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**Psychosocial factors and hospitalisations for Covid-19: Prospective cohort study of the general population**

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*Pre-print deposition*: medRxiv (XXXXXX)

**Abstract**

*Objective:* To.

*Design:* Prospective cohort study

*Setting:* England.

*Participants:* The analytical sample in the main analyses in UK Biobank comprised 499,701 people (response rate 5.5%) XXXX linked to the same nationwide XXX registries

*Main outcome measure:* XXXXX

*Results:* XXXXX.

*Conclusion:* XXXXX.

*Key words: XXXXXXX*

**Box**

*What is already known on this subject*

* XXXX

*What this study adds*

* XXXXX

**Introduction**

With outbreaks described across XXX countries, the novel coronavirus referred to as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared pandemic by the World Health Organization on XXXX. As of XXX 2020, in the absence of widespread testing, there has been global notification of XXXX cases of coronavirus disease 2019 (COVID-19) – the disease caused by SARS-CoV-2 – with XXXX deaths reported.

The influenza pandemics of 1918 (Spanish) and 2009 (Swine) were notable for marked inequalities in their occurrence, whereby more socioeconomically disadvantaged countries, cities, neighbourhoods, and individuals experienced the highest mortality rates from the infection.[citations in mamelund] Outside the eras of these pandemics, other respiratory diseases such as tuberculosis,[] pneumonia,[] and the common cold,[] a species of coronavirus, also appear to be similarly socioeconomically patterned. The mechanisms that underlie these socioeconomic gradients may include overcrowded living and working conditions, comorbidity, and a lack of understanding of prevention advice such as hand washing, physical distancing, and vaccination programmes among socially disadvantaged individuals. Indirect pathways of effect have also been advanced, such as the higher prevalence of unfavourable health behaviours – cigarette smoking, alcohol intake, and suboptimal nutrition – in lower social groups which in themselves have been linked to selected lower respiratory tract infections.[]

While correlated with socioeconomic status, mental health and cognitive function may have independent utility in understanding the burden of infectious disease. Although described as a potential consequence of Covid-19 based on unfavourable mental health outcomes in survivors of the (mars/sers) pandemics,[ref] poor psychological health may influence the risk of contracting respiratory infection by impairing innate and adaptive immunity.[in Hamer] In cohort studies generated using linked electronic registries people with a depressive episode serious enough to warrant treatment in a psychiatric care facility subsequently experienced elevated rates of all respiratory infections combined.[andersen] Alternatively, when the full range of psychological distress (depression and anxiety) symptoms are self-reported in the general population, an elevated risk of death from pneumonia is apparent even at moderate distress levels and despite adjustment for confounding factors which include poverty.[hamer]

­­While mental health problems may also influence the risk of acquiring a respiratory infection by negatively impacting cognitive function, so compromising the ability to adequately recognise a deterioration in health, actively seek medical attention, and communicate effectively with health care professionals,[in semiog] cognition in itself may offer predictive capacity for disease risk. Although traditionally studied in the context of non-communicable disease,[ref] higher levels of cognitive ability in both childhood[ref] and adulthood,[ref]– a psychological trait that involves the storage, selection, manipulation, and organisation of information – appear to be related lower rates of mortality from infectious disease. One explanation for this gradient is that people with better performance on standard tests of cognitive function are more likely to take-up influenza and pneumococcal inoculation [in Gale]. XXXothersXXX

With this evidence base giving us reason to anticipated links between these psychosocial characteristics and hospitalisation for incident Covid-19 infection, for the first time to our knowledge, we explored these relationships using new data from UK Biobank, a prospective cohort study.

**Methods**

We used data from both UK Biobank,1 a prospective cohort study, the sampling and procedures of which have been well described.2,3 In brief, baseline data collection took place between 2006 and 2010 in twenty-two research assessment centres across t­­­he UK, resulting in a sample of 502,655 people aged 40 to 69 years (response rate 5.5%).1 In UK Biobank, ethical approval was received from the North-West Multi-centre Research Ethics Committee, and the research was carried out in accordance with the Declaration of Helsinki of the World Medical Association, and participants gave informed consent. No specific ethical approval was required for the present data analyses.

*Assessment of socioeconomic factors*

We used four indicators of socioeconomic status. Total annual household income before tax was self-reported using a 5-point scale (<18,000, -30,999, -51,999, -100,000, >100,000 GBP). We derived a three category educational qualification variable (XXXXX). Age leaving education? Using the XXX index, we grouped job types into manual and non-manual groups. Lastly, we used the Townsend deprivation index as our indicator of neighbourhood socioeconomic status.[ref] Based on four characteristics (home and car ownership, employment, and number of households resident), participants’ postcodes at recruitment were matched to output areas from the preceding national census. A continuously scored variable, higher values denote greater deprivation.

*Assessment of psychological factors*

We captured five psychological factors. Study members were asked if they had ever been under the care of a psychiatrist for any mental health problem; in the UK, referral to a mental health professional would ordinarily have been made by a general practitioner. Symptoms of psychological distress was measured using the 4-item version of the Patient Health Questionnaire (PHQ-4).6 Items are rated on a 4-point Likert scale from 0 (“not at all”) to 3 (“nearly every day”) such that total scores range from 0 to 12 (higher scores denote greater distress). Scores on the PHQ-4 show good agreement with longer scales, and show known correlations with demographic risk factors for depression and anxiety.7 Neuroticism was measured with the 12-item Eysenck Personality Questionnaire-Revised Short Form;8 higher scores reflect XXXX.

Two tests of cognitive functioning were administered. Verbal and numerical reasoning was measured using a computerized 13-item multiple-choice test with a two-minute time limit. The score was the number of correct answers. This test was introduced after the beginning of the baseline assessment period so data are available for a subset of study members (N=XXXXX). Reaction time was measured using a computerized Go/No-Go “Snap” game. Participants were presented with electronic images of two cards. If symbols on the cards were identical, participants were instructed to immediately push the button-box using their dominant hand. The first five pairs were used as a practice with the remaining seven pairs, containing four identical cards, forming the assessment. Reaction time score was the mean time (milliseconds) to press the button when each of these four pairs was presented. Choice reaction time correlates strongly with single mental tests that involve complex reasoning and knowledge and which are strongly g-loaded.[gale]

*Assessment of confounding factors*

Ethnicity was self-reported and categorised as white, Asian, Black, Chinese, Mixed, or other ethnic group. A social isolation scale contained enquiries concerning number of people in household, visiting friends/family, and social activities. One point was allocated for living alone, one for friends/family visits less than once/month, and one for no weekly participation in social activities. Social isolation was denoted by a score of 3. Self-reported physician diagnosis was collected for vascular or heart problems, hypertension, diabetes, chronic lung disease, asthma, and cancer. Cigarette smoking, physical activity, and alcohol consumption was measured using standard enquiries. Height and weight were measured directly during a medical examination. Forced expiratory volume in one second, a measure of pulmonary function, was quantified using spirometry with the best of three technically satisfactory exhalations used in our analyses. Handgrip strength was measured using a hydraulic hand dynamometer (Jamar J00105) with participant seated and maximally squeezing the handle of the dynamometer for 3 seconds. An average of the right and left hand was used. Seated systolic and diastolic blood pressure measurements were made twice using the Omron HEM-7015IT digital blood pressure monitor (Omron Healthcare)20 or, exceptionally, a manual sphygmomanometer (6652 people). An average of the two readings was used herein. We defined hypertension according to existing guidelines as systolic/diastolic blood pressure ≥140/90 mmHg and/or self-reported use of antihypertensive medication.4 Non-fasting venous blood was drawn with assaying conducted at dedicated central laboratory for C-reactive protein, glycated haemoglobin, and high-density lipoprotein cholesterol.5,6 .6,7

*Ascertainment of hospitalisation for Covid-19*

Provided by Public Health England, data on Covid-19 status covered the period 16 March, after which testing was largely restricted to those with symptoms in hospital, to XXX 2020.[ref] These data can therefore be regarded as a proxy for hospitalisations for severe cases of the disease for England only; study members from Scotland and Wales were therefore omitted from our analytical sample. In the present data download from XXXX April 2020, XXXX (X%) of the Biobank study members were positive for Covid-19, and XXX of these individuals were in-patients when the biological sample was taken. A total of XXX swabs were taken from combined nose/throat swabs and XXXX were samples from the lower respiratory tract. (table XX)

In preliminary analyses, we used three different Covid-19 case definitions based on these data: all apparent cases of the disease (N=XXXX); cases based on samples from in-patients only (N=XXXX); and cases based on two or more samples from in-patients (N=XXXX) – the notion being that those people tested on more frequently were more likely to be in hospital at the time of testing. Evidence from prognostic studies of hospitalised patients in the USA[ref] and China[ref] suggest that men, older individuals, ethnic minorities, and those with existing disease experience greater rates of progression to intensive care and death.[ref] Preliminary analyses of the present data on incidence of severe disease revealed the same associations irrespective of case definition (supplemental table). On the basis of this apparent predictive validity, we therefore proceeded with our main analyses in which we used all Covid-19 cases as our outcome of interest.

*Statistical analyses*

We omitted from our analyses men and women who had died before XXXXdateXXX as they could not contribute to the risk set for Covid-19. Odds ratios and accompanying 95% confidence intervals were computed using logistic regression models to summarise the relationship between psychosocial factors and Covid-19 hospitalisations. We initially adjusted odds ratios for age, sex, and ethnicity, then covariates grouped into health behaviours (cigarette smoking, alcohol intake, and physical activity), biomarkers (XXXXX), and comorbidity (XXXX). Effect estimates for socioeconomic factors and psychological factors were mutually adjusted. In preliminary analyses, controlling for biomarkers which were only available on a subgroup of the study sample (XXX cases in XXXXXX people) had no impact on the association of psychosocial factors with Covid-19 (supplemental table X); these covariates therefore did not feature in the main analyses. Analyses were conducted using Stata version 15.

**Results**

There were XXXX hospitalisations for Covid-19 between XXX and YYY in XXXXXX individuals (XXXX women). Of the 28 baseline characteristics featured in table 1, only 5 – extant cancer, current smoking, grip strength, neuroticism, and social isolation – did not reveal relationships with Covid-19 in unadjusted analyses at conventional levels of statistical significance. These covariates were therefore excluded from subsequent multiple regression analyses.

Table 2 illustrates the associations between psychological traits and the risk of Covid-19. People with higher levels of psychological distress had an elevated risk of covid-19 hospitalisation, and there was evidence of a gradient across the distress scale (P for trend <= 0.007). Adjustment for confounding factors which including socioeconomic status did not appreciably affect these conclusions although attenuation was marked after taking into account lifestyle factors such as alcohol intake and physical activity. Study members who reported contact with a psychiatrist for any mental health problem experienced around a 50% increase in the likelihood of being hospitalised for Covid-19, an effect that was comparable to that seen in the high distress group. The association for psychiatric consultation was robust to a range of statistical adjustments. Neuroticism was essentially unrelated to the prevalence of Covid-19 in any of our analyses. Both indices of cognitive function – verbal numerical reasoning and reaction time – were associated with the infection whereby the most disadvantaged participants for each characteristic had the lowest concentration of Covid-19 hospital cases. The magnitude of this relationships was, however, weaker for reaction time and controlling for lifestyle factors eliminated its effect. Reasoning was more robust to such adjustments and in most analyses people with the lowest reasoning scores experienced around twice the burden of covid-19.

In table 3 we depict the association between various socio-economic characteristics and risk of Covid-19. After adjustment for age and sex, those study members who were most disadvantaged educationally, financially, and geographically experienced around a doubling in the risk of Covid-19. Effects were apparent across the full socioeconomic continuum (p for trend XXXX). While controlling for ethnicity has little impact on these gradients, partial attenuation was apparent after taking into account comorbidity and health behaviours. Adjusting for psychological characteristics, particularly cognitive function (XXXneed to show thisXXXX), had the most explanatory power, whereby the relation of both lower levels of educational and income with Covid-19 were largely lost. The effect of neighbourhood deprivation was also diminished but a gradient remained such that people from poorer areas experienced elevated risk.

We also carried out some sensitivity analyses. With the reasoning test having been introduced part way through baseline data collection, analyses featuring this variable were based on a subgroup of study members. To ensure direct comparison across statistical models, we therefore recomputed our analyses based on a non-missing dataset. We found that XXXXX

**Discussion**

*Principal findings*

Our main findings were that, in fully adjusted analyses, the two indicators of poor mental health and lower cognition function were related to an increased risk of hospitalisation for Covid-19. For psychological distress and the reasoning test, there was also evidence of graded effects across the exposure categories. Of the indicators of socioeconomic status, education and neighbourhood deprivation revealed consistent relationships with Covid-19 in most analyses but were eliminated after multiple adjustment for confounding factors with reasoning having the greatest attenuating effect. Thus, in the sample comprising study members who have data for both reasoning and psychological distress, adding psychological distress to a model of education as a predictor changes its effect only slightly: the odds ratio in those with no qualifications changes from 1.80 (CIs) to 1.75 (CIs), whereas if one adds reasoning, the OR in those with no qualifications changes from 1.80 (CIs) to 1.27 (CIs).

*Results from other studies*

Most of the evidence for risk factors for Covid-19 has been gleaned from prognostic studies in which the characteristics of patients upon hospitalisation are related to progression, where applicable, to intensive care and death.[ref, Jama] In another approach which provide some insights into the aetiology of the disease, the characteristics of patients on admission were compared to a general population external comparison group.[ref] Taken together, these approaches have suggested that ethnic minorities, men, the elderly, and people with co-morbidities experience a higher risk of hospitalisations and poorer prognosis.[] In the only study of which we are aware to have explored any of the present psychosocial factors, Manhattan, the most advantaged borough of New York City based on the prevalence of university degrees and XXX, had the lowest rates of hospitalisations for Covid-19 relative to the four remaining boroughs.[jama] By contrast, the Bronx, the least favourable socioeconomically, had the highest disease rates. We are unaware of any studies exploring the relation of cognitive function and mental health with hospitalisation or any other proxy for Covid-19.

*Mechanisms of effect*

Unhealthy lifestyle, lack of self-care, physical circumstances including poor housing and homelessness, and health-risk activities are common in people with mental illness, and these are associated with adverse health outcomes. .[in semiog]

Selected mechanisms may link these psychosocial variables. Others specific: Individuals who experience higher levels of psychological distress may have diminished learned resistance to infection due to fewer social interactions.

While higher seroprevalence of such infections may in part reflect increased exposure to pathogens among individuals living in disadvantaged environments due to overcrowded living or work conditions and/ or lack of proper sanitation, there is also evidence that those of lower socioeconomic status experience a higher force of infection (i.e. instantaneous per capita rate of acquisition) upon exposure (Colugnati et al., 2007 ).

In 2007, Nazmi and co- workers conducted a systematic review of studies examining the

association between various measures of SES (i.e. education level, occupational class, income

level, employment status) and levels of circulating CRP across numerous population- based

studies, finding that some, but not all, studies identified statistically significant inverse relation

ships between SES and CRP levels (Nazmi & Victora, 2007 ).

Viral infections and CRP: Increased blood CRP levels have been found in patients with avian flu H7N9 as compared to H1N1 (more common) influenza strains [50] and a review of ten studies of H1N1 influenza found significantly elevated CRP in more severe presentations. [51]

In 2020, clinics in Wuhan, China have reported that elevated CRP is an observed clinical feature of coronavirus COVID-19 infection.[52] [53][54]

*Study limitations*

Case definition.

Similar results to those for pneumonia death in UKBB? Pneumonia is a common complication of COVID-19. If we are able to show IQ, mental health, and SES are also linked to death from pneumonia (already shown for IQ in relation to deaths from pneumonia and influenza combined: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6362031/>), albeit in a pre-Covid19 era, this might elevate confidence in our novel results for covid-19.

Generalisability.

*Policy significance*

Identifying the characteristics of people with an elevated risk of Covid-19 is also important because vaccines, assuming they arrive, may be deployed in specific high-risk groups. Immunisation guidelines in the UK and the USA designed to protect groups most vulnerable to pneumococcal disease, for instance, as adults aged 65 and over, taken individuals people with selected medical conditions.[in semiog] In future prioritisation for vaccinations for Covid-19, provided the findings of other studies are supportive, it may be that people with mental health problems are considered higher risk. Education as a proxy for low IQ?

*Conclusions*

XXXXX

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**Table 1. Psychosocial factors and covariates at baseline according to hospitalisations for Covid-19**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** | **Covid-19 hospitalisation** | | **P value** | **Unadjusted OR**  **(95% CI)a** |
|  | **Yes**  **(n=669)** | **No**  **(n=430,382)** |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
| *Demographic factors* |  |  |  |  |
| Age (yrs), mean (SD) | 57.5 (8.67) | 56.4 (8.10) | 0.0004 | 1.15 (1.06, 1.24) |
| Female, no. (%) | 291 (43.5) | 236,434 (54.9) | <0.0001 | 0.63 (0.54, 0.74) |
| Non-white ethnicity | 98 (14.8) | 25,200 (5.89) | <0.0001 | 2.77 (2.24, 3.44) |
| Socially isolated, no (%) | 64 (9.57) | 38,379 (8.92) | 0.556 | 1.08 (0.83, 1.40) |
|  |  |  |  |  |
| *Comorbidities* |  |  |  |  |
| Vascular or heart disease, no. (%) | 286 (43.33) | 124,403 (29.0) | <0.0001 | 1.89 (1.60, 2.18) |
| Hypertension, no (%) (does this include measured BP?) | 417 (65.0) | 238,260 (56.4) | <0.0001 | 1.44 (1.22, 1.69) |
| Diabetes, no. (%) | 66 (9.97) | 21,340 (4.98) | <0.0001 | 2.11 (1.64, 2.72) |
| Chronic bronchitis or emphysema, no. (%) | 24 (3.59) | 6,315 (1.47) | <0.0001 | 2.50 (1.66, 3.76) |
| Asthma, no. (%) | 99 (14.8) | 49,627 (11.5) | 0.008 | 1.33 (1.08, 1.65) |
| Cancer, no. (%) | 58 (8.84) | 31,068 (7.26) | 0.119 | 1.24 (0.95, 1.62) |
|  |  |  |  |  |
| *Lifestyle factors* |  |  |  |  |
| Current smoker, no (%) (was there an effect for former smokers) | 71 (10.8) | 42,667 (9.97) | 0.501 | 1.09 (0.89, 1.39) |
| No physical activity, no (%) | 95 (14.7) | 26,118 (6.16) | <0.0001 | 2.63 (2.12, 3.27) |
| Drinks alcohol daily/almost daily, no (%) | 113 (17.0) | 87,789 (20.5) | 0.03 | 0.80 (0.64, 0.97) |
| Body mass index, mean (SD) | 29.2 (5.50) | 27.4 (4.77) | <0.0001 | 1.36 (1.30, 1.45) |
|  |  |  |  |  |
| *Biomarkers* |  |  |  |  |
| Lung function, mean (SD) | 2.68 (0.81) | 2.82 (0.80) | <0.0001 | 0.83 (0.76, 0.90) |
| Hand grip strength, mean (SD) | 32.7 (11.2) | 32.5 (11.3) | 0.633 | 1.02 (0.94, 1.10) |
| C-reactive protein, median (IQR) | 1.67 (0.86-3.06) | 1.24 (0.63-2.44) | 0.0001 | 1.34 (1.23, 1.46) |
| High-density lipoprotein, median (IQR) | 1.33 (1.12-1.57) | 1.43 (1.20-1.71) | 0.0007 | 0.71 (0.63, 0.79) |
| HbA1C, median (IQR) | 35.8 (33.4-38.5) | 35.0 (32.6-37.4) | 0.0001 | 1.33 (1.22, 1.45) |
|  |  |  |  |  |
| *Psychological factors* |  |  |  |  |
| Psychological distress score ≥3, no (%) | 172 (30.1) | 91,033 (23.7) | <0.0001 | 1.39 (1.16, 1.66) |
| Psychiatric consultation, no (%) | 110 (16.7) | 48,629 (11.4) | <0.0001 | 1.56 (1.27, 1.91) |
| Neuroticism, mean (SD) | 4.39 (3.39) | 4.27 (3.28) | 0.373 | 1.01 (0.96, 1.12) |
| Reasoning, mean (SD) | 5.24 (2.10) | 6.03 (2.16) | <0.0001 | 1.47 (1.30, 1.56) |
| Reaction time, mean (SD) | 580.1 (138.5) | 558.8 (117.8) | <0.0001 | 1.17 (1.09, 1.24) |
|  |  |  |  |  |
| *Socioeconomic factors* |  |  |  |  |
| No university education | 283,872 (67.4) | 468 (72.9) | 0.003 | 1.30 (1.09, 1.55) |
| Annual household income<£18,000 | 81,033 (22.3) | 174 (32.3) | <0.0001 | 1.66 (1.39, 1.99) |
| Neighbourhood deprivation score | -1.32 (3.06) | 0.05 (3.56) | <0.0001 | 1.47 (1.38, 1.58) |
| Manual social class | 106 (24.6) | 58,809 (19.1) | 0.004 | 1.38 (1.11, 1.72) |
| Early life SES (sorry to go back to this; there is a literature on early SES and coronaviruses) | 106 (24.6) | 58,809 (19.1) | 0.004 | 1.38 (1.11, 1.72) |
|  |  |  |  |  |

aOdds ratios are expressed per category, or per SD increase for continuous variables with the exception of reasoning which is expressed per SD decrease.

**Table 2. Odds ratios (95% CI) for the relation of psychological factors with Covid-19 hospitalisation**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Case no./Riskno.1** | **Adjustments** | | | | | |
|  |  | **None**  **(recompute for age+sex?)** | **Age, sex & ethnicity** | **Age, sex, ethnicity & comorbidity2** | **Age, sex, ethnicity & lifestyle factors3** | **Age, sex, ethnicity & socioeconomic factors4 (result minus education?)** | **All covariates** |
| **Psychological distress** |  | (n=384909) | (n=383655) | (n=377290) | (n=376562) | (n=329180) | N=324050 |
| 1 (low) | 185/153504 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref.) | 1.0 (ref.) | 1.0 (ref) |
| 2 | 215/140200 | 1.27 (1.05, 1.55) | 1.39 (1.14, 1.69) | 1.29 (1.05, 1.58) | 1.23 (1.01, 1.51) | 1.32 (1.06, 1.64) | 1.21 |
| 3 | 172/91205 | 1.57 (1.27, 1.93) | 1.69 (1.37, 2.09) | 1.52 (1.22, 1.89) | 1.34 (1.08, 1.68) | 1.47 (1.16, 1.87) | 1.25 |
| P for trend |  | <0.0001 | <0.0001 | 0.004 | 0.007 | 0.004 | 0.066 |
| Per SD increase |  | 1.20 (1.12, 1.28) | 1.21 (1.13, 1.30) | 1.17 (1.09, 1.26) | 1.12 (1.04, 1.21) | 1.17 (1.06, 1.30) | 1.11 (1.02, 1.20) |
|  |  |  |  |  |  |  |  |
| **Psychiatric consultation** |  | n=427819 | n=426823 | n=418218 | n=417481 | n=359947 | N=353458 |
| No | 559/379080 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |
| Yes | 110/487739 | 1.56 (1.27, 1.91) | 1.46 (1.17, 1.79) | 1.55 (1.26, 1.92) | 1.44 (1.16, 1.78) | 1.50 (1.19, 1.89) | 1.37 (1.07, 1.73) |
|  |  |  |  |  |  |  |  |
| **Neuroticism** |  | N=425707 | N=424212 | N=416378 | N=415622 | N=358754 | N=352401 |
| 1 (low) | 167/106910 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |
| 2 | 252/174705 | 0.92 (0.76, 1.12) | 1.01 (0.83, 1.23) | 0.96 (0.78, 1.17) | 0.98 (0.80, 1.20) | 0.99 (0.80, 1.23) | 0..98 (0.78, 1.22) |
| 3 | 239/144092 | 1.06 (0.87, 1.29) | 1.23 (1.00, 1.50) | 1.09 (0.89, 1.38) | 1.09 (0.89, 1.34) | 1.10 (0.87, 1.37) | 1.01 (0.80, 1.28) |
| P for trend |  | 0.458 | 0.034 | 0.368 | 0.352 | 0.391 | 0.874 |
| Per SD increase |  | 1.03 (0.96, 1.12) | 1.09 (1.00, 1.18) | 1.05 (0.97, 1.13) | 1.04 (0.96, 1.12) | 1.04 (0.95, 1.13) | 1.01 (0.92, 1.10) |
|  |  |  |  |  |  |  |  |
| **Verbal numerical reasoning** |  | n=175267 | n=174581 | n=172530 | n=415777 | N=150604 | N=148063 |
| 1 (low) | 114/43988 | 2.52 (1.88, 3.37) | 2.19 (1.61, 1.97) | 2.05 (1.49, 1.81) | 1.81 (1.32, 2.49) | 2.05 (1.42, 3.00) | 1.92 (1.31, 2.82) |
| 2 | 83/58446 | 1.38 (1.01, 1.39) | 1.33 (0.97, 1.83) | 1.34 (1.97, 1.85) | 1.27 (0.92, 1.74) | 1.42 (1.01, 2.01 | 1.43 (1.01, 2.04) |
| 3 | 75/72833 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |
| P for trend |  | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.001 | 0.001 |
| Per SD decrease |  | 1.47 (1.30, 1.56) | 1.37 (1.20, 1.55) | 1.33 (1.16, 1.51) | 1.26 (1.10, 1.43) | 1.32 (1.12, 1.54) | 1.28 (1.09, 1.51) |
|  |  |  |  |  |  |  |  |
| **Reaction time** |  | n=426127 | n=424432 | n=417366 | n=415777 | n=358720 | N=352331 |
| 1 (low) | 185/140934 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |
| 2 | 199/141575 | 1.07 (0.88, 1.31) | 1.02 (0.83, 1.25) | 0.98 (0.80, 1.21) | 0.95 (0.77, 1.17) | 0.90 (0.72, 1.12) | 0.88 (0.70, 1.10) |
| 3 | 269/143368 | 1.43 (1.18, 1.72) | 1.27 (1.04, 1.54) | 1.23 (1.00, 1.50) | 1.15 (0.94, 1.41) | 1.04 (0.84, 1.30) | 1.01 (0.81, 1.10) |
| P for trend |  | <0.0001 | 0.015 | 0.037 | 0.148 | 0.646 | 0.859 |
| Per SD increase |  | 1.17 (1.09, 1.24) | 1.10 (1.03, 1.18) | 1.09 (1.02, 1.17) | 1.07 (1.00, 1.15) | 1.05 (0.96, 1.130 | 1.04 (0.96, 1.14) |
|  |  |  |  |  |  |  |  |

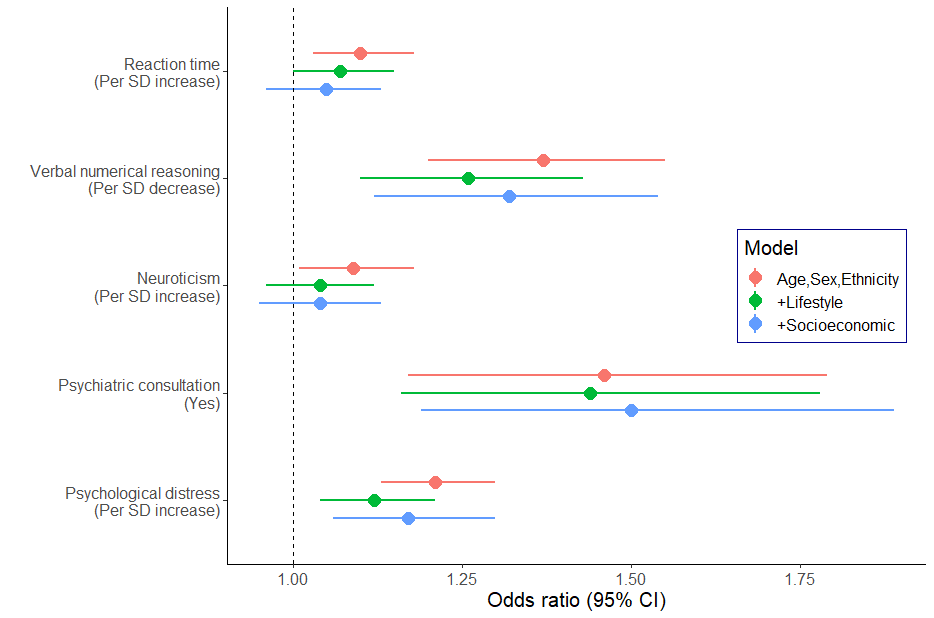
1 Numbers based on unadjusted model. 2 Comorbidity includes diagnoses of vascular or heart disease, diabetes, chronic bronchitis or emphysema, asthma, and hypertension defined according to measured blood pressure and/or use of anti-hypertensive drugs. 3Lifestyle factors included body mass index, smoking status, alcohol intake frequency & number of types of physical activity taken in last four weeks. 4Socioeconomic factors included highest educational attainment, Townsend deprivation index, & household income before tax

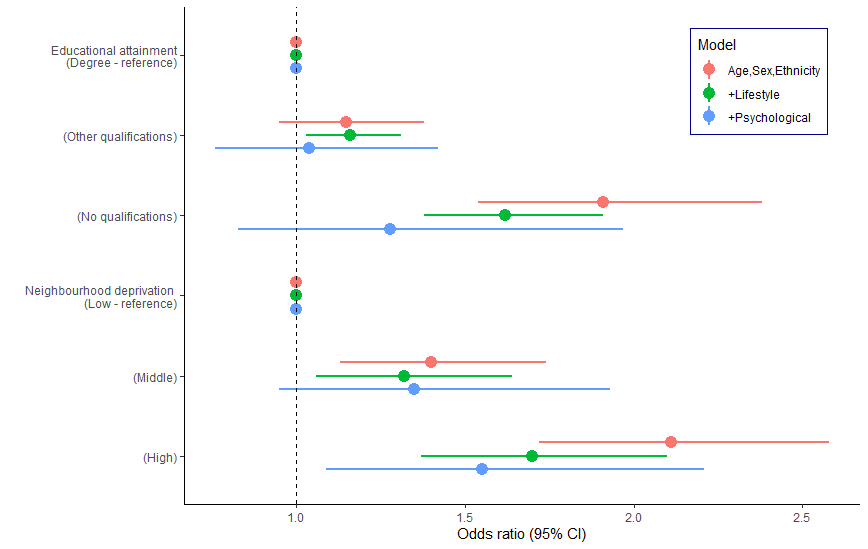
**Table 3. Odds ratios (95% CI) for the relation of socioeconomic factors with Covid-19 hospitalisation**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Case no./Risk no.1** | **Adjustments** | | | | | |
|  |  | **None(recompute for age+sex?)** | **Age, sex & ethnicity** | **Age, sex, ethnicity & comorbidity2** | **Age, sex, ethnicity & lifestyle factors3** | **Age, sex, ethnicity & psychological factors4**  **(result without IQ, particularly for education?)** | **All covariates** |
| **Educational attainment** |  | N=422057 | N=420502 | N=415945 | N=415367 | N=155244 (no. cases) | N=152739 |
| Degree | 174/137717 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |
| Other qualifications | 295/214337 | 1.09 (0.90, 1.31) | 1.15 (0.95, 1.38) | 1.11 (0.92, 1.35) | 1.16 (1.03, 1.31) | 1.04 (0.76, 1.42) | 0.90 (0.66, 1.25) |
| No qualifications | 173/70003 | 1.96 (1.59, 2.42) | 1.91 (1.54, 2.38) | 1.69 (1.35, 2.12) | 1.62 (1.38, 1.91) | 1.28 (0.83, 1.97) | 0.92 (0.58, 1.45) |
| P for trend |  | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.308 | 0.642 |
|  |  |  |  |  |  |  |  |
| **Annual household income (move ‘ref’ to opposite end of continuum)** |  | N=364219 | N=363175 | N=359853 | N=359491 | N=138207 | N=135773 |
| <£18,000 | 174/81207 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |
| £18,000-£30,999 | 128/92461 | 0.65 (0.51, 0.81) | 0.68 (0.54, 0.85) | 0.70 (0.55, 0.88) | 0.78 (0.61, 0.98) | 0.99 (0.66, 1.47) | 1.07 (0.71, 1.63) |
| £31,000-£51,999 | 126/95454 | 0.62 (0.49, 0.77) | 0.68 (0.53, 0.86) | 0.72 (0.50, 0.86) | 0.84 (0.66, 1.07) | 0.91 (0.60, 1.40) | 1.09 (0.70, 1.69) |
| £52,000-£100,000 | 87/74856 | 0.54 (0.42, 0.70) | 0.61 (0.47, 0.80) | 0.65 (0.50, 0.86) | 0.82 (0.62, 1.08) | 0.88 (0.54, 1.42) | 1.02 (0.62, 1.69) |
| >£100,000 | 24/20241 | 0.55 (0.36, 0.85) | 0.62 (0.40, 0.96) | 0.69 (0.45, 1.07) | 0.90 (0.58, 1.41) | 1.27 (0.66, 2.42) | 1.64 (0.84, 3.20) |
| P for trend |  | <0.0001 | <0.0001 | 0.003 | 0.283 | 0.958 | 0.431 |
|  |  |  |  |  |  |  |  |
| **Neighbourhood deprivation** |  | N=430538 | N=427986 | N=419593 | N=418942 | N=156919 | N=153384 |
| 1 (low) | 143/143483 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) |
| 2 | 201/143548 | 1.41 (1.13, 1.74) | 1.40 (1.13, 1.74) | 1.35 (1.08, 1.68) | 1.32 (1.06, 1.64) | 1.35 (0.95, 1.93) | 1.25 (0.87, 1.79) |
| 3 | 143/143517 | 2.28 (1.87, 2.77) | 2.11 (1.72, 2.58) | 1.91 (1.56, 2.35) | 1.70 (1.37, 2.10) | 1.55 (1.09, 2.21) | 1.19 (0.82, 1.71) |
| P for trend |  | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.015 | 0.404 |
|  |  |  |  |  |  |  |  |
| **Occupational social class?** |  |  |  |  |  |  |  |
| **Early life SES ?** |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

1 Numbers based on unadjusted model. 2 Comorbidity includes diagnoses of vascular or heart disease, diabetes, chronic bronchitis or emphysema, asthma, and hypertension defined according to measured blood pressure and/or use of anti-hypertensive medication. 3 Lifestyle factors includes body mass index, smoking status, alcohol intake frequency & number of types of physical activity taken in last four weeks. 4 Psychological factors includes psychological distress, psychiatric consultation, neuroticism, verbal and numerical reasoning, & reaction time.

**Figure options – Psychological characteristics in relation to hospitalisation for Covid-19**





**Supplemental Table 1. Preliminary analyses of covid-19 data in UK Biobank (N=488,284) – odds ratios for apparent risk factors for disease progression in covid-19 (based on clinical studies)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All Covid-19 cases**  **(N=669)** | **Covid-19 cases known to have been hospitalised (‘origin’=1) (N=574)** | **Covid-19 cases known to have been hospitalised (‘origin’=1) \*and\* with >=2 tests conducted (N=355)** |
|  |  |  |  |
| *Age* |  |  |  |
| 40-49 | Ref (1.0) | Ref (1.0) | Ref (1.0) |
| 50-59 | 0.76 (0.61, 0.94) | 0.86 (0.83,1.05) | 0.94 (0.70, 1.26) |
| 60+ | 1.16 (0.96, 1.40) | 1.23 (1.00, 1.51) | 1.29 (0.99, 1.69) |
| Per decade increase | 1.18 (1.08, 1.30) | 1.21 (1.09, 1.24) | 1.20 (1.05, 1.27) |
|  |  |  |  |
| *Sex* |  |  |  |
| Female | Ref (1.0) | Ref (1.0) | Ref (1.0) |
| Male | 1.58 (1.36, 1.84) | 1.58 (1.34, 1.86) | 1.59 (1.29, 1.96) |
|  |  |  |  |
| *Ethnicity* |  |  |  |
| White | Ref (1.0) | Ref (1.0) | Ref (1.0) |
| Non-white | 1.55 (1.26, 1.90) | 1.59 (1.27, 1.98) | 1.70 (1.30, 2.24) |
|  |  |  |  |
| *Long-standing illness* |  |  |  |
| No | Ref (1.0) |  |  |
| Yes | 2.07 (1.76, 2.40) | 2.06 (1.74, 2.43) | 2.26 (1.83, 2.79) |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

**Supplemental Table 2. Multiply-adjusted odds ratios (95% CI) for incident COVID-19 hospitalisation according to baseline psychological characteristics – based on complete data**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Psychological characteristics** | **Number of cases/**  **number at risk** | **Adjustments** | | | | | |  |
|  |  | **None** | **Age, sex & ethnicity** | **Age, sex, ethnicity & comorbidity1** | **Age, sex, ethnicity & lifestyle factors2** | **Age, sex, ethnicity & socioeconomic factors3** | **Adjusted for all covariates** | |
| Psychological distress  (n=324050) |  |  |  |  |  |  |  | |
| 1 (low) | 151/129135 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref.) | 1.0 (ref.) | 1.0 (ref) | |
| 2 | 170/119447 | 1.22 (0.98, 1.52) | 1.32 (1.06, 1.64) | 1.27 (1.01, 1.58) | 1.23 (0.99, 1.54) | 1.30 (1.04, 1.62) | 1.21 (0.97, 1.50) | |
| 3 | 134/75468 | 1.52 (1.20, 1.92) | 1.64 (1.29, 2.08) | 1.49 (1.17, 1.90) | 1.36 (1.07, 1.74) | 1.46 (1.16, 1.87) | 1.25 (0.98, 1.60) | |
| P for trend |  | <0.0001 | <0.0001 | 0.001 | 0.010 | 0.001 | 0.066 | |
| Per SD increase |  | 1.22 (1.13, 1.31) | 1.23 (1.13, 1.34) | 1.19 (1.10, 1.29) | 1.15 (1.06, 1.25) | 1.17 (1.08, 1.27) | 1.11 (1.02, 1.20) | |
|  |  |  |  |  |  |  |  | |
| Psychiatric consultation  (n=353458) |  |  |  |  |  |  |  | |
| No | 427/313778 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | |
| Yes | 84/39720 | 1.56 (1.23, 1.97) | 1.62(1.28, 2.05) | 1.53 (1.21, 1.94) | 1.45 (1.15, 1.84) | 1.48 (1.17, 1.88) | 1.37 (1.07, 1.73) | |
|  |  |  |  |  |  |  |  | |
| Neuroticism |  |  |  |  |  |  |  | |
| 1 (low) | 131/90337 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | |
| 2 | 201/144659 | 0.96 (0.77, 1.19) | 1.03 (0.82, 1.28) | 1.00 (0.85, 1.22) | 0.99 (0.80, 1.24) | 1.00 (0.80, 1.25) | 0..98 (0.78, 1.22) | |
| 3 | 179/141353 | 1.05 (0.84, 1.32) | 1.19 (0.95, 1.50) | 1.12 (0.89, 1.40) | 1.07 (0.85, 1.35) | 1.10 (0.87, 1.38) | 1.01 (0.80, 1.28) | |
| P for trend |  | 0.612 | 0.120 | 0.325 | 0.517 | 0.407 | 0.874 | |
| Per SD increase |  | 1.03 (0.96, 1.12) | 1.08 (0.99, 1.18) | 1.05 (0.96, 1.15) | 1.05 (0.92, 1.13) | 1.04 (0.95, 1.14) | 1.01 (0.92, 1.10) | |
|  |  |  |  |  |  |  |  | |
| Verbal numerical reasoning  (n=148063) |  |  |  |  |  |  |  | |
| 1 (low) | 77/33615 | 2.40 (1.72, 3.36) | 2.00 (1.41, 2.84) | 1.92 (1.35, 2.73) | 1.77 (1.24, 2.52) | 1.99 (1.35, 2.92) | 1.92 (1.31, 2.82) | |
| 2 | 71/49497 | 1. 50 (1.07, 2.11) | 1.43 (1.01, 2.02) | 1.41 (1.00, 1.98) | 1.35 (0.96, 1.91) | 1.45 (1.02, 2.06 | 1.43 (1.01, 2.04) | |
| 3 | 62/64951 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | |
| P for trend |  | <0.0001 | <0.0001 | <0.0001 | 0.002 | <0.001 | 0.001 | |
| Per SD decrease |  | 1.43 (1.24, 1.65) | 1.31 (1.13, 1.52) | 1.29 (1.11, 1.49) | 1.34 (1.07, 1.44) | 1.31 (1.11, 1.53) | 1.28 (1.09, 1.51) | |
|  |  |  |  |  |  |  |  | |
| Reaction time (n=352321) |  |  |  |  |  |  |  | |
| 1 (low) | 161/121611 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | |
| 2 | 151/117776 | 0.97 (0.78, 1.21) | 0.92 (0.74, 1.16) | 0.92 (0.73, 1.15) | 0.90 (0.71, 1.12) | 0.89 (0.71, 1.12) | 0.88 (0.70, 1.10) | |
| 3 | 193/112934 | 1.29 (1.05, 1.59) | 1.14 (0.91, 1.42) | 1.11 (0.89, 1.39) | 1.07 (0.85, 1.33) | 1.04 (0.83, 1.30) | 1.01 (0.81, 1.10) | |
| P for trend |  | 0.015 | 0.234 | 0.322 | 0.523 | 0.705 | 0.859 | |
| Per SD increase |  | 1.16 (1.07, 1.25) | 1.10 (1.01, 1.19) | 1.09 (1.00, 1.18) | 1.07 (0.98, 1.16) | 1.04 (0.83, 1.30) | 1.04 (0.96, 1.14) | |
|  |  |  |  |  |  |  |  | |

1 Comorbidity includes diagnoses of vascular or heart disease, diabetes, chronic bronchitis or emphysema, asthma, and hypertension defined according to measured blood pressure and/or use of anti-hypertensive drugs

2 Lifestyle factors included body mass index, smoking status, alcohol intake frequency & number of types of physical activity taken in last four weeks

3 Socioeconomic factors included highest educational attainment, Townsend deprivation index, & household income before tax

**Supplemental Table 3. Multiply-adjusted odds ratios (95% CI) for incident COVID-19 hospitalisation according to baseline socioeconomic characteristics – based on complete data**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Number of cases/**  **number at risk** | **Adjustments** | | | | | |  |
|  |  | **None** | **Age, sex & ethnicity** | **Age, sex, ethnicity & comorbidity1** | **Age, sex, ethnicity & lifestyle factors2** | **Age, sex, ethnicity & psychological factors3** | **Adjusted for all covariates** | |
| Educational attainment  (n=152739) |  |  |  |  |  |  |  | |
| Degree | 68/55905 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | |
| Other qualifications | 105/77597 | 1.11 (0.82, 1.51) | 1.15 (0.84, 1.56) | 1.10 (0.81, 1.50) | 0.99 (0.72, 1.35) | 1.03 (0.75 1.41) | 0.90 (0.66, 1.25) | |
| No qualifications | 38/19237 | 1.96 (1.09, 2.41) | 1.56 (1.05, 2.37) | 1.44 (1.95, 2.19) | 1.15 (0.75, 1.76) | 1.19 (0.76, 1.86) | 0.92 (0.58, 1.45) | |
| P for trend |  | 0.031 | 0.042 | 0.109 | 0.607 | 0.503 | 0.642 | |
|  |  |  |  |  |  |  |  | |
| Annual household income  (n=135773) |  |  |  |  |  |  |  | |
| <£18,000 | 45/26578 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | |
| £18,000-£30,999 | 49/34301 | 0.84 (0.56, 1.26) | 0.86 (0.57, 1.29) | 0.91 (0.60, 1.37) | 0.95 (0.63, 1.44) | 0.97 (0.65, 1.45) | 1.07 (0.71, 1.63) | |
| £31,000-£51,999 | 46/36526 | 0.74 (0.49, 1.12) | 0.78 (0.41, 1.06) | 0.84 (0.55, 1.28) | 0.91 (0.59, 1.39) | 0.97 (0.61, 1.45) | 1.09 (0.70, 1.69) | |
| £52,000-£100,000 | 31/29819 | 0.61 (0.39, 0.97) | 0.66 (0.41, 1.06) | 0.72 (0.45, 1.16) | 0.81 (0.50, 1.33) | 0.84 (0.52, 1.38) | 1.02 (0.62, 1.69) | |
| >£100,000 | 13/8549 | 0.90 (0.48, 1.65) | 0.97 (0.51, 1.82) | 1.08 (0.57, 2.03) | 1.28 (0.67, 2.45) | 1.29 (0.67, 2.49) | 1.64 (0.84, 3.20) | |
| P for trend |  | 0.094 | 0.211 | 0.409 | 0.846 | 0.951 | 0.431 | |
|  |  |  |  |  |  |  |  | |
| Townsend Deprivation Index  (n=153384) |  |  |  |  |  |  |  | |
| 1 (low) | 50/48529 | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | 1.0 (ref) | |
| 2 | 76/53718 | 1.37 (0.96, 1.95) | 1.35 (0.95, 1.93) | 1.33 (0.93, 1.90) | 1.27 (0.89, 1.82) | 1.32 (0.92, 1.88) | 1.25 (0.87, 1.79) | |
| 3 | 88/51407 | 1.65 (1.17, 2.34) | 1.56 (1.09, 2.22) | 1.47 (1.03, 2.09) | 1.29 (0.90, 1.85) | 1.42 (0.99, 2.03) | 1.19 (0.82, 1.71) | |
| P for trend |  | 0.005 | 0.015 | 0.039 | 0.193 | 0.064 | 0.404 | |
|  |  |  |  |  |  |  |  | |
| **Occupational social class?** |  |  |  |  |  |  |  | |
|  |  |  |  |  |  |  |  | |
|  |  |  |  |  |  |  |  | |

1Comorbidity includes diagnoses of vascular or heart disease, diabetes, chronic bronchitis or emphysema, asthma, and hypertension defined according to measured blood pressure and/or use of anti-hypertensive medication. 2 Lifestyle factors includes body mass index, smoking status, alcohol intake frequency & number of types of physical activity taken in last four weeks. 2 Psychological factors includes psychological distress, psychiatric consultation, neuroticism, verbal and numerical reasoning, & reaction time.