine intentionality as an indicator of 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% who expressed a commitment to being inoculated subsequently reported have received a vaccination two months later.47 Elsewhere, in a US adult population at high risk of seasonal influenza, over half of those intending to be vaccinated had done so 5 months later.48**

**In conclusion, people with lower scores on standard tests of cognitive function were less willing to take up the future offer of vaccination for COVID-19. Erroneous messaging around the roll-out of the vaccine programme may have complicated decision-making.**

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

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

Wave 1 (N=50,994) Main Survey

(2009-11)

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

(Nov 2020)

*(vaccine hesitancy, psychological distress)*

40,730 participants in Wave 3

(2011-13) of Main Survey (*cognitive function*)

34,318 participants in Wave 10 of the Main Survey (*educational level, ethnicity, current and past comorbidities*)

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

Wave 1 (N=17,761) COVID Survey

(April 2020)

**Figure 2. Odds ratios (95% CI) for the relation of cognitive function with COVID-19 vaccine hesitancy in Understanding Society**

|  |
| --- |
|  |
|  |
| All cavariates are: age, sex, ethnicity, somatic comorbidity, psychological distress, shielding, and education. In both models, the p-value for trend across deciles was <0.0001 |

**Table 1. Study member characteristics according to COVID-19 vaccine hesitancy in**

**Understanding Society**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Vaccine hesitant** | | **P value** |
|  | **Yes** | **No** |  |
|  |  |  |  |
| Numbers of people\* | 1842 | 10113 |  |
|  |  |  |  |
| **Demographic factors** |  |  |  |
| Age, yr, mean (SD) | 45.0 (14.5) | 54.6(15.6) | < 0.0001 |
| Female, N (%) | 1162 (63) | 5530 (55) | < 0.0001 |
| Non-white ethnicity, N (%) | 406 (22.0) | 698 (7.0) | < 0.0001 |
|  |  |  |  |
| **Socioeconomic factors** |  |  |  |
| No university education, N (%) | 939 (51.0) | 4298 (42.5) | < 0.0001 |
|  |  |  |  |
| **Comorbidities** |  |  |  |
| Cardiometabolic disease, N (%) | 268 (15.0) | 2513 (25.2) | < 0.0001 |
| Respiratory disease, N (%) | 219 (12.3) | 1372 (13.8) | 0.144 |
| Any cancer, N (%) | 45 (2.5) | 525 (5.3) | < 0.0001 |
| Psychological distress, N (%) | 509 (27.6) | 2399 (23.7) | < 0.0001 |
| Shielding in the household, N (%) | 196 (10.6) | 1187 (11.7) | < 0.0001 |
|  |  |  |  |
| **Cognitive function** |  |  |  |
| *g* factor, mean (SD) | 96.6 (15.7) | 100.5 (14.8) | < 0.0001 |
|  |  |  |  |

\*Numbers corresponds to those with complete data on vaccine intentionality

**Table 2. Odds ratios (95% CI) for the relation of cognitive function (*g*) with COVID-19 vaccine hesitancy in Understanding Society**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Number hesitant / Total at risk** | **Age, sex, & ethnicity** | **Age, sex, ethnicity, & somatic comorbidity** | **Age, sex, ethnicity, & psychological distress** | **Age, sex, ethnicity, & shielding** | **Age, sex, ethnicity, & education** | **All covariates** |
|  |  |  |  |  |  |  |  |
| Tertile 3 (high) | 236 / 2048 | 1 (ref) | 1 (ref) | 1 (ref) | 1 (ref) | 1 (ref) | 1 (ref) |
| Tertile 2 | 352 / 2566 | 1.28 (1.07, 1.54) | 1.29 (1.08, 1.55) | 1.28 (1.07, 1.54) | 1.29 (1.08, 1.55) | 1.17 (0.98, 1.41) | 1.18 (0.99, 1.42) |
| Tertile 1 | 365 / 1794 | 1.99 (1.66, 2.40) | 2.01 (1.67, 2.43) | 1.99 (1.66, 2.40) | 2.01 (1.67, 2.42) | 1.64 (1.35, 1.99) | 1.67 (1.37, 2.03) |
| P for trend |  | p < 0.0001 | p < 0.0001 | p < 0.0001 | p < 0.0001 | p < 0.0001 | p < 0.0001 |
| Per SD decrease | 953/7361 | 1.76 (1.62, 1.90) | 1.77 (1.63, 1.91) | 1.76 (1.62, 1.90) | 1.78 (1.64, 1.91) | 1.52 (1.37, 1.67) | 1.54 (1.40, 1.69) |

Thresholds for categories of g: Tertile 1 (>=108.3); tertile 2 (108.2- 93.3); and tertile 1 (>=93.2). A standard deviation (SD) in general cognitive function was 15 units.