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**Pre-pandemic Cognitive Function and COVID-19 Vaccine Intentionality: Evidence from the Understanding Society and Generation Scotland Cohort Studies**

G. David Batty (E. [david.batty@ucl.ac.uk](mailto:david.batty@ucl.ac.uk) / ORCID: 0000-0003-1822-5753)

*Department of Epidemiology and Public Health, University College London, UK*

Drew Altschuld ([drew.altschul@ed.ac.uk](mailto:drew.altschul@ed.ac.uk) / 0000-0001-7053-4209)

*Department of Psychology, University of Edinburgh, UK*

Chloe Fawns-Ritchie ([c.fawns-ritchie@ed.ac.uk](mailto:c.fawns-ritchie@ed.ac.uk) / XXXXXX)

*Department of Psychology, University of Edinburgh, UK*

Catharine R. Gale ([crg@mrc.soton.ac.uk](mailto:crg@mrc.soton.ac.uk) / 0000-0002-3361-8638)

*Medical Research Council Lifecourse Epidemiology Unit, University of Southampton, UK*

*Lothian Birth Cohorts, Department of Psychology, University of Edinburgh, UK*

Ian J. Deary ([i.deary@ed.ac.uk](mailto:i.deary@ed.ac.uk) / 0000-0002-1733-263X)

*Lothian Birth Cohorts, Department of Psychology, University of Edinburgh, UK*

Correspondence: David Batty, Department of Epidemiology & Public Health, University College London, 1-19 Torrington Place, London, UK, WC1E 6BT. E. david.batty@ucl.ac.uk

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**Abstract**

*Importance*: While several predictors of COVID-19 vaccine intentionality have been examined – ethnicity, education gender, age – the role of cognitive function, particularly post-announcement of the successful trial results of the Oxford-AstraZeneca vaccination, is unknown.

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

*Design, Setting, and Participants*: We used individual-level baseline data the Understanding Society COVID Survey. Aged XXXX at study induction, cohort members responded XXXXX.

*Main Outcomes and Measures*: Self-reported intention to take up a COVID-19 vaccination. To summarise our results, we computed odds ratios with accompany 95% confidence intervals adjusted for a series of covariates. XXXXXXX.

*Results*: XXXXXXX.

*Conclusions and Relevance*: XXXXXX

**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.[ref] Assessed using standard tests, there is wide inter-person variation in how rapidly and precisely people carry out these mental tasks.[ref]

Health protection and health care can be regarded as a complex set of tasks that require assimilation of knowledge, decision-making, and planning. It has posited that people with higher cognitive function manage preventative behaviours and treatment more effectively,[ref] 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,[ref] choose dietary supplements,[ 12949843] be physically activity,[ref] and have superior oral hygiene.[ref] People who score better on cognitive tests are also less likely to smoke cigarettes,[ref] and drink harmful levels of alcohol.[ref] Cessation rates are also elevated in smokers with higher mental ability.[ref] Further, in individuals with a greater risk of a first cardiovascular disease event,[ref] and in those at increased risk of re-infarction,[ref] improved compliance with known efficacious drug therapies – aspirin and statins, respectively – is associated with a higher cognition score.

These observations provide circumstantial evidence for a link between cognitive ability and another health-protecting behaviour, vaccine uptake. In the only empirical investigation of vaccination uptake and cognition of which we are aware, investigators administered a measure of analytical reasoning to two small samples from the UK (XXX) and Ireland (XXXX).[ref] 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..[ref] These data were collected around April 2020 when no vaccine was available. Around 8 months later, the development of the first efficacious vaccine for COVID-19 was announced (https://www.bbc.co.uk/news/health-55040635), progress that may have impacted upon individual intentionality.[ref] 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. Based a clustered-stratified probability sample of UK households, study members have been interviewed annually since 2009 [ref 11 BBI] (hereafter, the ‘main survey’). Households who had participated in at least one of the last two 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’). 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 questions on vaccine intention were first administered.12 Sampling study members who had taken part in a minimum of one of the preceding five COVID-19 surveys, and had neither died, emigrated, or declined to continue participation in the interim, wave 6 comprised a total of 12,035 individuals who responded to the 19,294 invitations issued (response proportion, 62%).13 Data collection in wave 6 (24th November) commenced the day immediately following the announcement of the Oxford University/AstraZeneca vaccine[https://www.bbc.co.uk/news/health-55040635] and continued until 1st December 2020.

*Assessment of cognitive function*

In the third wave of data collection in the main survey (January 2011-April 2013), six cognitive function measures were administered to represent an array of cognitive skills using tests that have been employed across multiple large scale population-based studies.[refs] *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. They were then asked to recall the words immediately after the reading and, again, at a later stage in the interview without the words being repeated. 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. In a subtraction test, and a component of screening instruments for *cognitive impairment* including the Mini Mental State Examination (Crum, Anthony, Bassett, & Folstein, 1993) and the Cambridge Cognitive Examination (CAMCOG), 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 out 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 who did not appear to understand after two examples 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 described 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*

Covariates were self-reported and included age, sex, ethnicity (taken from wave 10, non-white *n* = 1,126, 9.4%), education level (wave 10, higher degree *n* = 4,873, 40.5%), if anyone in the participant’s household was shielding (indicated between April and October 2020), physical comorbidity (derived at wave 10 and drawing on data reported during previous waves), and psychological distress (from November & December 2020) were derived from previous waves of the main study. Cardiometabolic disease was denoted by self-report of physician diagnosis of congestive heart failure, coronary heart disease, angina, heart attack or infarction, stroke, diabetes, and/or hypertension; respiratory disease comprised bronchitis, emphysema, COPD, and/or asthma. Study members were administered the 12-item version of the General Health Questionnaire (GHQ-12).18 Validated against standardised psychiatric interviews,19;20 this is a widely used measure of psychological distress in population studies. It comprises items capturing symptoms of depression and anxiety over the prior 4 week period with responses based on a 4-point scale which signals the presence of a symptom (not at all = 0, same as usual = 0, more than usual = 1, much more than usual = 1). Consistent with published analyses,8;10;21;22 we used a score of >= 3 to denote psychological distress.

*Assessment of vaccine intentionality*

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 cognition and vaccine hesitancy, we used logistic regression to compute odds ratios with accompanying 95% confidence intervals. General cognitive function was computed using principal components analysis: the first unrotated component of the six cognitive tests from wave 3 was used as a single measure of cognitive function, conventionally termed ‘g’. In these analyses we calculated effect estimates for tertiles of ‘g’ scores alongside odds ratios for a unit (standard deviation, 15) 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.

**Results**

In the sample of 11740 individuals (6702 women), 1842 individuals (1162 women) (17.2%) 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 at wave 3 (p-value for difference: <0.0001). We investigated these differentials in table 2 where we present 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). Simultaneous adjustment for all covariates had no additional impact on effects estimates 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 after both basic- (figure 1A) and multiple-adjustment (figure 2A).

The Kendall rank correlation between g and educational attainment was *τ* = 0.27 (p < 0.0001)

**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 of an efficacious vaccination, the Oxford-AstroZeneca XXXXX. That we were able to replicate know predictors of COVID-19 vaccine hesitancy – being female, younger, non-white ethnicity, having a higher morbid load[refs] – gives grounds for our novel results for cognitive function to be trusted.**

Although education correlates positively with cognition in the present cohort and many other studies,[refs] ours is not the first to suggest that better educated people report being less likely to take up a COVID-19 vaccination. For other inoculations, including those developed during prior pandemics, results are inconsistent across studies **with both ‘U’-shaped[ref] and inverse relationships reported.[ref]**

We have recently shown that, of a range of baseline factors which included socioeconomic status, education, 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.1 We have also shown that individuals with higher cognitive function experience a lower risk of death from other respiratory diseases, including influenza and pneumonia.[ref] Plausible explanations include XXXXX. The notion that people with lower cognitive ability may have greater rates of severe COVID-19, and are simultaneously less likely to take up the offer of vaccination, may represent a dual burden as has already been described in the context of ethnic minority groups.[ref]

***Plausible mechanisms***

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,2 itself a risk factor for pneumonia.3 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 literacy4 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 in Cantonese-speaking adults, less than 10% who expressed a commitment to being inoculated subsequently reported have received a vaccination two months later.[ref] Elsewhere, in a US adult population deemed high risk of seasonal influenza, over half of those intending to be vaccinated had done so 5 months later.[ref]**

**In conclusion, XXXXXX**

**References**

1. Batty GD, Deary IJ, Luciano M, Altschul DM, Kivimaki M, Gale CR. Psychosocial factors and hospitalisations for COVID-19: Prospective cohort study based on a community sample. *Brain Behav Immun.* 2020;89:569-578.

2. Batty GD, Deary IJ, MacIntyre S. Childhood IQ in relation to risk factors for premature mortality in middle-aged persons: the Aberdeen Children of the 1950s study. *J Epidemiol Community Health.* 2007;61(3):241-247.

3. Baik I, Curhan GC, Rimm EB, Bendich A, Willett WC, Fawzi WW. A prospective study of age and lifestyle factors in relation to community-acquired pneumonia in US men and women. *Arch Intern Med.* 2000;160(20):3082-3088.

4. Wolf MS, Serper M, Opsasnick L, et al. Awareness, Attitudes, and Actions Related to COVID-19 Among Adults With Chronic Conditions at the Onset of the U.S. Outbreak: A Cross-sectional Survey. *Annals of internal medicine.* 2020.

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

Wave 1 (N=XXXX) Main Survey

(2009-11)

Wave 6 (N=XXXX) of COVID Survey

(Nov 2020)

*Vaccine hesitancy assessment*

Wave 1 (N=XXXX) COVID Survey

(April 2020)

Wave 3 (N=XXXX) Main Survey

(2011-13)

*Cognitive function assessment*

Wave 9 (N=XXXX) Main Survey

(2017-19)

Wave 8 (N=XXXX) Main Survey

(2016-18)

**Figure 2. Odds ratios (95% CI) for the relation of cognitive function with COVID-19 vaccine hesitancy (panel A – ORs are age-, sex- and ethnicity-adjusted, Panel B – ORs are multiply-adjusted as per table 2)**

|  |
| --- |
|  |
|  |
| P-value for trend across deciles after age-, sex- and ethncity-adjustment (p<0.0001) and after adjustment for all covariates (p<0.0001). |

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

**Understanding Society**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Understanding Society** | | |
|  | **Vaccine hesitant** | | **P value** |
|
|  | **Yes** | **No** |  |
| **(n=1842\*)** | **(n=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 (%) | 613 (34.3) | 4233 (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 of study member corresponds to those with data on XXXXX

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

*Note.* Tertile 1 corresponds to scores of 108.3 and above, tertile 2 contains scores between 108.2 and 93.3, and tertile 1 contains scores of 93.2 and under.