

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository:<https://orca.cardiff.ac.uk/id/eprint/176686/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Lin, Bochao Danae, Pries, Lotta-Katrin, Arias-Magnasco, Angelo, Klingenberg, Boris, Linden, David E.J. , Blokland, Gabriëlla A.M., van der Meer, Dennis, Luykx, Jurjen J., Rutten, Bart P.F. and Guloksuz, Sinan 2025. Exposome-wide gene-environment interaction study of psychotic experiences in the UK Biobank. *Biological Society Global Open Science* , 100460. 10.1016/j.bpsgos.2025.100460

Publishers page: <http://dx.doi.org/10.1016/j.bpsgos.2025.100460>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Journal Pre-proof

Exposome-wide gene-environment interaction study of psychotic experiences in the UK Biobank

Bochao Danae Lin, PhD, Lotta-Katrin Pries, PhD, Angelo Arias-Magnasco, Boris Klingenberg, MD, David E.J. Linden, MD, PhD, Gabriëlla A.M. Blokland, PhD, Dennis van der Meer, PhD, Jurjen J. Luykx, MD, PhD, Bart P.F. Rutten, MD, PhD, Sinan Guloksuz, MD, PhD



PII: S2667-1743(25)00014-X

DOI: <https://doi.org/10.1016/j.bpsgos.2025.100460>

Reference: BPSGOS 100460

To appear in: *Biological Psychiatry Global Open Science*

Received Date: 29 October 2024

Revised Date: 26 January 2025

Accepted Date: 29 January 2025

Please cite this article as: Lin B.D., Pries L.-K., Arias-Magnasco A., Klingenberg B., Linden D.E.J., Blokland G.A.M., van der Meer D., Luykx J.J., Rutten B.P.F. & Guloksuz S., Exposome-wide gene-environment interaction study of psychotic experiences in the UK Biobank, *Biological Psychiatry Global Open Science* (2025), doi: <https://doi.org/10.1016/j.bpsgos.2025.100460>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2025 Published by Elsevier Inc. on behalf of Society of Biological Psychiatry.

Exposome-wide gene-environment interaction study of psychotic experiences in the UK Biobank

Bochao Danae Lin, PhD^{1,2}; Lotta-Katrin Pries, PhD¹; Angelo Arias-Magnasco¹, Boris Klingenberg MD¹, David E. J. Linden MD, PhD^{1,3} Gabriëlla A. M. Blokland PhD¹, Dennis van der Meer PhD^{1,4}, Jurjen J. Luykx MD, PhD^{1,5-8}, Bart P. F. Rutten MD, PhD¹, Sinan Guloksuz, MD, PhD^{1,9}

1. Department of Psychiatry and Neuropsychology, Mental Health and Neuroscience Research Institute, Faculty of Health, Medicine, and Life Sciences, Maastricht University Medical Centre, Maastricht, The Netherlands.
2. Department of Preventive Medicine, Institute of Biomedical Informatics, Bioinformatics Center, School of Basic Medical Sciences, Henan University, Kaifeng, China.
3. Division of Psychological Medicine and Clinical Neurosciences, School of Medicine, Cardiff University
4. Centre for Precision Psychiatry, Division of Mental Health and Addiction, Oslo University Hospital, and Institute of Clinical Medicine, University of Oslo, Oslo, Norway
5. Department of Psychiatry, Amsterdam University Medical Center, Amsterdam, The Netherlands
6. GGZ inGeest Mental Health Care, Amsterdam, The Netherlands
7. Neuroscience Mood, Anxiety, Psychosis, Stress & Sleep Research Program, Amsterdam University Medical Center, Amsterdam, The Netherlands
8. Public Health Mental Health Research Program, Amsterdam University Medical Center, Amsterdam, The Netherlands
9. Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA.

Corresponding author:

Sinan Guloksuz,

Department of Psychiatry and Neuropsychology, Mental Health and Neuroscience Research Institute, Maastricht University Medical Center, P.O. Box 616 6200 MD Maastricht, The Netherlands; tel: 31-433-88-4071, fax: 31433-88-4122, e-mail:

sinan.guloksuz@maastrichtuniversity.nl.

word abstract: 250

word full text: 3859

tables:3; # figures: 1

Running title: XWIS of PEs in UKB

Keywords: psychotic experiences, exposome, gene-environment interaction, XWIS, disability, diathesis-stress model.

Abstract

Background. A previous study successfully identified 148 out of 23,098 exposures associated with any psychotic experiences (PEs) in the UK Biobank using an exposome-wide association study (XWAS). Furthermore, research has shown that the polygenic risk score for schizophrenia (PRS-SCZ) is associated with PEs. However, the interaction of these exposures with PRS-SCZ remains unknown.

Method. To systematically investigate possible gene-environment interactions underlying PEs through data-driven agnostic analyses, we conducted 1) conditional XWAS adjusting for PRS-SCZ to estimate the main effects of the exposures and of PRS-SCZ; 2) exposome-wide interaction study (XWIS) to estimate multiplicative and additive interactions between PRS-SCZ and exposures; and 3) correlation analyses between PRS-SCZ and exposures. The study included 148,502 participants from the UK biobank.

Results. In the conditional XWAS models, significant effects of PRS-SCZ and 148 exposures on PEs remained statistically significant. In the XWIS model, we found significant multiplicative (multiplicative scale, Ms, 1.23, 95%CI, 1.10-1.37; $P=4.0 \times 10^{-4}$) and additive (Relative excess risk due to interaction, RERI, 0.55; 95%CI, 0.32-0.77; SI, 0.22; 95%CI, 0.14-0.30; AP, 1.59; 95%CI, 1.30-1.91; all $P < 0.05/148$) interactions of PRS-SCZ and variable “serious medical conditions/disability” with PEs. We additionally identified six additive gene-environment interactions for mental distress, help/treatment-seeking behaviors (3 variables), sadness and sleep problems. In the correlation test focused on seven exposures exhibiting significant interactions with PRS-SCZ, non-significant or small ($r < 0.04$) gene-environment correlations were estimated.

Conclusions. These findings reveal evidence for gene-environment interaction underlying PEs and suggest that intertwined pathways of genetic vulnerability and exposures may contribute to psychosis risk.

Introduction

Psychotic experiences (PEs) are common and disabling conditions, comprising delusions (unreal beliefs or impressions) or hallucinations (unreal visual or auditory perceptions) in people who do not fulfil the criteria for psychotic disorders. They have a lifetime prevalence of 5-10% in the general population (1). Behavioral, genetic and epidemiological research found that PEs might represent subtle, subclinical symptoms across the psychosis spectrum and often precede or accompany the onset of clinical psychosis (2). Longitudinal studies and familial aggregation research suggest a substantial overlap between PEs and the development of schizophrenia spectrum disorders (3, 4). PEs are moderately heritable and show considerable environmental influence (5). Understanding the genetic and environmental mechanisms of PEs is crucial for the development of tailored prevention, targeted interventions and the improvement of clinical outcomes in individuals with mental disorders. Hypothesis-driven research has identified several environmental factors associated with psychosis such as bullying (6), stressful life events (7), cannabis use (8), tobacco use (9), and low birth weight (10), as well as less studied exposures such as physical activity (11), toxins (12), and nutrients. However, these one-exposure-to-one-outcome hypothesis-testing studies fail to embrace the multiplicity of (and complex relationships among) exposures and are prone to selective reporting and publication bias, involving arbitrary decisions. The availability of large public datasets, along with increased transparency in data processing and standardized analytical algorithms, has significantly advanced agnostic data-driven approaches in human epidemiology. A recent exposome-wide analysis of PEs in the UK Biobank has confirmed previous environmental factors associated with PEs, as well as factors that have not been considered thus far, such as major dietary changes in the last 5 years, and playing computer games (13).

While twin studies suggest moderate heritability of PEs, the contribution of common genetic variants (as measured by SNP heritability) to PEs is considered relatively small, with a SNP heritability < 2% (14, 15), especially when compared to clinical psychotic disorders. Although the GWAS of PEs identified genome-wide significant loci, none showed evidence of colocalization with schizophrenia (16). Significant genetic correlations (r_g) between PEs and psychiatric diseases such as schizophrenia have been detected. However, findings of studies

investigating the associations between PEs and polygenic risk score for schizophrenia (PRS-SCZ) have been inconsistent, showing no (17, 18), weak (15, 16), or significant positive association(19, 20). These studies might be limited by the statistical power of GWAS and target sample size. Therefore, the genetic association of PRS-SCZ with PEs remains to be verified using the most recent SCZ GWAS(21).

In a twin study of PEs (20), heritability of PEs decreased with increasing environmental exposure, highlighting the importance of a diathesis-stress or bioecological framework for understanding adolescent PEs. Previous candidate gene-environment interactions (GxE) studies of PEs have yielded inconsistent results (22-25). The advent of polygenic scores (PRS), which aggregate genome-wide common variants to index a person's genetic propensities for a trait, has created opportunities for testing gene-environment interactions . Recent GxE studies testing the interaction of PRS-SCZ with high birth weight (26) and smoking (27) also need to be replicated. Hereby, we conducted the first systematic and agnostic exposome-wide interaction analyses to identify GxE underlying PEs.

Methods and Materials

Sample

The current study included participants from the UK Biobank (UKB), a large prospective population-based cohort that included around half a million participants from the United Kingdom (28). All participants provided written consent and ethical approval was given by the National Research Ethics Service Committee North West Multi-Centre Haydock, Committee reference: 11/NW/0382 (29). The current study (UKB project number: 55392) analyzed participants with complete data on the Mental Health Questionnaire (29) that assessed PEs (n=155,247; 57% female; mean age=55.94 [SD=7.74] years).

Psychotic experiences

Guided by previous reports (13, 16, 27), a binary variable of any PEs (n=7,803) was defined as an endorsement of any of the following four-lifetime items: visual hallucination, auditory hallucination, reference delusion, and persecutory delusion. The specific wording of, operationalized by the items was: variables 'ever seen an un-real vision', 'ever heard an un-

real voice', 'ever believed in un-real communications or signs', and 'ever believed in an un-real conspiracy against self', respectively.

Correlates of psychotic experiences

For the current analyses, we included 148 variables (**Supplementary Material and eTable 1**) which were significantly associated with PEs in a previous exposome-wide association study (XWAS) after applying Bonferroni correction (13). These 148 exposures, consisting of 109 binary and 39 continuous variables, belong to 13 UKB categories including environmental, lifestyle, behavioral, and sociodemographic factors. Most exposures are associated with increased PEs, except for 26 exposures (such as vitamin D intake, and general health rating) that were associated with decreased PEs.

In this study, we further dichotomized the 39 continuous exposures at the 75th percentile assigning values of 1 and 0, concordant with our previous GxE analyses (30, 31). As previously suggested for additive interactions, we reverse-coded the 26 negative correlates of PE, with 1 indicating "high-risk" and 0 indicating "low-risk" (32). This approach was used across all analyses to ensure comparable and consistent results (32). Therefore, the direction of effects of these 26 correlates on PEs differs from the previous study (**eTable 2**).

Polygenic risk score estimation

Detailed methodology can be found in the Supplementary Material. We calculated the PRS-SCZ for 151,627 participants who had available genetic and phenotypic information. We used summary statistics from the most recent GWAS of schizophrenia derived from European-ancestry (21) to calculate PRS-SCZ. To estimate the PRSs, we used PRS-continuous shrinkage (33) (PRS-cs-auto) for the main analyses and PRSice2 (p-value threshold = 0.05) (34) for sensitivity analyses. PRS-SCZ was dichotomized using quartile cut-off points based on the control distribution. Consistent with our previous work testing gene-environment interaction in psychosis (1-3), the highest quartile (PRS-SCZ > 75% of the controls) was considered the binary genetic risk state for schizophrenia for more interpretable and comparable testing of additive interactions. This cut-off was chosen based on previous research demonstrating its

effectiveness in identifying individuals at higher genetic risk for schizophrenia (35). Additionally, sensitivity analyses in prior studies have shown that additive interactions between PRS-SCZ and candidate exposures (e.g., regular cannabis use, childhood bullying, emotional abuse, sexual abuse, and emotional neglect) were consistent across different PRS-SCZ cut-points (50% and 25%) (31). These findings support the rationale of the 75th percentile as an appropriate threshold for our analyses.

Statistical analyses

Analyses were performed using R (version 4.0.4) (36) from November 1, 2023, to February 1, 2024. There were three sequential analytical steps (**eFigure 1**). First, the correlations of PRS-SCZ with each of the 148 exposures were estimated using the Pearson correlation test. Second, we tested the main effects of PRS-SCZ on PEs using baseline logistic models with covariates, including sex, age and the first 3 genetic Principal components (PCs) ($PEs \sim sex + age + PC1 + PC2 + PC3 + PRS-SCZ$). In our previous work testing model specifications for adjusting for population stratification in polygenic risk score analyses in the UKB, we demonstrated that the first three PCs captured a substantial proportion of genetic variation related to population structure in the UK Biobank cohort (eFigure2), correlating well with geographic and ancestral differences within the British population (37). Then we added each of the 148 exposures into the PRS model ($PEs \sim sex + age + PC1 + PC2 + PC3 + PRS-SCZ + Exposure$), using the "interactionR" package (38) to estimate GxE interactions. Third, the correlations of PRS-SCZ with each of the 148 exposures were estimated using Pearson correlation (38). Bonferroni correction was applied for adjusting p-values for multiple testing ($p < 0.05/148$). We also attempted to replicate previously demonstrated gene-environment interactions for birth weight and smoking behavior (26, 27). Sensitivity analyses were conducted using PRSice-SCZ₇₅ across all analytical steps.

Multiplicative and additive interaction

Interactions on the multiplicative scale assess whether the joint effect of the PRS and exposure is greater than the product of their individual effects. For multiplicative interaction, we integrated a product term (Multiplicative scale, Ms) of PRS-SCZ with each exposure on PEs

in the logistic regression models. Besides the Ms coefficients, corresponding p-values and 95% confidence intervals (CIs) were also reported.

Interactions on the additive scale assess whether the joint effect of exposure and the PRS-SCZ is greater than the sum of their individual effects. Relative excess risk due to interaction (RERI), attributable proportion of interaction (AP), and synergy index (SI), along with corresponding p-values and 95% CIs were utilized to perform effect modification analysis on the additive scale. We also estimated ORs, 95% CIs, and P values in each exposure and PRS strata to evaluate whether the effect of the exposure differed within the strata of PRS-SCZ. To estimate the CIs for the additive interactions, the simple asymptotic delta method (39) and the variance recovery ('MOVER') method (40) were applied. As sensitivity analyses, we additionally estimated the CIs of the interactions with the 39 continuous exposures and the continuous PRSs using the non-parametric bootstrapping method with 1000 bootstrap resampling (41).

Replication of previous gene-environment interactions

Recent studies have shown GxE in PEs related to birth weight and smoking behavior, employing PRS-SCZ derived from PGC2 (42) across different datasets. In addition to the exposome-wide interaction analyses, we attempted to replicate the genetic association findings using PRS-SCZ PGC3 (21).

Results

Main effects

In the baseline model (PEs ~ sex + age + PC1 + PC2 + PC3 + PRS-SCZ), PRS-cs-auto-SCZ₇₅ significantly predicted PEs (OR, 1.14; 95 %CI, 1.11-1.17; P=7.27x10⁻²⁴, R²=0.21%). In the 148 conditional XWAS models (PEs ~ sex + age + PC1 + PC2 + PC3 + PRS-SCZ + Exposure), adding exposure into the logistic models, the significant effects of PRS-cs-auto-SCZ₇₅ on PEs remained significant (ORs, 1.11-1.15; R², 0.12-0.24%; P-values 6.6 x10⁻¹³ to 1.1x10⁻²⁶; **eTable 3**). Under the condition of PRS-cs-auto-SCZ₇₅, all the ORs of the 148 exposures remained significant (**eFigure 3**). The sensitivity analyses with PRSice-SCZ₇₅ confirmed these results (**eTable 3**).

Multiplicative scales

Among the 148 exposures, the only significant multiplicative interaction with PRS-SCZ was found for disability (“other serious medical condition disability diagnosed by the doctor”, with the Multiplicative scale (Ms) 1.23 (**Table 1**, 95 %CI, 1.10-1.37; P=4.0x10⁻⁴). For the exposures “visiting a psychiatrist for mental health”, “mental distress”, “vitamin D”, and “visiting a GP for mental health”, analyses indicated nominally statistically significant interactions (**Table 2**). In the sensitivity test using PRSice-SCZ₇₅, disability remained the top multiplicative interaction (Ms, 1.22; 95 %CI, 1.092-1.37, P=0.0005), but it was not statistically significant after Bonferroni correction. Furthermore, three nominally significant interactions remained: mental distress, visiting a psychiatrist for mental health, and vitamin D (**eTable 4**).

Additive interaction

Among the 148 variables, significant additive interactions were found for seven exposures (disability, mental distress, sadness, help for mental distress, sleeping difficulties, visiting a GP for mental health, and visiting a psychiatrist for mental health) (**Figure 1 & Table 3**). Similarly to the multiplicative interaction analyses, disability interacted with PRS-cs-auto-SCZ₇₅ on an additive scale (**eTable 1**: RERI,0.55; 95%CI, 0.32-0.77; SI, 0.22; 95%CI, 0.14-0.30; AP, 1.59; 95%CI, 1.30-1.91; all P < 0.05/148). The MOVER method identified similar confidence intervals (**eTable 5**).

An additional 48 interactions were detected with nominal significance levels (**eTable 5 and eFigure 4**). The majority of these exposures were from the UKB mental health (n=25) and psychosocial factors (n=15) categories, including cannabis use, self-harm, eating problems, sexual molestation as a child, and loneliness isolation. Furthermore, interactions with exposures from the following categories were found: health and medical history (n=8: e.g. chest, dental, infirmity, hearing problem and vitamin supplements), lifestyle and environment (n=4: insomnia, diet change, milk types used, and hot drink temperature), physical measures (n=2: fat mass and hand grip strength) and medical conditions (number of illnesses).

The sensitivity analyses using PRSice-SCZ₇₅ confirmed the seven significant additive interactions. Furthermore, 39 out of the 48 nominal significant additive interactions were confirmed (**eTable 5**).

Gene-environment correlations

The correlation analyses found small (correlation coefficient r range from -0.021 to 0.058) but significant ($P < 2.02 \times 10^{-4}$) correlations between 102 exposures and PRS-cs-auto-SCZ₇₅ (**eTable 6**). Ninety-four (r range from -0.028 to 0.042) of these correlations remained significant using PRSice-SCZ₇₅ in sensitivity tests.

Focusing on the exposures with significant interactions with PRS, disability and sleeping problems were not correlated with PRS-SCZ. Although the rest of the exposures that interacted with PRS-SCZ were positively correlated with PRS-cs-auto-SCZ₇₅, the magnitude of the correlations was very small (< 0.04). These correlations were replicated in the sensitivity tests using PRSice-SCZ₇₅.

GxE interaction with birth weight and smoking

Birth weight was initially excluded from the previous XWAS due to a missing rate of $> 10\%$. Smoking status, pack years of smoking and maternal smoking around birth were also excluded due to collinearity, missingness, and being a follow-up variable, respectively. However, we extracted these variables to replicate previous findings and estimated the additive and multiplicative interactions with PRSice-SCZ₇₅ on PEs (**eTable 7 and eFigure 5**). Among these four variables, only a nominally significant additive interaction of smoking status with PRS-SCZ on PEs was found (RERI, 0.13; 95%CI, 0.014- 0.266; $P = 0.038$).

Discussion

To the best of our knowledge, this study represents the most extensive systematic inquiry into the exposome-wide gene-environment interaction of PEs. It encompasses several sequential analytical steps, including an exposome-wide association study conditional on PRS-SCZ, an exposome-wide gene-environment interaction investigation, an exposome-wide gene-environment correlation estimation, and replication of previous GxE analyses.

Our exposome-wide gene-environment interaction study identified significant multiplicative and additive interactions between disability and genetic risk of schizophrenia on PE, as well as seven significant additive interactions: 3 help and treatment-seeking behaviours, mental distress, sadness and sleep problems. Besides the significant interactions, four multiplicative and 48 additive nominally significant interactions were identified, mainly in the domains of physical health outcomes, non-psychotic disorders, mental distress, stress, trauma, help and treatment-seeking behaviors, and sleep problems. Multiplicative interaction occurs when the combined effect of two factors differs from the product of their individual effects. This is commonly used in logistic regression models. In contrast, additive interaction occurs when the combined effect differs from the sum of individual effects. Overall, more significant additive interactions were detected compared to multiplicative interactions. Compared to multiplicative interaction tests, additive interaction tests may offer greater statistical power and reveal more interpretable results from biomedical and epidemiological data (43).

Our study found that the impact of physical disability on PEs increased with higher PRS-SCZ, as revealed by both multiplicative and additive GxE models. To the best of our knowledge, this is the first report indicating that the sensitivity to adverse physical conditions is moderated by PRS-SCZ. PE, an indicator of general health, has been associated with increased risk for disability across a broad range of functional domains, including social-, role-, cognitive functioning, mobility, and self-care (44). We showed that both conditional XWAS tests and XWIS models, which include PRS-SCZ and GxE, explained more variance of PEs than models testing only environmental factors. This finding supports the idea that polygenic risk, poor physical health, and their combined influence are associated with subthreshold psychosis expression.

Additionally, we identified nominally significant additive interactions with milder physical health issues like chronic illness or recent fatigue, with smaller RERI (0.23, 0.17) and AP (0.09, 0.07) values compared to Bonferroni significant interaction of 'disability with more serious condition' (RERI=0.56, AP=0.24), indicating stronger GxE effects with severe health outcomes. Furthermore, GxE interactions have also been detected for other physical health outcomes, such as wheezing or whistling in the chest in the last year, chest pain, dental problems, taking other prescription medications, number of self-reported noncancer illnesses, and hearing problems. Our findings highlight GxE of serious medical conditions or disabilities with genetic propensities for schizophrenia on PEs. This supports a conceptual framework where underlying (nonspecific) immune dysfunction (e.g. autoantibodies, T- and B cells), with an estimated heritability of 30% (45), might serve as a foundational mechanism leading to a broad spectrum of health outcomes, including psychosis, contingent on disease burden. Of note, the GxE interactions became stronger with increasing severity of the physical condition, suggesting a dose-response relationship where increased disease burden might exacerbate PE, akin to sickness behavior during illness (46, 47). In this regard, immune system dysregulation and neuroinflammation might underlie behavioural and functional impairments (48). We acknowledge that some of the included variables may not strictly adhere to traditional environmental exposure definitions. However, these were included to maintain consistency with the analytical pipeline applied in our previous work of exposome-wide association study of PEs in the UKB, which aimed to eliminate data dredging and selective reporting that could be produced by preconceptions when determining what the environment is. However, this approach might introduce Type-II error due to the increased number of tests.

In the XWIS study, three significant additive interactions were identified for treatment-seeking behavior linked to mental health problems: 'seeing a psychiatrist for nerves, anxiety, tension or depression', 'seen doctor/GP for nerves, anxiety, tension or depression', and 'ever sought or received professional help for mental distress'. In accordance with our findings, this suggests that targeting high PRS-SCZ and help-seeking individuals may aid in intervening in psychotic disorders. Furthermore, our findings identified suggestive interactions of well-known exposures such as cannabis use, self-harm, medical prescription, and sexually

molested as a child, which is consistent with previous studies with independent samples (13, 30).

According to the diathesis-stress theory, it is crucial to identify cumulative stressors that contribute to the manifestation of psychiatric symptoms in vulnerable populations like those with PEs. The diathesis, or inherent vulnerabilities, are crucial in explaining why some individuals are more susceptible to developing psychiatric symptoms. Individuals with a high genetic predisposition to psychosis may experience cognitive deficits that could influence their response to environmental stressors and increase the likelihood of experiencing psychiatric symptoms (49). Cumulative stressors, such as ongoing life difficulties and acute stress events, can exacerbate vulnerability, potentially triggering adverse psychotic symptoms and increasing the need for intervention. It is critical to identify and manage cumulative stressors in genetically vulnerable populations, particularly those with high genetic liability for schizophrenia. Overall, our results align with the diathesis-stress model theory, suggesting that a combination of genetic predisposition and environmental stress contribute the manifestation of PEs. Identifying these high-risk individuals who are actively seeking help presents an opportunity for early intervention and better management of mental health concerns.

Several prior investigations have evaluated the interplay between PRS-SCZ and environmental variables underlying PEs. However, these studies have predominantly focused on a limited number of environmental factors such as stress (50), smoking behavior (27), and birth weight (26), which have not been verified in independent cohorts. In our study, we have replicated previous findings with suggestive interaction for stress (“felt very upset when reminded of a stressful experience in the past month and avoided activities” or “situations because of previous stressful experience in the past month”) and smoking status.

Our findings highlight the complex interplay between genetic predisposition and environmental factors in the etiology of PEs. Previous exposome-wide analyses identified 148 exposures associated with PEs(13). The subsequent conditional cross-phenotype-wide association study (XWAS) reaffirms that the relative impact of genetic factors on PEs (with only 0.2% variance explained by PRS-SCZ) is notably lower compared to environmental exposures. Our results were consistent with the findings of a twin study suggesting that environmental factors might play a greater role than genetic factors in the etiology of PEs (20).

However, it is crucial to emphasize that while environmental factors appear to have a larger impact, the role of genetic predisposition remains significant and cannot be overlooked. Even after adjusting environmental exposures associated with PEs, we observed a persistent significant association between PRS-SCZ and PEs. This underscores that genetic risk for schizophrenia, although contributing a smaller proportion of variance, plays an essential role in the manifestation of PEs that is distinct from and complementary to environmental influences. Our findings thus support a model where both genetic and environmental factors contribute to the development of PEs, with environment explaining a slightly larger variance, but genetic predisposition remaining an integral part of the equation. This emphasizes the need for a comprehensive approach in understanding and potentially intervening in the development of PEs, considering both genetic vulnerability and environmental exposures.

It is crucial to consider whether PEs assessed in our older adult population (mean age >55 years) are related to, or on the same continuum as, PEs expressed by young adults who might be more prone to schizophrenia risk. Although our study provides valuable insights into the long-term manifestation of PEs, we acknowledge that the nature and implications of PEs may differ across age groups.

Our research has several strengths. First, the UKB's deep phenotyping and large sample size provide the requisite statistical robustness to discern subtle GxE, even within complex multifactorial outcomes such as PEs. This capability enables the identification of interactions with heightened precision. Second, we employed two widely recognized methods for PRS calculation: PRS-cs-auto and PRSice2. The PRS-cs-auto generation method allows for the efficient processing of vast amounts of genetic data and yields more statistically robust results, particularly in the context of larger sample sizes (33). Additionally, we utilized PRSice2 to generate PRS-SCZ, employing a liberal p-value threshold of 0.05 for sensitivity analyses, thereby enhancing the predictive power of genetic scores. Third, our study benefited from access to the most extensive GWAS summary statistics available to date (21). The variance of PEs explained by PRS-SCZ in our study (0.2%) is larger than another study using summary statistics from Psychiatric Genomic Consortium freeze 2 (PGC2) (27). Still, the R^2 is relatively low, which suggests a small effect size. However, this should not be the sole criterion for assessing the importance of variables, especially in complex phenotypes like PEs. The biological plausibility, and consistency with other findings should also be considered. Although our systematic approach was designed to mitigate biases and increase

reproducibility, it was not without limitations. First, the sequential replication procedure and stringent multiple-testing correction might have inadvertently increased the likelihood of type II errors. Conversely, statistically significant yet trivial effects can also emerge in analyses of large datasets. Second, we have not investigated any subtypes of PE; therefore, the contribution of genetic risk and exposures on specific types of PEs remains unknown. Secondly, our cross-sectional design limits causal inferences. Some of the correlates of PE might be consequences rather than causes of PEs (for example, visiting a psychiatrist could be a result of experiencing PEs rather than a causal factor.). We acknowledge the potential for reverse causality in our findings. Further studies of causal inference, such as Mendelian Randomization, would be valuable in identifying potential causal mechanisms underlying PEs. Lastly, the proportion of variance of PEs explained by PRS-SCZ was minimal (<2%). Additional investigation is necessary to clarify the other genetic contributors (rare variants and Copy Number Variants) to phenotypic variance. Our study focused on white British aged 48-63, which allows examination of cumulative environmental effects but may limit generalizability to younger populations and other ethnic groups. Future research should investigate these gene-environment interactions across different ethnic and age groups, particularly in younger individuals during critical developmental periods. To enhance the reproducibility of our results, future studies could validate the identified exposures and their GxE interactions through hypothesis-driven research in independent cohorts.

Conclusion

The current study marks the first documentation of numerous exposures associated with PEs, after adjusting for polygenic risk for schizophrenia. These findings reveal preliminary evidence for gene-environment interaction in PEs and suggest that genetic vulnerability and exposures specifically physical health conditions might be intertwined in the pathway leading to psychosis. Our findings support the diathesis-stress theory and underscore the necessity of evaluating both environmental and genetic influences in conjunction to elucidate biological mechanisms underlying psychosis.

Journal Pre-proof

Data availability

All results data generated and analyzed during this study are included in the supplementary materials accompanying this manuscript. These supplementary materials provide the complete dataset necessary to interpret, verify, and extend the research presented in the article.

For any additional information or access to specific datasets beyond what is provided in the supplementary materials, reasonable requests can be made to the corresponding author.

Acknowledgments

Drs Lin and Guloksuz had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Drs Lin and Guloksuz. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Dr Lin. Statistical analysis: Dr Lin. Critical revision of the manuscript for important intellectual content: Lin, Pries, Arias-Magnasco, Klingenberg, Guloksuz. Obtained funding: Rutten, Guloksuz. Supervision: Dr Guloksuz. This manuscript was previously posted as a preprint on medRxiv (Lin et al., 2024; doi: <https://doi.org/10.1101/2024.09.06.24313177>).

Disclosures

Conflict of Interest Disclosures: The authors report no biomedical financial interests or potential conflicts of interest.

Funding/Support: Dr Guloksuz is supported by the Ophelia research project, ZonMw grant 636340001. Dr Rutten is funded by a Vidi award (91718336) from the Netherlands Scientific Organisation. Dr Lin, Dr Pries, Arias-Magnasco, Dr Rutten, and Dr Guloksuz, are supported by the YOUTH-GEMs project, funded by the European Union's Horizon European program under the grant agreement number: 101057182. Dr. van der Meer is supported by a Research Council of Norway grant #324252.

Supplement Description (2 files):

Supplement Methods, Figures e1-e5, Table e8

Tables e1-e7

Table 1. Interaction of disability and PRS-cs-auto-SCZ₇₅ on psychotic experience.

	Disability: No	Disability: Yes	Disability Yes, vs No within strata of PRSice-SCZ
	OR [95%CI] P	OR [95%CI] P	OR [95%CI] P
PRS-cs-auto-SCZ ₇₅ =0	1[Reference]	1.82[1.72-1.94] P<10 ⁻⁵	1.82[1.74-1.94] P<10 ⁻⁵
PRS-cs-auto-SCZ ₇₅ =1	1.10[1.04-1.17] P=0.023	2.47[2.27-2.69] P<10 ⁻⁵	2.24[2.04-2.47] P<10 ⁻⁵
High PRS vs low PRS within strata of disability	1.10[1.04-1.17] P=0.023	1.36[1.23-1.49] P<10 ⁻⁵	
Ms	1.23, [1.10-1.38], P=3.3X10 ⁻⁴ .		
RERI	0.55, [delta:0.32-0.77], [mover:0.33-0.78], P<10 ⁻⁵		
SI	0.22, [delta:0.14-0.30], [mover:0.14-0.29], P<10 ⁻⁵		
AP	1.59, [delta:1.32-1.91], [mover:1.32-1.91,] P<10 ⁻⁵		

Note: Disability: other serious medical condition disability diagnosed by a doctor, Multiplicative scale, RERI= relative excess risk due to interaction, AP= attributable proportion, and SI= synergy index.

Table 2. Significant multiplicative interactions of PRS-cs-auto-SCZ₇₅ and exposures on psychotic experiences were identified using an exposome-wide interaction study.

Exposure	Category	Ms	95% CIs	P-value
Disability*	Health and medical history	1.23	1.10-1.38	4.0x10⁻⁴
visit psychiatrist for mental health*	Psychosocial factors	1.18	1.05-1.32	0.006
mental distress*	Mental health	1.15	1.03-1.28	0.013
vitamin D*	Biological samples	0.94	0.89-0.99	0.042
visit GP for mental health	Psychosocial factors	1.12	1.00-1.23	0.046

Note: MS= Multiplicative scales, 95% CIs 95% confidence intervals. The full name of exposure: disability = other serious medical condition disability diagnosed by a doctor, visit psychiatrist for mental health = seen a psychiatrist for nerves anxiety tension or depression, mental distress = Ever suffered mental distress preventing usual activities, visit GP for mental health = seen doctor gp for nerves anxiety tension or depression. The variable in bold is identified as having significant multiplicative interaction with Bonferroni correction ($p < 0.05/148$).

The variables with asterisk are results that have been replicated from sensitivity tests using PRSice-SCZ₇₅.

Table 3. Significant additive interaction between PRS-cs-auto-SCZ₇₅ and exposures on psychotic experiences were identified using an exposome-wide interaction study.

Exposure	Category	Relative excess risk due to interaction (RERI)		Attributable proportion (AP)		Synergy index (SI)	
		estimate	P-value	estimate	P-value	estimate	P-value
disability*	Health and medical history	0.562	<10 ⁻⁵	0.224	<10 ⁻⁵	1.595	<10 ⁻⁵
mental distress*	Mental health	0.601	<10 ⁻⁵	0.158	<10 ⁻⁵	1.275	<10 ⁻⁵
Sadness*	Mental health	0.498	10 ⁻⁵	0.141	<10 ⁻⁵	1.244	<10 ⁻⁵
visit psychiatrist for mental health*	Psychosocial factors	0.894	10 ⁻⁵	0.210	<10 ⁻⁵	1.378	10 ⁻⁵
visit GP for mental health*	Psychosocial factors	0.450	10 ⁻⁵	0.152	<10 ⁻⁵	1.298	10 ⁻⁵
help of mental distress*	Mental health	0.465	3.0x10 ⁻⁴	0.136	10 ⁻⁵	1.239	3.0x10 ⁻⁵
sleeping problem*	Mental health	0.292	2.9x10 ⁻⁴	0.127	1.4x10 ⁻⁴	1.294	5.2x10 ⁻⁴

Note: The variables are identified as having significant additive interaction with Bonferroni correction ($p < 0.05/148$). disability = other serious medical condition disability diagnosed by a doctor, mental distress = ever suffered mental distress preventing usual activities, sadness = ever had prolonged feelings of sadness or depression, visit psychiatrist for mental health = seen a psychiatrist for nerves anxiety tension or depression, visit GP for mental health = seen doctor gp for nerves anxiety tension or depression, help of mental distress = ever sought or received professional help for mental distress, sleeping problem = trouble falling or staying asleep or sleeping too much.

The variable in bold is identified as having significant multiplicative interaction with Bonferroni correction ($p < 0.05/148$). The variables with asterisk are results have been replicated from sensitivity tests using PRSice-SCZ₇₅.

Figure 1. Odds ratios of PEs in 55 exposures and PRS subgroups. 55 exposures are nominal significant from the additive interaction test.

Journal Pre-proof

Reference:

1. McGrath JJ, Saha S, Al-Hamzawi AO, Alonso J, Andrade L, Borges G, et al. (2016): Age of Onset and Lifetime Projected Risk of Psychotic Experiences: Cross-National Data From the World Mental Health Survey. *Schizophr Bull.* 42:933-941.
2. Staines L, Healy C, Coughlan H, Clarke M, Kelleher I, Cotter D, et al. (2022): Psychotic experiences in the general population, a review; definition, risk factors, outcomes and interventions. *Psychol Med.* 52:1-12.
3. Isaksson J, Angenfelt M, Frick MA, Olofsdotter S, Vadlin S (2022): Psychotic-like experiences from adolescence to adulthood: A longitudinal study. *Schizophr Res.* 248:1-7.
4. Gregersen M, Jepsen JRM, Rohd SB, Søndergaard A, Brandt JM, Ellersgaard D, et al. (2022): Developmental Pathways and Clinical Outcomes of Early Childhood Psychotic Experiences in Preadolescent Children at Familial High Risk of Schizophrenia or Bipolar Disorder: A Prospective, Longitudinal Cohort Study - The Danish High Risk and Resilience Study, VIA 11. *American Journal of Psychiatry.* 179:628-639.
5. Ronald A (2015): Recent quantitative genetic research on psychotic experiences: new approaches to old questions. *Current Opinion in Behavioral Sciences.* 2:81-88.
6. Chen LH, Touloupoulou T (2022): Pathways linking school bullying and psychotic experiences: Multiple mediation analysis in Chinese adolescents and young adults. *Frontiers in Psychiatry.* 13.
7. Shakoor S, Zavos HM, Haworth CM, McGuire P, Cardno AG, Freeman D, et al. (2016): Association between stressful life events and psychotic experiences in adolescence: evidence for gene-environment correlations. *Br J Psychiatry.* 208:532-538.
8. Wright AC, Cather C, Farabaugh A, Terechina O, Pedrelli P, Nyer M, et al. (2021): Relationship between cannabis use and psychotic experiences in college students. *Schizophr Res.* 231:198-204.
9. Jones HJ, Gage SH, Heron J, Hickman M, Lewis G, Munafò MR, et al. (2018): Association of Combined Patterns of Tobacco and Cannabis Use in Adolescence With Psychotic Experiences. *JAMA psychiatry.* 75:240-246.
10. Lipner E, O'Brien KJ, Pike MR, Ered A, Ellman LM (2023): Environmental Risk Factors and Cognitive Outcomes in Psychosis: Pre-, Perinatal, and Early Life Adversity. *Curr Top Behav Neurosci.* 63:205-240.
11. Firth J, Solmi M, Wootton RE, Vancampfort D, Schuch FB, Hoare E, et al. (2020): A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. *World Psychiatry.* 19:360-380.
12. Newbury JB, Arseneault L, Beevers S, Kitwiroon N, Roberts S, Pariante CM, et al. (2019): Association of Air Pollution Exposure With Psychotic Experiences During Adolescence. *JAMA psychiatry.* 76:614-623.
13. Lin BD, Pries LK, Sarac HS, van Os J, Rutten BPF, Luykx J, et al. (2022): Nongenetic Factors Associated With Psychotic Experiences Among UK Biobank Participants: Exposome-Wide Analysis and Mendelian Randomization Analysis. *JAMA psychiatry.*
14. Ronald A, Pain O (2018): A systematic review of genome-wide research on psychotic experiences and negative symptom traits: new revelations and implications for psychiatry. *Hum Mol Genet.* 27:R136-R152.
15. Pain O, Dudbridge F, Cardno AG, Freeman D, Lu Y, Lundstrom S, et al. (2018): Genome-wide analysis of adolescent psychotic-like experiences shows genetic overlap with psychiatric disorders. *Am J Med Genet B Neuropsychiatr Genet.* 177:416-425.

16. Legge SE, Jones HJ, Kendall KM, Pardinas AF, Menzies G, Bracher-Smith M, et al. (2019): Association of Genetic Liability to Psychotic Experiences With Neuropsychotic Disorders and Traits. *JAMA psychiatry*. 76:1256-1265.
17. Zammit S, Hamshere M, Dwyer S, Georgiva L, Timpson N, Moskvina V, et al. (2014): A population-based study of genetic variation and psychotic experiences in adolescents. *Schizophr Bull*. 40:1254-1262.
18. Sieradzka D, Power RA, Freeman D, Cardno AG, McGuire P, Plomin R, et al. (2014): Are genetic risk factors for psychosis also associated with dimension-specific psychotic experiences in adolescence? *PLoS One*. 9:e94398.
19. Jones HJ, Stergiakouli E, Tansey KE, Hubbard L, Heron J, Cannon M, et al. (2016): Phenotypic Manifestation of Genetic Risk for Schizophrenia During Adolescence in the General Population. *JAMA psychiatry*. 73:221-228.
20. Taylor MJ, Martin J, Lu Y, Brikell I, Lundström S, Larsson H, et al. (2019): Association of Genetic Risk Factors for Psychiatric Disorders and Traits of These Disorders in a Swedish Population Twin Sample. *JAMA psychiatry*. 76:280-289.
21. Trubetskov V, Pardiñas AF, Qi T, Panagiotaropoulou G, Awasthi S, Bigdeli TB, et al. (2022): Mapping genomic loci implicates genes and synaptic biology in schizophrenia. *Nature*. 604:502-508.
22. Zammit S, Owen MJ, Evans J, Heron J, Lewis G (2011): Cannabis, COMT and psychotic experiences. *British Journal of Psychiatry*. 199:380-385.
23. Misiak B, Stramecki F, Gawęda Ł, Prochwicz K, Sąsiadek MM, Moustafa AA, et al. (2018): Interactions Between Variation in Candidate Genes and Environmental Factors in the Etiology of Schizophrenia and Bipolar Disorder: a Systematic Review. *Molecular Neurobiology*. 55:5075-5100.
24. de Castro-Catala M, van Nierop M, Barrantes-Vidal N, Cristóbal-Narváez P, Sheinbaum T, Kwapil TR, et al. (2016): Childhood trauma, BDNF Val66Met and subclinical psychotic experiences. Attempt at replication in two independent samples. *J Psychiatr Res*. 83:121-129.
25. de Castro-Catala M, Peña E, Kwapil TR, Papiol S, Sheinbaum T, Cristóbal-Narváez P, et al. (2017): Interaction between FKBP5 gene and childhood trauma on psychosis, depression and anxiety symptoms in a non-clinical sample. *Psychoneuroendocrinology*. 85:200-209.
26. Liuhanen J, Suvisaari J, Kajantie E, Miettunen J, Sarin AP, Järvelin MR, et al. (2018): Interaction between compound genetic risk for schizophrenia and high birth weight contributes to social anhedonia and schizophrenia in women. *Psychiatry Res*. 259:148-153.
27. García-González J, Ramírez J, Howard DM, Brennan CH, Munroe PB, Keers R (2020): The effects of polygenic risk for psychiatric disorders and smoking behaviour on psychotic experiences in UK Biobank. *Translational Psychiatry*. 10:330.
28. Bycroft C, Freeman C, Petkova D, Band G, Elliott LT, Sharp K, et al. (2018): The UK Biobank resource with deep phenotyping and genomic data. *Nature*. 562:203-209.
29. Davis KA, Coleman JR, Adams M, Allen N, Breen G, Cullen B, et al. (2020): Mental health in UK Biobank—development, implementation and results from an online questionnaire completed by 157 366 participants: a reanalysis. *BJPsych Open*. 6:1-8.
30. Guloksuz S, Pries LK, Delespaul P, Kenis G, Luyckx JJ, Lin BD, et al. (2019): Examining the independent and joint effects of molecular genetic liability and environmental exposures in schizophrenia: results from the EUGEI study. *World Psychiatry*. 18:173-182.
31. Guloksuz S, Pries LK, Ten Have M, de Graaf R, van Dorsselaer S, Klingenberg B, et al. (2020): Association of preceding psychosis risk states and non-psychotic mental disorders

- with incidence of clinical psychosis in the general population: a prospective study in the NEMESIS-2 cohort. *World Psychiatry*. 19:199-205.
32. Knol MJ, VanderWeele TJ, Groenwold RH, Klungel OH, Rovers MM, Grobbee DE (2011): Estimating measures of interaction on an additive scale for preventive exposures. *Eur J Epidemiol*. 26:433-438.
 33. Ge T, Chen C-Y, Ni Y, Feng Y-CA, Smoller JW (2019): Polygenic prediction via Bayesian regression and continuous shrinkage priors. *Nature Communications*. 10:1776.
 34. Choi SW, O'Reilly PF (2019): PRSice-2: Polygenic Risk Score software for biobank-scale data. *Gigascience*. 8.
 35. Guloksuz S, Pries L-K, Delespaul P, Kenis G, Luykx JJ, Lin BD, et al. (2019): Examining the independent and joint effects of molecular genetic liability and environmental exposures in schizophrenia: results from the EUGEI study. *World Psychiatry*. 18:173-182.
 36. Team R Development Core (2020): R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, pp <https://www.R-project.org>.
 37. Lin BD, Pries LK, van Os J, Luykx JJ, Rutten BPF, Guloksuz S (2023): Adjusting for population stratification in polygenic risk score analyses: a guide for model specifications in the UK Biobank. *J Hum Genet*. 68:653-656.
 38. Alli BY (2021): InteractionR: An R package for full reporting of effect modification and interaction. *Software Impacts*. 10:100147.
 39. Hosmer DW, Lemeshow S (1992): Confidence Interval Estimation of Interaction. *Epidemiology*. 3.
 40. Zou GY (2008): On the Estimation of Additive Interaction by Use of the Four-by-two Table and Beyond. *American Journal of Epidemiology*. 168:212-224.
 41. Assmann SF, Hosmer DW, Lemeshow S, Mundt KA (1996): Confidence intervals for measures of interaction. *Epidemiology*. 7:286-290.
 42. Pardiñas AF, Holmans P, Pocklington AJ, Escott-Price V, Ripke S, Carrera N, et al. (2018): Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. *Nature Genetics*. 50:381-389.
 43. VanderWeele TJ, Knol MJ (2014): A Tutorial on Interaction. 3:33-72.
 44. Oh H, Koyanagi A, Kelleher I, DeVlyder J (2018): Psychotic experiences and disability: Findings from the Collaborative Psychiatric Epidemiology Surveys. *Schizophr Res*. 193:343-347.
 45. de Craen AJM, Posthuma D, Remarque EJ, van den Biggelaar AHJ, Westendorp RGJ, Boomsma DI (2005): Heritability estimates of innate immunity: an extended twin study. *Genes & Immunity*. 6:167-170.
 46. Estroff SE (1994): Knowledge, Power, and Practice
11 Identity, Disability, and Schizophrenia: The Problem of Chronicity. In: Lindenbaum S, Lock MM, editors. *The Anthropology of Medicine and Everyday Life*: University of California Press, pp 247-286.
 47. Mechanic D (1968): *Medical Sociology: a Selective View*. Free Press.
 48. Rhie SJ, Jung EY, Shim I (2020): The role of neuroinflammation on pathogenesis of affective disorders. *J Exerc Rehabil*. 16:2-9.
 49. Dean K, Murray RM (2005): Environmental risk factors for psychosis. *Dialogues Clin Neurosci*. 7:69-80.

50. Hatzimanolis A, Avramopoulos D, Arking DE, Moes A, Bhatnagar P, Lencz T, et al. (2018): Stress-Dependent Association Between Polygenic Risk for Schizophrenia and Schizotypal Traits in Young Army Recruits. *Schizophr Bull.* 44:338-347.

Journal Pre-proof

Predictors	Group	Variable Type	riable Type (Recorded Values)	Recorded Values
able to confide f2110	Psychosoc	Categorical	Ord Binary	Never or almost never =0 Once every few months=1 About once a month=1 About once a week=1 2-4 times a week=1 Almost daily=1 Do not know =NA Prefer not to answer =NA
alcohol drinker status f20117	Lifestyle ai	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
attendantsdisabilitymobility	Sociodemc	Categorical	Unc Binary	(Reference) C Do not know=NA Prefer not to answer=NA
avoided activities or situation	Mental he	Categorical	Ord Binary	Not at all=0 A little bit=1 Quite a bit=1 Moderately=1 Extremely=1 Prefer not to answer=NA
been in serious accident belii	Mental he	Categorical	Ord Binary	Never=0 Yes, but not in the last 12 months=1 Yes, within the last 12 months=1 Prefer not to answer=NA
been involved in combat or e	Mental he	Categorical	Ord Binary	Never=0 Yes, but not in the last 12 months=1 Yes, within the last 12 months=1 Prefer not to answer=NA
belief that own life is meanin	Mental he	Categorical	Ord Binary	Not at all=0 A little=1 A moderate amount=1 Very much=1 An extreme amount=1 Prefer not to answer=NA Do not know=NA
belittlement by partner or ex	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
blood clot dvt bronchitis emf	Health anc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
chest pain or discomfort f23	Health anc	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
contraindications for spirom	Physical m	Categorical	Ord Binary	No=0 Yes=1 Unsure=NA
current employment status f	Sociodemc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
daytime dozing sleeping narc	Lifestyle ai	Categorical	Ord Binary	Never/rarely=0 Sometimes=1 Often=1 All of the time=1 Prefer not to answer=NA Do not know=NA
diagnosed with lifethreatenir	Mental he	Categorical	Ord Binary	Never=0 Yes, but not in the last 12 months=1 Yes, within the last 12 months=1 Prefer not to answer=NA
drive faster than motorway s	Lifestyle ai	Categorical	Ord Binary	Never/rarely=0 Sometimes=1 Often=1 Most of the time=1 Prefer not to answer=NA Do not know=NA Do not drive on the motorway=NA
ever addicted to any substan	Mental he	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
ever been injured or injured	Mental he	Categorical	Ord Binary	No=0 Yes, but not in the last year Yes, during the last year Do not know=NA Prefer not to answer=NA
ever contemplated selfharm	Mental he	Categorical	Ord Binary	No=0 Yes, once=1 Yes, more than once =1 Prefer not to answer=NA
ever felt worried tense or an	Mental he	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
ever had bowel cancer screei	Health anc	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
ever had known person conc	Mental he	Categorical	Ord Binary	No=0 Yes, but not in the last year=1 Yes, during the last year =1 Prefer not to answer=NA
ever had period extreme irrit	Mental he	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
ever had period of mania exc	Mental he	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
ever had prolonged feelings r	Mental he	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer =NA
ever selfharmmed f20480	Mental he	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA
ever smoked f20160	Lifestyle ai	Categorical	Ord Binary	No=0 Yes=1
ever sought or received profi	Mental he	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
ever suffered mental distress	Mental he	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
ever taken cannabis f20453	Mental he	Categorical	Ord Binary	No=0 Yes, 1-2 times=1 Yes, 3-10 times=1 Yes, 11-100 times=1 Yes, more than 100 times=1 Prefer not to answer=NA
ever thought that life not wo	Mental he	Categorical	Ord Binary	No=0 Yes, once=1 Yes, more than once =1
falls in the last year f2296	Health anc	Categorical	Ord Binary	No falls=0 Only one fall=1 More than one fall=1 Prefer not to answer=NA
fedup feelings f1960	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
felt hated by family member	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
felt loved as a child f20489	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
felt very upset when remind	Mental he	Categorical	Ord Binary	Not at all=0 A little bit=1 Quite a bit=1 Moderately=1 Extremely=1 Prefer not to answer=NA
fractured broken bones in	Health an	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
frequency of depressed moo	Psychosoc	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Do not know=NA Prefer not to answer=NA
frequency of friendfamily visi	Psychosoc	Categorical	Ord Binary	No friends/family outside household =0 Never or almost never =0 Once every few months=1 About once a month=1 About once a week=1 2-4 times a week=1 Almost daily=1 Do not know=NA Prefer not to answer=NA
frequency of tiredness restle	Psychosoc	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Do not know=NA Prefer not to answer=NA
frequency of tiredness lethar	Psychosoc	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Do not know=NA Prefer not to answer=NA
frequency of unenthusiasim c	Psychosoc	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Do not know=NA Prefer not to answer=NA
general happiness f20458	Mental he	Categorical	Ord Binary	Extremely unhappy=0 Very unhappy=1 Moderately unhappy=1 Moderately happy=1 Very happy=1 Extremely happy=1 Do not know=NA Prefer not to answer=NA
general happiness with own i	Mental he	Categorical	Ord Binary	Extremely unhappy=0 Very unhappy=1 Moderately unhappy=1 Moderately happy=1 Very happy=1 Extremely happy=1 Do not know=NA Prefer not to answer=NA
getting up in morning f1170	Lifestyle ai	Categorical	Ord Binary	Not at all easy=0 Not very easy=1 Fairly easy=1 Very easy=1 Prefer not to answer=NA Do not know=NA
guilty feelings f2030	Mental he	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
hearing difficultyproblems f2	Health anc	Categorical	Ord Binary	No=0 Yes=1 I am completely deaf=1 Do not know=NA Prefer not to answer=NA
hot drink temperature f1518	Lifestyle ai	Categorical	Ord Binary	Warm=0 Hot=1 Very hot=1 Do not drink hot drinks=NA Prefer not to answer=NA
illness injury bereavement st	Psychosoc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
irritability f1940	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
leisure/social activities f6160	Psychosoc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
loneliness isolation f2020	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
longstanding illness disability	Health anc	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
major dietary changes in the	Lifestyle ai	Categorical	Ord Binary	No=0 Yes, because of illness=1 Yes, because of other reasons=1 Prefer not to answer=NA
medication for pain relief cor	Health anc	Categorical	Ord Binary	(Reference) C Do not know=NA Prefer not to answer=NA
milk type used f1418	Lifestyle ai	Categorical	Unc Binary	(Reference) C Do not know =NA Prefer not to answer=NA
miserableness f1930	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
mood swings f1920	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
mouthteeth dental problems	Health anc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
nap during day f1190	Lifestyle ai	Categorical	Ord Binary	Never/rarely=0 Sometimes=1 Usually=1 Prefer not to answer=NA
nervous feelings f1970	Mental he	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
nitrogen dioxide air pollution	Local Envir	Numerical	Continuous	
other eye problems f2227	Health anc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA
other serious medical conditi	Health anc	Categorical	Ord Binary	No=0 Yes - you will be asked about this later by an interviewer=1 Prefer not to answer=NA Do not know=NA
overall health rating f2178	Health anc	Categorical	Ord Binary	Poor=0 Fair=1 Good=1 Excellent=1 Do not know=NA Prefer not to answer=NA
pain types experienced in las	Health anc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
particulate matter air polluti	Local Envir	Numerical	Continuous	
physical violence by partner r	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
physically abused by family a	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
plays computer games f2237	Lifestyle ai	Categorical	Ord Binary	Never/rarely=0 Sometimes=1 Often=1 Prefer not to answer=NA
pork intake f1389	Lifestyle ai	Categorical	Ord Binary	Never=0 Less than once a week=1 Once a week=1 2-4 times a week=1 5-6 times a week=1 Once or more daily=1 Prefer not to answer=NA Do not know=NA
poultry intake f1359	Lifestyle ai	Categorical	Ord Binary	Never=0 Less than once a week=1 Once a week=1 2-4 times a week=1 5-6 times a week=1 Once or more daily=1 Prefer not to answer=NA Do not know =NA
recent changes in speedamo	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent easy annoyance or irri	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent feelings of depression	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent feelings of foreboding	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent feelings of inadequacy	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent feelings of tiredness o	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent feelings or nervousne	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent poor appetite or overi	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent restlessness f20516	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent thoughts of suicide or	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent trouble concentrating	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent trouble relaxing f2051	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
recent worrying too much ab	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
repeated disturbing thought:	Mental he	Categorical	Ord Binary	Not at all=0 A little bit=1 Moderately=1 Quite a bit=1 Extremely=1 Prefer not to answer=NA
risk taking f2040	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
seen a psychiatrist for nerves	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
seen doctor gp for nerves an:	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
sensitivity hurt feelings f195C	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
sexual interference by partnr	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
sexually molested as a child f	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
sleeplessness insomnia f120C	Lifestyle ai	Categorical	Ord Binary	Never/rarely=0 Sometimes=1 Usually=1 Prefer not to answer=NA
snoring f1210	Lifestyle ai	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
someone to take to doctor w	Mental he	Categorical	Ord Binary	Never true=0 Rarely true=1 Sometimes true=1 Often=1 Very often true=1 Prefer not to answer =NA
suffer from nerves f2010	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Do not know=NA Prefer not to answer=NA
taking other prescription me	Health anc	Categorical	Ord Binary	No=0 Yes - you will be asked about this later by an interviewer=1 Prefer not to answer=NA Do not know=NA
tense highly strung f1990	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
trouble falling or staying asle	Mental he	Categorical	Ord Binary	Not at all=0 Several days=1 More than half the days=1 Nearly every day=1 Prefer not to answer=NA
type of accommodation lived	Sociodemc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
use of sunuv protection f226	Lifestyle ai	Categorical	Ord Binary	Do not go out in sunshine=0 Never/rarely=0 Sometimes=1 Most of the time=1 Always=1 Do not know=NA Prefer not to answer=NA
variation in diet f1548	Lifestyle ai	Categorical	Ord Binary	Never/rarely=0 Sometimes=1 Often=1 Do not know=NA Prefer not to answer=NA
victim of physically violent cri	Mental he	Categorical	Ord Binary	Never=0 Yes, but not in the last 12 months=1 Yes, within the last 12 months=1 Prefer not to answer=NA
victim of sexual assault f2053	Mental he	Categorical	Ord Binary	Never=0 Yes, but not in the last 12 months=1 Yes, within the last 12 months=1 Prefer not to answer=NA
vitamin and mineral supplm	Health anc	Categorical	Unc Binary	(Reference) C Prefer not to answer=NA
weight change compared wit	Health anc	Categorical	Ord Binary	No - weigh about the same=0 Yes - gained weight =1 Yes - lost weight=1 Do not know=NA Prefer not to answer=NA
wheeze or whistling in the ch	Health anc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
witnessed sudden violent de:	Mental he	Categorical	Ord Binary	Never=0 Yes, but not in the last 12 months=1 Yes, within the last 12 month=1 Prefer not to answer=NA
worrier anxious feelings f198	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
worry too long after embarr:	Psychosoc	Categorical	Ord Binary	No=0 Yes=1 Prefer not to answer=NA Do not know=NA
age first had sexual intercour	Lifestyle ai	Numerical	Continuous	(-)3=NA (-)2 =NA (-)1 =NA
alkaline phosphatase f30610	Biological :	Numerical	Continuous	
arm fat mass left f23124	Physical m	Numerical	Continuous	
body mass index bmi f21001	Physical m	Numerical	Continuous	
cereal intake f1458	Lifestyle ai	Numerical	Continuous	
creative protein f30710	Biological :	Numerical	Continuous	
cystatin c f30720	Biological :	Numerical	Continuous	
forced expiratory volume in :	Physical m	Numerical	Continuous	
gamma glutamyltransferase f	Biological :	Numerical	Continuous	
glycated haemoglobin hba1c	Biological :	Numerical	Continuous	

hand grip strength right f47	Physical m Numerical	Continuous
high light scatter reticulocyte	Biological : Numerical	Continuous
hip circumference f49	Physical m Numerical	Continuous
igf1 f30770	Biological : Numerical	Continuous
immature reticulocyte fractic	Biological : Numerical	Continuous
impedance of leg left f23108	Physical m Numerical	Continuous
impedance of whole body f2:	Physical m Numerical	Continuous
length of time at current add	Sociodemc Numerical	Continuous
mean time to correctly identi	Cognitive f Numerical	Continuous
natural environment percent	Local Envir Numerical	Continuous
neutrophill count f30140	Biological : Numerical	Continuous
number of daysweek of vigor	Lifestyle a Numerical	Binary
number of operations selfrep	Operation Numerical	Continuous
number of selfreported nonc	Medical cc Numerical	Continuous
number of treatmentsmedic:	Medicatio Numerical	Continuous
peak expiratory flow pef f306	Physical m Numerical	Continuous
pulse rate automated readin	Biological : Numerical	Continuous
tea intake f1488	Lifestyle a Numerical	Continuous
time spent using computer f:	Lifestyle a Numerical	Continuous
townsend deprivation index :	Populatio Numerical	Continuous
triglycerides f30870	Biological : Numerical	Continuous
trunk fat percentage f23127	Physical m Numerical	Continuous
urate f30880	Biological : Numerical	Continuous
vitamin d f30890	Biological : Numerical	Continuous
waist circumference f48	Physical m Numerical	Continuous
weight f21002	Physical m Numerical	Continuous
white blood cell leukocyte co	Biological : Numerical	Continuous

(-)3=NA | (-)1 =NA|0=0, the rest=1

(-)10=0 | (-)3=NA | (-)1=NA
 (-)10=0 | (-)3=NA | (-)1=NA

Journal Pre-proof

Predictors	Discovery dataset					Replication dataset					Combined dataset				
	R2 (%)	OR	lower.CI	upper.CI	P-value	R2 (%)	OR	lower.CI	upper.CI	P-value	R2 (%)	OR	lower.CI	upper.CI	P-value
able to confide f2110	0.697	0.706	0.645	0.772	2.90E-14	0.640	0.781	0.712	0.858	2.08E-07	0.663	0.742	0.696	0.792	1.39E-19
age first had sexual intercourse f2139	0.646	0.885	0.852	0.919	2.25E-10	0.627	0.901	0.867	0.935	5.51E-08	0.635	0.893	0.869	0.917	7.96E-17
alcohol drinker status f20117	0.743	1.647	1.464	1.852	8.53E-17	0.714	1.475	1.308	1.663	2.27E-10	0.725	1.558	1.433	1.695	3.75E-25
alkaline phosphatase f30610	0.686	1.106	1.076	1.138	1.43E-12	0.794	1.103	1.071	1.135	2.49E-11	0.738	1.104	1.083	1.127	2.28E-22
arm fat mass left f23124	1.077	1.189	1.158	1.221	9.84E-38	1.116	1.184	1.154	1.216	3.89E-36	1.096	1.187	1.165	1.209	3.97E-72
attendancedisabilitymobility allowance f6146	1.579	3.351	2.956	3.798	8.94E-80	1.678	3.435	3.027	3.899	1.51E-81	1.627	3.392	3.103	3.708	2.60E-159
avoided activities or situations because of previous stressful e	3.137	2.534	2.369	2.711	1.80E-160	3.148	2.520	2.355	2.696	5.60E-158	3.142	2.527	2.409	2.651	5.00E-324
been in serious accident believed to be lifethreatening f20526	1.560	2.182	2.001	2.379	1.09E-69	1.652	2.199	2.016	2.398	8.20E-71	1.605	2.190	2.060	2.329	1.50E-138
been involved in combat or exposed to warzone f20527	0.773	1.924	1.670	2.217	1.22E-19	0.866	1.965	1.708	2.261	3.91E-21	0.819	1.945	1.760	2.148	4.00E-39
belief that own life is meaningful f20460	1.060	0.332	0.282	0.391	2.86E-40	1.047	0.338	0.286	0.399	3.55E-37	1.053	0.335	0.298	0.376	1.20E-75
belittlement by partner or expartner as an adult f20521	2.972	2.436	2.277	2.606	2.10E-147	3.171	2.487	2.325	2.661	1.10E-154	3.070	2.462	2.347	2.582	5.60E-300
blood clot dvt bronchitis emphysema asthma rhinitis eczema	0.860	1.385	1.297	1.479	2.83E-22	0.873	1.347	1.261	1.439	7.28E-19	0.865	1.366	1.304	1.431	2.01E-39
body mass index bmi f21001	1.275	1.237	1.202	1.272	2.79E-48	1.288	1.226	1.191	1.261	4.44E-45	1.280	1.231	1.207	1.256	1.68E-91
cereal intake f1458	0.604	0.921	0.892	0.951	4.52E-07	0.673	0.921	0.892	0.951	4.99E-07	0.638	0.921	0.900	0.942	1.04E-12
chest pain or discomfort f2335	1.960	2.213	2.051	2.387	9.72E-94	1.688	2.037	1.885	2.202	8.25E-72	1.819	2.124	2.012	2.243	5.60E-163
contraindications for spirometry f3088	0.584	1.331	1.179	1.502	3.55E-06	0.660	1.367	1.212	1.542	3.58E-07	0.621	1.349	1.238	1.469	6.23E-12
creactive protein f30710	0.611	1.079	1.050	1.108	3.26E-08	0.715	1.071	1.043	1.099	3.31E-07	0.661	1.075	1.055	1.095	5.73E-14
current employment status f6142	0.629	1.262	1.166	1.366	7.52E-09	0.668	1.221	1.128	1.322	7.84E-07	0.647	1.241	1.174	1.313	3.48E-14
cystatin c f30720	0.706	1.118	1.085	1.151	9.58E-14	0.957	1.145	1.112	1.180	4.21E-19	0.828	1.131	1.108	1.155	1.45E-31
daytime dozing sleeping narcolepsy f1220	0.855	1.457	1.352	1.570	5.43E-23	0.825	1.378	1.278	1.486	9.10E-17	0.837	1.417	1.344	1.494	7.19E-38
diagnosed with lifethreatening illness f20528	0.933	1.555	1.435	1.685	3.34E-27	0.832	1.428	1.316	1.550	1.32E-17	0.878	1.491	1.408	1.579	1.38E-42
drive faster than motorway speed limit f1100	0.575	0.817	0.761	0.877	2.35E-08	0.587	0.872	0.812	0.936	1.53E-04	0.576	0.844	0.803	0.888	3.51E-11
ever addicted to any substance or behaviour f20401	1.840	2.730	2.478	3.007	8.28E-92	1.893	2.727	2.473	3.006	3.20E-90	1.865	2.728	2.547	2.922	5.00E-180
ever been injured or injured someone else through drinking a	1.173	2.364	2.102	2.658	5.98E-47	1.040	2.111	1.866	2.387	1.38E-32	1.102	2.238	2.055	2.436	3.29E-77
ever contemplated selfharm f20485	5.632	3.926	3.662	4.209	5.00E-324	5.412	3.777	3.523	4.050	1.80E-305	5.521	3.851	3.666	4.045	5.00E-324
ever felt worried tense or anxious for most of a month or long	4.011	2.799	2.612	2.998	5.80E-188	4.550	2.981	2.784	3.192	2.40E-214	4.279	2.889	2.752	3.033	5.00E-324
ever had bowel cancer screening f2345	0.579	1.175	1.089	1.267	2.92E-05	0.662	1.228	1.139	1.324	8.91E-08	0.618	1.201	1.139	1.267	1.65E-11
ever had known person concerned about or recommend redu	1.165	1.963	1.785	2.158	4.55E-44	1.170	1.921	1.744	2.116	4.53E-40	1.166	1.942	1.815	2.078	2.72E-82
ever had period extreme irritability f20502	3.996	2.784	2.603	2.977	2.90E-196	4.181	2.837	2.653	3.035	1.50E-203	4.087	2.810	2.680	2.947	5.00E-324
ever had period of mania excitability f20501	5.461	6.540	5.969	7.165	5.00E-324	4.955	5.955	5.428	6.533	5.00E-324	5.201	6.240	5.847	6.660	5.00E-324
ever had prolonged feelings of sadness or depression f20446	4.310	3.208	2.964	3.472	7.20E-183	3.892	2.944	2.724	3.183	8.90E-163	4.096	3.072	2.906	3.248	5.00E-324
ever selfharmmed f20480	3.282	4.430	4.021	4.880	1.30E-199	3.689	4.719	4.291	5.190	2.30E-224	3.484	4.574	4.274	4.895	5.00E-324
ever smoked f20160	0.871	1.397	1.305	1.496	1.07E-21	0.931	1.391	1.299	1.489	2.96E-21	0.900	1.394	1.328	1.463	2.71E-41
ever sought or received professional help for mental distress t	4.276	2.890	2.698	3.094	2.30E-202	4.497	2.952	2.756	3.163	6.90E-209	4.385	2.921	2.782	3.066	2.60E-159
ever suffered mental distress preventing usual activities f2050	5.430	3.345	3.124	3.580	8.70E-265	5.185	3.206	2.996	3.432	4.10E-248	5.306	3.275	3.121	3.436	5.00E-324
ever taken cannabis f20453	1.316	1.722	1.602	1.850	9.84E-50	1.358	1.703	1.585	1.829	8.50E-48	1.336	1.712	1.627	1.801	1.11E-95
ever thought that life not worth living f20479	5.773	3.467	3.242	3.708	2.30E-289	5.227	3.220	3.012	3.442	8.40E-258	5.495	3.341	3.187	3.503	5.00E-324
falls in the last year f2296	1.295	1.757	1.631	1.893	8.45E-50	1.446	1.811	1.681	1.950	2.34E-55	1.369	1.784	1.692	1.880	3.30E-103
fedup feelings f1960	1.580	1.750	1.638	1.869	2.89E-62	1.662	1.751	1.639	1.870	2.18E-62	1.620	1.750	1.670	1.833	9.70E-123
felt hated by family member as a child f20487	3.458	2.845	2.652	3.053	2.80E-186	3.415	2.805	2.613	3.010	5.20E-180	3.436	2.825	2.688	2.969	5.00E-324
felt loved as a child f20489	0.948	0.341	0.287	0.406	1.17E-33	1.179	0.293	0.248	0.347	2.14E-46	1.060	0.316	0.280	0.357	9.88E-78
felt very upset when reminded of stressful experience in past	3.191	2.415	2.260	2.581	4.90E-149	3.075	2.346	2.196	2.507	5.60E-140	3.132	2.380	2.271	2.495	7.00E-287
forced expiratory volume in 1second fev1 f3063	0.707	0.855	0.817	0.895	2.60E-11	0.790	0.842	0.803	0.882	7.34E-13	0.747	0.849	0.821	0.877	1.31E-22
fracturedbroken bones in last 5 years f2463	0.558	1.245	1.120	1.383	4.56E-05	0.658	1.289	1.162	1.431	1.66E-06	0.607	1.267	1.177	1.364	3.56E-10
frequency of depressed mood in last 2 weeks f2050	2.622	2.333	2.176	2.501	5.20E-126	2.350	2.164	2.018	2.321	4.10E-104	2.480	2.247	2.139	2.360	1.70E-227
frequency of friendfamily visits f1031	0.683	0.445	0.361	0.548	2.57E-14	0.724	0.464	0.373	0.576	4.25E-12	0.702	0.454	0.391	0.528	7.73E-25
frequency of tenseness restlessness in last 2 weeks f2070	2.198	2.084	1.948	2.230	4.60E-100	2.183	2.055	1.920	2.199	3.67E-96	2.190	2.069	1.972	2.171	3.30E-194
frequency of tiredness lethargy in last 2 weeks f2080	1.837	1.882	1.756	2.016	4.82E-72	1.755	1.817	1.696	1.947	9.78E-65	1.795	1.849	1.761	1.942	8.90E-135
frequency of unenthusiasm disinterest in last 2 weeks f2060	2.264	2.251	2.095	2.419	2.90E-108	1.962	2.065	1.920	2.220	2.13E-85	2.106	2.156	2.049	2.269	5.50E-191
gamma glutamyltransferase f30730	0.564	1.059	1.030	1.089	4.22E-05	0.727	1.074	1.045	1.103	2.09E-07	0.643	1.066	1.046	1.087	4.87E-11
general happiness f20458	0.915	0.149	0.110	0.202	1.85E-34	0.907	0.165	0.120	0.227	9.77E-29	0.910	0.157	0.126	0.195	2.27E-61
general happiness with own health f20459	1.220	0.252	0.212	0.300	2.36E-54	1.144	0.282	0.236	0.337	2.55E-44	1.180	0.267	0.236	0.302	1.46E-96
getting up in morning f1170	0.877	0.486	0.425	0.555	1.86E-26	0.993	0.476	0.418	0.542	6.01E-29	0.934	0.481	0.438	0.528	1.12E-53
glycated haemoglobin hba1c f30750	0.716	1.116	1.086	1.148	6.63E-15	0.806	1.112	1.081	1.144	2.21E-13	0.759	1.114	1.093	1.137	9.93E-27
guilty feelings f2030	1.427	1.718	1.605	1.838	4.77E-55	1.411	1.665	1.555	1.782	4.80E-49	1.417	1.691	1.612	1.774	3.90E-102
hand grip strength right f47	0.772	0.816	0.777	0.856	7.76E-17	0.829	0.817	0.779	0.858	3.50E-16	0.800	0.816	0.789	0.845	2.03E-31
hearing difficultyproblems f2247	0.893	1.466	1.362	1.578	2.22E-24	1.062	1.543	1.434	1.660	2.46E-31	0.975	1.504	1.428	1.584	8.78E-54
high light scatter reticulocyte percentage f30290	0.553	1.074	1.044	1.106	8.03E-07	0.739	1.104	1.073	1.136	1.00E-11	0.640	1.089	1.067	1.111	7.26E-17
hip circumference f49	0.908	1.169	1.135	1.204	1.13E-25	1.055	1.185	1.152	1.220	1.42E-30	0.980	1.177	1.153	1.202	2.00E-54

hot drink temperature f1518	0.647	0.767	0.707	0.833	2.00E-10	0.767	0.737	0.680	0.800	1.84E-13	0.706	0.752	0.710	0.797	3.06E-22
igf1 f30770	0.583	0.929	0.897	0.962	3.56E-05	0.767	0.899	0.868	0.931	3.52E-09	0.671	0.914	0.891	0.937	1.23E-12
illness injury bereavement stress in last 2 years f6145	1.283	1.596	1.495	1.703	4.80E-45	1.286	1.558	1.460	1.663	1.05E-40	1.283	1.577	1.506	1.651	6.98E-84
immature reticulocyte fraction f30280	0.642	1.126	1.089	1.164	3.12E-12	0.677	1.090	1.055	1.127	2.90E-07	0.653	1.108	1.082	1.134	1.21E-17
impedance of leg left f23108	0.705	0.874	0.843	0.906	2.26E-13	0.847	0.858	0.828	0.889	3.36E-17	0.774	0.866	0.844	0.888	7.27E-29
impedance of whole body f23106	0.694	0.854	0.817	0.891	7.42E-13	0.864	0.826	0.792	0.863	3.86E-18	0.776	0.840	0.815	0.866	3.61E-29
irritability f1940	0.965	1.472	1.373	1.577	7.36E-28	1.088	1.503	1.403	1.611	7.25E-31	1.025	1.487	1.416	1.562	6.03E-57
leg fatfree mass right f23113	0.756	1.256	1.191	1.325	4.16E-17	0.854	1.262	1.198	1.330	3.48E-18	0.804	1.259	1.213	1.307	1.13E-33
leisuresocial activities f6160	0.837	1.392	1.296	1.496	1.43E-19	0.910	1.401	1.304	1.506	3.25E-20	0.873	1.397	1.328	1.470	3.81E-38
length of time at current address f699	0.584	0.915	0.882	0.950	2.81E-06	0.714	0.891	0.858	0.925	1.19E-09	0.646	0.903	0.880	0.927	2.65E-14
loneliness isolation f2020	1.967	2.162	2.008	2.328	6.32E-93	2.034	2.146	1.993	2.309	4.98E-92	1.999	2.154	2.044	2.269	6.00E-183
longstanding illness disability or infirmity f2188	2.402	2.155	2.015	2.305	1.70E-111	2.347	2.090	1.954	2.235	8.00E-103	2.372	2.122	2.024	2.225	3.80E-212
major dietary changes in the last 5 years f1538	1.206	1.563	1.465	1.667	1.49E-41	1.210	1.531	1.435	1.634	5.14E-38	1.207	1.547	1.478	1.619	9.87E-78
mean time to correctly identify matches f20023	0.589	1.082	1.048	1.118	1.57E-06	0.679	1.092	1.058	1.128	5.48E-08	0.633	1.087	1.063	1.112	4.44E-13
medication for pain relief constipation heartburn f6154	1.130	1.513	1.418	1.615	8.26E-36	0.833	1.315	1.232	1.404	1.88E-16	0.963	1.411	1.347	1.477	1.13E-48
milk type used f1418	0.565	1.151	1.077	1.229	3.23E-05	0.696	1.208	1.131	1.291	2.06E-08	0.627	1.179	1.125	1.235	5.13E-12
miserableness f1930	2.348	2.081	1.946	2.225	4.00E-102	2.135	1.957	1.831	2.092	3.83E-87	2.237	2.018	1.925	2.115	6.00E-187
mood swings f1920	1.926	1.887	1.766	2.016	1.71E-78	1.820	1.824	1.708	1.949	2.05E-71	1.871	1.855	1.770	1.944	7.30E-148
mouthteeth dental problems f6149	0.880	1.394	1.305	1.488	4.62E-23	0.919	1.374	1.286	1.468	3.65E-21	0.898	1.384	1.321	1.450	1.53E-42
nap during day f1190	1.047	1.492	1.397	1.593	7.99E-33	0.986	1.416	1.326	1.512	3.14E-25	1.013	1.453	1.388	1.523	4.36E-56
natural environment percentage buffer 1000m f24506	0.568	0.932	0.902	0.963	3.05E-05	0.639	0.929	0.898	0.960	1.20E-05	0.603	0.930	0.909	0.952	1.47E-09
nervous feelings f1970	1.060	1.577	1.467	1.695	6.57E-35	1.153	1.575	1.465	1.693	7.96E-35	1.105	1.576	1.497	1.658	6.00E-68
neutrophill count f30140	0.621	1.103	1.069	1.138	7.15E-10	0.703	1.099	1.066	1.134	2.18E-09	0.661	1.101	1.077	1.126	8.80E-18
nitrogen dioxide air pollution 2007 f24018	0.582	1.071	1.038	1.104	1.56E-05	0.633	1.063	1.030	1.097	1.41E-04	0.607	1.067	1.044	1.091	8.89E-09
number of daysweek of vigorous physical activity 10 minutes	0.689	0.786	0.735	0.840	1.73E-12	0.658	0.846	0.791	0.905	1.20E-06	0.668	0.815	0.777	0.855	3.61E-17
number of operations selfreported f136	0.885	1.174	1.138	1.211	1.70E-24	0.845	1.146	1.111	1.182	5.02E-18	0.862	1.160	1.135	1.185	1.37E-40
number of selfreported noncancer illnesses f135	2.139	1.348	1.312	1.384	2.20E-106	1.993	1.323	1.288	1.359	4.25E-92	2.063	1.335	1.310	1.361	3.30E-196
number of treatmentsmedications taken f137	1.729	1.304	1.268	1.340	2.58E-79	1.560	1.272	1.237	1.308	8.21E-64	1.641	1.288	1.263	1.313	9.70E-141
other eye problems f2227	0.765	1.444	1.326	1.572	3.07E-17	0.776	1.398	1.283	1.523	1.95E-14	0.769	1.421	1.337	1.509	5.24E-30
other serious medical conditiondisability diagnosed by doctor	1.746	1.982	1.844	2.130	4.07E-77	1.658	1.898	1.765	2.041	8.52E-67	1.700	1.939	1.843	2.041	8.30E-142
overall health rating f2178	1.622	0.279	0.245	0.317	4.50E-83	1.676	0.276	0.242	0.315	5.36E-82	1.648	0.278	0.253	0.304	4.40E-163
pain types experienced in last month f6159	1.184	1.574	1.470	1.685	1.20E-38	1.285	1.589	1.484	1.702	3.74E-40	1.234	1.582	1.507	1.660	5.39E-77
particulate matter air pollution pm10 2007 f24019	0.615	1.089	1.055	1.124	1.27E-07	0.721	1.105	1.070	1.140	8.74E-10	0.666	1.097	1.073	1.122	7.00E-16
peak expiratory flow pef f3064	0.611	0.907	0.871	0.945	2.64E-06	0.706	0.889	0.853	0.926	1.45E-08	0.656	0.898	0.872	0.924	2.33E-13
physical violence by partner or expartner as an adult f20523	2.027	2.296	2.125	2.481	2.85E-98	1.917	2.192	2.027	2.370	7.31E-86	1.970	2.244	2.124	2.371	5.60E-182
physically abused by family as a child f20488	1.901	2.032	1.893	2.180	3.25E-86	1.965	2.036	1.897	2.186	6.04E-86	1.933	2.034	1.935	2.138	3.30E-170
plays computer games f2237	0.750	1.347	1.254	1.447	3.08E-16	0.745	1.286	1.196	1.382	9.19E-12	0.745	1.316	1.251	1.385	2.97E-26
pork intake f1389	0.565	0.835	0.768	0.907	2.08E-05	0.652	0.817	0.752	0.886	1.19E-06	0.608	0.826	0.779	0.875	1.13E-10
poultry intake f1359	0.584	0.746	0.661	0.841	1.57E-06	0.671	0.727	0.647	0.816	7.59E-08	0.627	0.736	0.677	0.800	5.91E-13
pulse rate automated reading f102	0.699	1.121	1.085	1.158	4.69E-12	0.760	1.118	1.082	1.154	9.66E-12	0.729	1.119	1.094	1.145	2.78E-22
recent changes in speedamount of moving or speaking f20518	3.500	4.075	3.731	4.451	8.60E-214	3.235	3.872	3.538	4.238	1.30E-189	3.365	3.974	3.731	4.233	5.00E-324
recent easy annoyance or irritability f20505	2.164	2.035	1.904	2.174	6.95E-98	2.301	2.067	1.935	2.208	8.20E-103	2.231	2.051	1.957	2.149	1.20E-198
recent feelings of depression f20510	2.814	2.366	2.212	2.531	3.00E-139	2.634	2.264	2.116	2.422	1.80E-124	2.722	2.315	2.207	2.427	1.80E-261
recent feelings of foreboding f20512	2.996	2.588	2.413	2.776	1.30E-155	3.043	2.582	2.407	2.770	1.00E-154	3.019	2.585	2.460	2.717	5.00E-324
recent feelings of inadequacy f20507	2.904	2.468	2.304	2.644	2.20E-146	2.883	2.433	2.271	2.606	1.20E-141	2.893	2.451	2.334	2.573	6.30E-286
recent feelings of tiredness or low energy f20519	2.305	2.087	1.948	2.236	1.19E-96	2.499	2.144	2.000	2.298	1.00E-102	2.401	2.115	2.014	2.222	2.50E-197
recent feelings or nervousness or anxiety f20506	2.508	2.170	2.031	2.318	7.30E-117	2.544	2.160	2.022	2.308	9.60E-116	2.525	2.165	2.066	2.269	1.50E-230
recent poor appetite or overeating f20511	2.938	2.526	2.356	2.709	1.10E-149	2.709	2.397	2.235	2.571	5.50E-132	2.820	2.461	2.342	2.586	2.40E-279
recent restlessness f20516	2.539	2.587	2.398	2.792	2.60E-132	2.460	2.506	2.322	2.706	1.70E-122	2.498	2.547	2.413	2.688	1.20E-252
recent thoughts of suicide or selfharm f20513	3.141	4.355	3.948	4.805	2.80E-189	2.699	3.836	3.470	4.241	7.50E-152	2.913	4.088	3.811	4.386	5.00E-324
recent trouble concentrating on things f20508	3.522	2.768	2.585	2.964	3.00E-187	3.241	2.625	2.450	2.812	2.30E-166	3.379	2.696	2.568	2.830	5.00E-324
recent trouble relaxing f20515	2.644	2.224	2.082	2.376	1.60E-124	2.610	2.184	2.044	2.333	5.10E-119	2.626	2.204	2.103	2.309	1.80E-241
recent worrying too much about different things f20520	2.168	2.011	1.883	2.148	2.20E-96	2.300	2.041	1.911	2.179	2.20E-100	2.233	2.026	1.934	2.122	9.60E-195
repeated disturbing thoughts of stressful experience in past m	3.279	2.476	2.320	2.644	6.70E-163	3.266	2.449	2.294	2.615	1.20E-158	3.272	2.463	2.351	2.579	5.00E-180
risk taking f2040	1.098	1.562	1.457	1.676	7.85E-36	1.312	1.636	1.526	1.754	8.43E-44	1.203	1.599	1.522	1.680	1.22E-77
seen a psychiatrist for nerves anxiety tension or depression f2	3.719	3.376	3.129	3.643	4.60E-216	3.996	3.476	3.224	3.748	2.10E-230	3.856	3.426	3.247	3.614	5.00E-324
seen doctor gp for nerves anxiety tension or depression f2090	3.395	2.507	2.347	2.679	8.70E-164	3.359	2.458	2.301	2.626	1.60E-157	3.375	2.482	2.369	2.601	2.30E-179
sensitivity hurt feelings f1950	0.980	1.452	1.356	1.555	1.17E-26	1.022	1.454	1.358	1.556	4.28E-27	1.001	1.453	1.385	1.525	4.97E-52
sexual interference by partner or expartner without consent a	1.885	2.869	2.594	3.173	1.34E-93	1.870	2.759	2.496	3.049	7.91E-88	1.877	2.813	2.620	3.020	2.30E-179
sexually molested as a child f20490	1.798	2.401	2.200	2.621	1.64E-85	1.687	2.253	2.062	2.462	3.00E-72	1.739	2.326	2.185	2.475	1.70E-155
sleeplessness insomnia f1200	0.788	1.412	1.302	1.530	5.01E-17	0.827	1.379	1.273	1.494	3.63E-15	0.806	1.395	1.318	1.477	1.38E-30

snoring f1210	0.630	1.232	1.148	1.323	9.04E-09	0.740	1.293	1.205	1.388	9.35E-13	0.681	1.263	1.201	1.328	7.47E-20
someone to take to doctor when needed as a child f20491	0.660	0.561	0.470	0.671	2.14E-10	0.650	0.652	0.539	0.790	1.20E-05	0.652	0.603	0.530	0.687	2.97E-14
suffer from nerves f2010	1.281	1.733	1.609	1.866	8.38E-48	1.463	1.790	1.663	1.926	2.46E-54	1.371	1.761	1.671	1.855	3.50E-100
taking other prescription medications f2492	1.480	1.699	1.591	1.814	3.04E-56	1.294	1.575	1.475	1.682	6.55E-42	1.381	1.636	1.562	1.714	8.59E-96
tea intake f1488	0.564	1.066	1.035	1.099	2.88E-05	0.654	1.077	1.044	1.110	2.16E-06	0.608	1.071	1.049	1.095	2.88E-10
tense highly strung f1990	1.564	1.959	1.815	2.115	1.61E-66	1.441	1.850	1.712	1.999	1.60E-54	1.500	1.904	1.803	2.011	7.10E-119
time spent using computer f1080	0.931	1.165	1.133	1.197	1.30E-27	0.915	1.148	1.116	1.181	4.01E-22	0.921	1.156	1.134	1.179	6.77E-48
townsend deprivation index at recruitment f189	1.239	1.237	1.201	1.274	1.52E-44	1.196	1.218	1.182	1.255	1.51E-38	1.216	1.227	1.202	1.253	3.49E-81
triglycerides f30870	0.872	1.166	1.131	1.202	6.35E-23	0.900	1.140	1.106	1.174	1.37E-17	0.882	1.152	1.128	1.177	1.28E-38
trouble falling or staying asleep or sleeping too much f20517	1.754	1.833	1.713	1.962	8.16E-69	2.013	1.924	1.797	2.060	4.92E-79	1.881	1.878	1.790	1.970	9.40E-146
trunk fat percentage f23127	0.957	1.221	1.177	1.266	2.89E-27	0.912	1.185	1.143	1.228	1.91E-20	0.931	1.203	1.172	1.234	9.10E-46
type of accommodation lived in f670	0.731	1.490	1.352	1.643	1.02E-15	0.921	1.622	1.475	1.784	1.90E-23	0.822	1.556	1.454	1.665	3.84E-37
urate f30880	0.658	1.135	1.091	1.181	3.57E-10	0.757	1.121	1.077	1.165	1.28E-08	0.706	1.128	1.097	1.160	2.72E-17
use of sunuv protection f2267	0.628	0.713	0.638	0.798	2.80E-09	0.720	0.699	0.625	0.783	5.06E-10	0.673	0.706	0.653	0.765	8.18E-18
variation in diet f1548	0.634	1.226	1.143	1.315	1.03E-08	0.836	1.337	1.245	1.435	1.03E-15	0.729	1.280	1.218	1.345	2.34E-22
vascularheart problems diagnosed by doctor f6150	0.775	1.394	1.292	1.503	7.24E-18	0.812	1.363	1.263	1.470	1.22E-15	0.792	1.378	1.306	1.454	7.31E-32
victim of physically violent crime f20529	1.797	2.008	1.868	2.158	1.61E-79	1.829	1.993	1.854	2.142	3.42E-78	1.813	2.000	1.900	2.105	9.40E-156
victim of sexual assault f20531	3.036	2.734	2.539	2.944	4.60E-156	2.698	2.548	2.365	2.745	1.40E-133	2.863	2.639	2.504	2.782	4.10E-287
vitamin and mineral supplements f6155	0.679	1.261	1.179	1.348	1.39E-11	0.792	1.292	1.209	1.382	6.21E-14	0.734	1.276	1.217	1.338	6.36E-24
vitamin d f30890	0.829	0.855	0.825	0.886	7.10E-18	0.907	0.859	0.829	0.890	4.59E-17	0.867	0.857	0.836	0.879	2.34E-33
waist circumference f48	1.384	1.305	1.262	1.350	1.14E-53	1.382	1.291	1.248	1.335	1.13E-49	1.382	1.298	1.267	1.329	1.90E-101
weight change compared with 1 year ago f2306	0.901	1.405	1.316	1.500	2.37E-24	0.907	1.370	1.283	1.462	5.25E-21	0.903	1.387	1.325	1.453	1.25E-43
weight f21002	1.008	1.220	1.180	1.262	1.33E-31	1.078	1.221	1.181	1.262	5.80E-32	1.043	1.221	1.192	1.250	7.91E-62
wheeze or whistling in the chest in last year f2316	1.132	1.666	1.544	1.797	7.54E-40	1.445	1.808	1.678	1.948	2.54E-54	1.283	1.736	1.646	1.831	8.96E-92
white blood cell leukocyte count f30000	0.608	1.088	1.059	1.118	1.67E-09	0.690	1.075	1.047	1.104	9.05E-08	0.647	1.081	1.061	1.102	1.81E-15
witnessed sudden violent death f20530	1.293	1.866	1.720	2.024	5.98E-51	1.458	1.918	1.769	2.080	3.46E-56	1.374	1.892	1.787	2.004	3.20E-105
worrier anxious feelings f1980	0.878	1.400	1.309	1.499	2.27E-22	1.004	1.417	1.324	1.516	7.96E-24	0.939	1.409	1.343	1.478	1.66E-44
worry too long after embarrassment f2000	0.751	1.324	1.239	1.415	1.38E-16	0.902	1.349	1.262	1.442	1.16E-18	0.825	1.337	1.275	1.401	1.30E-33

R2 (%): explained variance (i.e. including the independent variable, age, and sex), OR: Odds ratios, lower.CI: confidence interval lower limit, upper.CI: confidence interval upper limit.

Predictors	category	PRS-cs-auto (main analyses)										PRSice (sensitivity analyses)									
		PRS					exposure					PRS					exposure				
		R2 (%)	OR	lower.CI	upper.CI	P-value	R2 (%)	OR	lower.CI	upper.CI	P-value	R2 (%)	OR	lower.CI	upper.CI	P-value	R2 (%)	OR	lower.CI	upper.CI	P-value
able_to_confide_f2110	Psychosocial factors	0.208	1.140	1.111	1.170	3.57E-23	0.171	0.731925	0.713215	0.751125	1.75E-20	0.177	1.125	1.097	1.154	4.9985E-20	0.17	0.733	0.714	0.751	2.37E-20
avoided_activities_or_situations_because_of_previous_stressful_experience_in_past_month_f20495	Mental health	0.144	1.115	1.087	1.144	1.72E-16	2.609	2.523394	2.458855	2.589627	9.1E-299	0.177	1.125	1.097	1.155	4.5809E-19	0.159	0.891	0.868	0.914	2.06E-16
been_in_serious_accident_believed_to_be_lifethreatening_f20526	Mental health	0.181	1.130	1.101	1.160	1.31E-20	1.052	2.170386	2.11517	2.227043	1E-128	0.186	1.128	1.101	1.157	3.028E-21	0.205	1.591	1.551	1.631	9.88E-26
been_involved_in_combat_or_exposed_to_warzone_f20527	Mental health	0.207	1.140	1.111	1.169	2.24E-23	0.26	1.888703	1.840743	1.937914	1.65E-33	0.187	1.129	1.101	1.158	1.3566E-20	0.174	1.103	1.075	1.132	3.07E-21
belief_that_own_life_is_meaningful_f20460	Mental health	0.2	1.137	1.108	1.167	3.74E-22	0.557	0.327621	0.319197	0.336266	3.53E-75	0.194	1.132	1.103	1.16	8.2715E-22	0.626	1.197	1.167	1.227	8.64E-75
belittlement_by_partner_or_expartner_as_an_adult_f20521	Mental health	0.154	1.119	1.090	1.148	1.58E-17	2.53	2.454218	2.391535	2.518543	1.2E-282	0.172	1.123	1.095	1.152	1.1135E-19	1.082	3.363	3.280	3.449	4.44E-148
chest_pain_or_discomfort_f2335	Health and medical history	0.198	1.136	1.107	1.166	3.76E-22	1.354	2.152106	2.097111	2.208543	7.3E-161	0.131	1.106	1.079	1.135	3.7813E-15	2.618	2.527	2.465	2.592	5.89E-300
contraindications_for_spirometry_f3088	Physical measures	0.206	1.139	1.111	1.169	2.74E-23	0.089	1.353233	1.318845	1.388518	1.08E-11	0.16	1.119	1.091	1.147	1.9289E-18	1.052	2.171	2.117	2.226	1.02E-128
daytime_dozing_sleeping_narcolepsy_f1220	Lifestyle and environment	0.21	1.141	1.112	1.170	1.1E-23	0.331	1.432902	1.396506	1.470247	2.31E-38	0.18	1.126	1.098	1.155	1.3789E-20	0.26	1.889	1.842	1.937	1.65E-33
diagnosed_with_lifethreatening_illness_f20528	Mental health	0.2	1.137	1.108	1.167	1.29E-22	0.351	1.495919	1.457868	1.534962	3.8E-41	0.176	1.125	1.097	1.154	9.0408E-20	0.559	0.327	0.319	0.335	1.83E-75
drive_faster_than_motorway_speed_limit_f1100	Lifestyle and environment	0.178	1.130	1.099	1.161	1.21E-18	0.094	0.844412	0.821828	0.867616	1.16E-10	0.136	1.109	1.081	1.137	1.168E-15	2.534	2.456	2.395	2.519	4.58E-283
ever_addicted_to_any_substance_or_behaviour_f20401	Mental health	0.163	1.123	1.094	1.153	2.19E-18	1.375	2.745796	2.675341	2.818107	1.4E-174	0.187	1.129	1.101	1.158	2.2721E-21	0.337	1.369	1.335	1.403	5.58E-38
ever_been_injured_or_injured_someone_else_through_drinking_alcohol_f20411	Mental health	0.192	1.134	1.105	1.164	8.9E-22	0.563	2.212979	2.156776	2.270647	8.61E-72	0.202	1.134	1.106	1.163	6.4469E-23	0.81	1.242	1.212	1.274	4.44E-94
ever_contemplated_selfharm_f20485	Mental health	0.127	1.107	1.079	1.137	1.6E-14	4.977	3.839021	3.740308	3.94034	5.00E-324	0.184	1.128	1.1	1.156	4.829E-21	0.099	0.921	0.898	0.944	3.96E-12
ever_felt_worried_tense_or_anxious_for_most_of_a_month_or_longer_f20421	Mental health	0.12	1.105	1.075	1.135	6.63E-13	3.73	2.882286	2.805084	2.961611	5.00E-324	0.174	1.124	1.096	1.153	1.0952E-19	1.352	2.151	2.097	2.206	1.33E-160
ever_had_known_person_concerned_about_or_recommend_reduction_of_alcohol_consumption_f20405	Mental health	0.193	1.135	1.106	1.164	6.35E-22	0.658	1.954916	1.905236	2.005891	2.66E-80	0.187	1.129	1.101	1.158	2.2526E-21	0.09	1.355	1.322	1.390	8.40E-12
ever_had_bowel_cancer_screening_f2345	Health and medical history	0.212	1.142	1.112	1.171	1.2E-23	0.09	1.201498	1.170791	1.23301	4.7E-11	0.186	1.128	1.1	1.158	2.0348E-20	0.099	1.074	1.047	1.102	2.58E-13
ever_had_period_extreme_irritability_f20502	Mental health	0.155	1.119	1.090	1.149	4.8E-17	3.493	2.789708	2.717237	2.864112	5.00E-324	0.185	1.128	1.1	1.157	3.5396E-21	0.116	1.246	1.216	1.278	5.22E-14
ever_had_period_of_mania_excitability_f20501	Mental health	0.141	1.114	1.085	1.144	1.76E-15	4.693	6.220818	6.057411	6.388633	5.00E-324	0.189	1.13	1.101	1.159	8.4237E-21	0.28	1.133	1.104	1.162	1.86E-31
ever_had_prolonged_feelings_of_sadness_or_depression_f20446	Mental health	0.132	1.110	1.081	1.139	3.12E-15	3.54	3.057292	2.979278	3.13735	5.00E-324	0.187	1.129	1.101	1.158	2.5964E-21	0.331	1.433	1.397	1.469	2.43E-38
ever_selfharm_f20480	Mental health	0.155	1.120	1.091	1.149	1.53E-17	2.946	4.549553	4.432815	4.669365	5.00E-324	0.18	1.126	1.098	1.155	1.6875E-20	0.352	1.496	1.459	1.534	3.24E-41
ever_smoked_f20160	Lifestyle and environment	0.193	1.135	1.106	1.164	6.59E-22	0.361	1.391311	1.355979	1.427563	9.87E-39	0.163	1.121	1.091	1.151	2.9349E-17	0.094	0.844	0.822	0.867	1.17E-10
ever_sought_or_received_professional_help_for_mental_distress_f20499	Mental health	0.13	1.109	1.080	1.138	6.09E-15	3.804	2.900637	2.826456	2.976764	5.00E-324	0.142	1.112	1.084	1.14	2.589E-16	1.378	2.749	2.680	2.820	5.36E-175
ever_suffered_mental_distress_preventing_usual_activities_f20500	Mental health	0.123	1.105	1.077	1.134	6.1E-14	4.668	3.236967	3.153552	3.322588	5.00E-324	0.168	1.122	1.094	1.15	2.6044E-19	0.561	2.210	2.156	2.267	1.41E-71
ever_taken_cannabis_f20453	Mental health	0.18	1.130	1.101	1.160	1.59E-20	0.782	1.700332	1.657021	1.744775	2.14E-88	0.112	1.098	1.07	1.126	5.2738E-13	4.984	3.843	3.747	3.942	5.00E-324
ever_thought_that_life_not_worth_living_f20479	Mental health	0.125	1.106	1.078	1.135	3.06E-14	4.933	3.32616	3.240677	3.413897	5.00E-324	0.096	1.091	1.063	1.12	1.0886E-10	3.749	2.889	2.814	2.967	5.00E-324
falls_in_the_last_year_f2296	Health and medical history	0.205	1.139	1.110	1.168	4.19E-23	0.86	1.792944	1.747428	1.839647	5.1E-100	0.197	1.133	1.104	1.162	4.0362E-22	0.091	1.203	1.173	1.234	3.61E-11
fedup_feelings_f1960	Psychosocial factors	0.212	1.141	1.112	1.171	1.61E-23	1.112	1.757946	1.712957	1.804117	2.1E-118	0.167	1.121	1.094	1.15	3.5823E-19	0.656	1.954	1.905	2.004	3.65E-80
felt_hated_by_family_member_as_a_child_f20487	Mental health	0.133	1.110	1.082	1.139	2.4E-15	2.882	2.815303	2.74337	2.889121	5.00E-324	0.138	1.109	1.081	1.138	2.0958E-15	3.495	2.791	2.720	2.863	5.00E-324
felt_loved_as_a_child_f20489	Mental health	0.193	1.135	1.106	1.164	7.06E-22	0.497	0.32572	0.31743	0.334226	1.11E-68	0.124	1.104	1.076	1.133	8.2145E-14	4.694	6.224	6.065	6.387	5.00E-324
felt_very_upset_when_reminded_of_stressful_experience_in_past_month_f20498	Mental health	0.152	1.118	1.090	1.148	2.15E-17	2.609	2.380561	2.319887	2.442821	6.3E-272	0.125	1.104	1.076	1.132	1.747E-14	3.555	3.063	2.987	3.141	5.00E-324
fractured_broken_bones_in_last_5_years_f2463	Health and medical history	0.205	1.139	1.110	1.169	4.06E-23	0.658	1.249344	1.217551	1.281967	1.04E-08	0.14	1.11	1.083	1.139	5.0277E-16	2.957	4.564	4.450	4.681	5.00E-324
frequency_of_depressed_mood_in_last_2_weeks_f2050	Psychosocial factors	0.176	1.128	1.099	1.158	2.17E-19	1.991	2.26379	2.205178	2.323959	1.5E-220	0.172	1.124	1.096	1.152	8.6149E-20	0.365	1.394	1.359	1.429	3.81E-39
frequency_of_friendfamily_visits_f1031	Psychosocial factors	0.207	1.140	1.111	1.169	2.29E-23	0.18	0.448048	0.436666	0.459726	9.33E-25	0.121	1.102	1.074	1.13	4.6759E-14	3.819	2.906	2.834	2.980	5.00E-324
frequency_of_tenseness_restlessness_in_last_2_weeks_f2070	Psychosocial factors	0.182	1.130	1.101	1.160	4.03E-20	1.674	2.066383	2.013139	2.121034	6.2E-184	0.106	1.095	1.067	1.123	3.1965E-12	4.681	3.242	3.161	3.326	5.00E-324
frequency_of_tiredness_lethargy_in_last_2_weeks_f2080	Psychosocial factors	0.196	1.135	1.106	1.165	8.88E-22	1.304	1.864087	1.816357	1.913072	3.9E-131	0.165	1.121	1.093	1.149	5.5033E-19	0.788	1.704	1.662	1.747	3.96E-89
frequency_of_unenthusiasm_disinterest_in_last_2_weeks_f2060	Psychosocial factors	0.177	1.128	1.099	1.158	1.19E-19	1.059	2.156914	2.101419	2.213875	1.3E-181	0.116	1.1	1.072	1.128	2.2149E-13	4.948	3.332	3.248	3.417	5.00E-324
general_happiness_f20458	Mental health	0.195	1.135	1.106	1.165	6.09E-22	0.409	0.150665	0.146821	0.154609	3.43E-61	0.178	1.125	1.098	1.154	2.5443E-20	0.858	1.792	1.747	1.837	9.01E-100
general_happiness_with_own_health_f20459	Mental health	0.194	1.135	1.106	1.165	5.73E-22	0.64	0.267601	0.260794	0.274586	1.98E-90	0.189	1.129	1.101	1.158	3.8328E-21	1.109	1.757	1.713	1.802	3.87E-118
getting_up_in_morning_f1170	Lifestyle and environment	0.196	1.136	1.107	1.166	2.79E-22	0.387	0.485129	0.472805	0.497775	1.02E-49	0.12	1.102	1.074	1.13	5.2488E-14	2.889	2.819	2.749	2.891	5.00E-324
guilty_feelings_f2030	Mental health	0.176	1.128	1.099	1.158	1.18E-19	0.882	1.687513	1.644202	1.731964	2.04E-96	0.174	1.124	1.096	1.153	6.4455E-20	0.5	0.324	0.316	0.333	3.57E-69
hot_drink_temperature_f1518	Lifestyle and environment	0.219	1.144	1.115	1.174	2.2E-24	0.175	0.753909	0.734657	0.773666	6.85E-21	0.132	1.107	1.079	1.135	2.4807E-15	2.611	2.382	2.322	2.442	3.38E-272
irritability_f1940	Psychosocial factors	0.19	1.134	1.104	1.164	9.01E-21	0.481	1.476015	1.43773	1.51532	4.07E-52	0.176	1.125	1.096	1.155	5.9629E-19	0.194	0.849	0.828	0.872	1.09E-20
loneliness_isolation_f2020	Psychosocial factors	0.187	1.132	1.103	1.162	6.93E-21	1.469	2.142204	2.087277	2.198576	7.9E-171	0.187	1.129	1.101	1.158	2.9085E-21	0.064	1.248	1.217	1.279	1.28E-08
longstanding_illness_disability_or_infirmary_f2188	Health and medical history	0.193	1.134	1.105	1.164	2.88E-21	1.892	2.13811	2.08304	2.194636	8.8E-206	0.154	1.116	1.088	1.145	3.7267E-17	1.996	2.266	2.209	2.325	3.90E-221
major_dietary_changes_in_the_last_5_years_f1538	Lifestyle and environment	0.207	1.139	1.111	1.169	2.37E-23	0.704	1.561476	1.521864	1.602118	6.1E-77	0.186	1.129	1.101	1.157	3.0946E-21	0.181	0.447	0.435	0.458	5.85E-25
miserableness_f1930	Psychosocial factors	0.198	1.136	1.107	1.166	4.29E-22	1.712	2.017485	1.965982	2.070339	2E-177	0.165	1.12	1.092	1.149	1.8822E-18	1.682	2.070	2.018	2.123	7.05E-185
mood_swings_f1920	Psychosocial factors	0.19	1.133	1.104	1.16																

variation_in_diet_f1548	Lifestyle and environment	0.21	1.141	1.112	1.170	1.07E-23	0.193	1.280486	1.248003	1.313814	1.94E-21	0.181	1.127	1.099	1.155	1.1296E-20	1.146	1.292	1.260	1.324	9.41E-138
victim_of_physiologically_violent_crime_f20529	Mental health	0.173	1.127	1.098	1.156	1.12E-19	1.276	1.993904	1.943085	2.046052	9.1E-147	0.18	1.126	1.098	1.155	1.3737E-20	0.235	1.416	1.381	1.452	4.30E-28
victim_of_sexual_assault_f20531	Mental health	0.144	1.115	1.086	1.144	2.71E-16	2.287	2.609622	2.542516	2.678499	1.2E-265	0.167	1.121	1.093	1.15	8.5924E-19	1.169	1.931	1.883	1.981	4.57E-133
weight_change_compared_with_1_year_ago_f2306	Health and medical history	0.22	1.144	1.115	1.174	1.84E-24	0.414	1.406803	1.370829	1.443722	5.93E-45	0.167	1.121	1.094	1.15	3.8389E-19	1.157	0.272	0.266	0.279	1.85E-160
wheeze_or_whistling_in_the_chest_in_last_year_f2316	Health and medical history	0.208	1.140	1.111	1.170	5.12E-23	0.788	1.751352	1.706398	1.797491	2.22E-90	0.18	1.126	1.098	1.155	1.5292E-20	0.689	1.572	1.534	1.612	1.53E-71
witnessed_sudden_violent_death_f20530	Mental health	0.202	1.138	1.109	1.168	8.17E-23	0.844	1.890836	1.842735	1.940192	4.9E-100	0.186	1.129	1.101	1.158	5.398E-21	0.14	1.103	1.075	1.131	2.45E-16
worrier_anxious_feelings_f1980	Psychosocial factors	0.199	1.137	1.108	1.167	3.95E-22	0.401	1.408624	1.372478	1.445722	3.18E-42	0.179	1.126	1.097	1.156	3.3982E-19	0.089	0.908	0.885	0.932	1.91E-10
worry_too_long_after_embarrassment_f2000	Psychosocial factors	0.229	1.147	1.118	1.178	6.63E-25	0.299	1.336533	1.302049	1.37193	6.18E-32	0.14	1.11	1.083	1.139	3.5335E-16	1.461	2.249	2.193	2.306	2.90E-174
hearing_difficulty_problems_f2247	Health and medical history	0.209	1.141	1.111	1.171	1.26E-22	0.466	1.502118	1.463072	1.542207	5.78E-51	0.148	1.114	1.086	1.142	4.442E-17	1.368	2.021	1.971	2.073	4.69E-158
alcohol_drinker_status_f20117	Lifestyle and environment	0.21	1.141	1.112	1.170	9.36E-24	0.206	1.59236	1.551985	1.633785	7.78E-26	0.203	1.135	1.107	1.164	3.9767E-23	0.246	1.344	1.311	1.378	1.08E-28
attendances_disability_mobility_allowance_f6146	Sociodemographics	0.197	1.136	1.107	1.166	3.14E-22	1.081	3.360237	3.274723	3.447985	7.6E-148	0.183	1.127	1.1	1.156	6.3467E-21	0.072	0.832	0.811	0.853	2.42E-09
blood_clot_dvt_bronchitis_emphysema_asthma_rhinitis_eczema_allergy_diagnosed_by_doctor_f6152	Health and medical history	0.209	1.140	1.111	1.170	1.38E-23	0.337	1.368301	1.333581	1.403924	6.33E-38	0.184	1.128	1.1	1.157	3.9462E-21	0.087	0.746	0.727	0.765	2.22E-11
current_employment_status_f6142	Sociodemographics	0.209	1.140	1.111	1.170	1.29E-23	0.117	1.246905	1.215261	1.279374	4.56E-14	0.198	1.133	1.104	1.162	1.1198E-21	0.206	1.125	1.096	1.154	4.51E-23
illness_injury_bereavement_stress_in_last_2_years_f6145	Psychosocial factors	0.199	1.137	1.108	1.166	1.7E-22	0.734	1.571971	1.532033	1.612951	8.66E-79	0.14	1.111	1.083	1.139	3.761E-16	2.891	3.995	3.895	4.097	5.00E-324
leisure_social_activities_f6160	Psychosocial factors	0.214	1.142	1.113	1.172	4.49E-24	0.345	1.398837	1.363334	1.435264	1.37E-36	0.168	1.122	1.094	1.15	4.0734E-19	1.714	2.052	2.001	2.105	3.74E-189
medication_for_pain_relief_constipation_heartburn_f6154	Health and medical history	0.212	1.142	1.112	1.171	8.67E-24	0.428	1.41386	1.377844	1.450817	6.14E-47	0.165	1.12	1.093	1.149	8.8711E-19	2.206	2.319	2.261	2.378	1.07E-249
milk_type_used_f1418	Lifestyle and environment	0.209	1.140	1.112	1.170	1.11E-23	0.084	1.169401	1.139748	1.199826	1.72E-10	0.141	1.111	1.083	1.139	3.356E-16	2.521	2.594	2.529	2.660	5.48E-295
mouthteeth_dental_problems_f6149	Health and medical history	0.202	1.138	1.109	1.167	7.13E-23	0.363	1.38459	1.349455	1.42064	1.12E-40	0.151	1.115	1.087	1.143	2.8352E-17	2.378	2.454	2.393	2.517	8.63E-273
pain_types_experienced_in_last_month_f6159	Health and medical history	0.205	1.139	1.110	1.168	4.26E-23	0.691	1.573562	1.533621	1.614543	9.23E-72	0.165	1.121	1.093	1.149	6.9884E-19	1.916	2.134	2.081	2.189	4.23E-191
type_of_accommodation_lived_in_f670	Sociodemographics	0.197	1.136	1.107	1.166	2.19E-22	0.275	1.542339	1.503218	1.582479	1.91E-33	0.157	1.117	1.089	1.146	6.4197E-18	2.009	2.169	2.115	2.225	4.04E-220
vascular_heart_problems_diagnosed_by_doctor_f6150	Health and medical history	0.203	1.138	1.109	1.168	5.41E-23	0.286	1.39776	1.362275	1.434169	4.68E-33	0.161	1.119	1.091	1.148	2.0976E-18	2.349	2.486	2.424	2.550	1.62E-271
vitamin_and_mineral_supplements_f6155	Health and medical history	0.207	1.140	1.111	1.169	2.19E-23	0.191	1.271756	1.239481	1.304872	3.57E-22	0.164	1.12	1.092	1.148	1.1665E-18	1.987	2.554	2.490	2.619	5.74E-242
age_first_had_sexual_intercourse_f2139	Lifestyle and environment	0.204	1.138	1.109	1.169	1.25E-21	0.159	0.890672	0.86729	0.914686	2.1E-16	0.161	1.119	1.091	1.148	3.6364E-18	2.403	4.102	3.999	4.207	5.00E-324
alkaline_phosphatase_f30610	Biological samples	0.2	1.137	1.108	1.167	7.48E-22	0.176	1.103605	1.075052	1.132916	1.95E-21	0.162	1.119	1.091	1.148	1.9559E-18	2.923	2.722	2.654	2.791	5.00E-324
arm_fat_mass_left_f23124	Physical measures	0.224	1.146	1.116	1.176	7.26E-25	0.636	1.198543	1.167906	1.229984	5.2E-76	0.16	1.118	1.091	1.147	2.8927E-18	2.083	2.199	2.144	2.255	5.80E-228
body_mass_index_bmi_f21001	Physical measures	0.239	1.151	1.121	1.181	1.05E-26	0.825	1.244853	1.213252	1.277278	9E-96	0.16	1.119	1.091	1.147	2.3342E-18	1.724	2.032	1.981	2.084	1.88E-186
cereal_intake_f1458	Lifestyle and environment	0.207	1.140	1.111	1.170	1.82E-23	0.1	0.920334	0.896973	0.944303	3.15E-12	0.123	1.103	1.076	1.131	2.392E-14	2.75	2.464	2.403	2.527	4.07E-303
creactive_protein_f30710	Biological samples	0.199	1.137	1.107	1.167	1E-21	0.101	1.075039	1.047187	1.103632	1.67E-13	0.164	1.12	1.092	1.149	2.6838E-18	0.66	1.590	1.550	1.631	7.45E-72
cystatin_c_f30720	Biological samples	0.209	1.140	1.111	1.171	8.85E-23	0.286	1.134197	1.104838	1.164336	4.05E-32	0.122	1.103	1.075	1.131	3.5925E-14	3.367	3.429	3.344	3.517	5.00E-324
forced_expiratory_volume_in_1second_fev1_f3063	Physical measures	0.223	1.146	1.115	1.177	1.84E-23	0.2	0.847429	0.825109	0.870354	2.9E-21	0.135	1.108	1.081	1.136	1.4343E-15	2.813	2.469	2.407	2.532	9.55E-299
gamma_glutamyltransferase_f30730	Biological samples	0.198	1.136	1.107	1.166	1.3E-21	0.08	1.067636	1.040012	1.095995	3.82E-11	0.177	1.125	1.097	1.154	9.3579E-20	0.462	1.446	1.410	1.483	3.47E-48
glycated_haemoglobin_hba1c_f30750	Biological samples	0.226	1.146	1.117	1.177	2.34E-24	0.225	1.119806	1.09074	1.149647	7.3E-28	0.163	1.12	1.092	1.148	1.3431E-18	1.374	2.837	2.767	2.909	3.05E-173
hand_grip_strength_right_f47	Physical measures	0.202	1.138	1.109	1.168	6.67E-23	0.249	0.821564	0.800718	0.842951	4.31E-28	0.156	1.117	1.089	1.146	1.1734E-17	1.207	2.321	2.263	2.381	6.99E-147
high_light_scatter_reticulocyte_percentage_f30290	Biological samples	0.234	1.149	1.120	1.179	8.59E-26	0.147	1.091637	1.063692	1.120316	1.39E-17	0.187	1.129	1.101	1.158	2.2602E-21	0.281	1.401	1.366	1.436	8.88E-30
hip_circumference_f49	Physical measures	0.235	1.149	1.120	1.179	2.46E-26	0.507	1.19082	1.160603	1.221824	1.22E-58	0.198	1.133	1.104	1.163	4.9715E-21	0.18	1.267	1.234	1.301	1.74E-19
igf1_f30770	Biological samples	0.202	1.138	1.108	1.168	5.84E-22	0.109	0.913076	0.889391	0.937391	2.16E-12	0.185	1.128	1.1	1.157	4.8659E-21	0.098	0.604	0.589	0.620	2.46E-13
immature_reticulocyte_fraction_f30280	Biological samples	0.233	1.149	1.119	1.179	1.08E-25	0.166	1.11319	1.084703	1.142426	6.63E-19	0.168	1.122	1.094	1.151	9.6246E-19	0.827	1.747	1.703	1.792	1.39E-92
impedance_of_leg_left_f23108	Physical measures	0.217	1.143	1.114	1.173	3.67E-24	0.275	0.858332	0.836413	0.880825	1.98E-30	0.181	1.127	1.099	1.155	1.1914E-20	0.848	1.636	1.596	1.678	3.54E-91
impedance_of_whole_body_f23106	Physical measures	0.218	1.144	1.114	1.174	2.87E-24	0.283	0.82973	0.808539	0.851477	3.73E-31	0.18	1.127	1.099	1.155	1.0936E-20	0.07	1.069	1.043	1.096	3.17E-09
leg_fatfree_mass_right_f23113	Physical measures	0.219	1.144	1.115	1.174	2.06E-24	0.33	1.28571	1.252849	1.319434	9.32E-38	0.129	1.106	1.078	1.135	1.0089E-14	0.958	1.888	1.840	1.937	1.35E-109
length_of_time_at_current_address_f699	Sociodemographics	0.202	1.138	1.109	1.168	6.3E-23	0.118	0.901952	0.879045	0.925456	6.41E-14	0.186	1.129	1.101	1.157	3.1246E-21	0.374	1.157	1.128	1.186	2.25E-45
mean_time_to_correctly_identify_matches_f20023	Cognitive function	0.199	1.137	1.108	1.166	1.59E-22	0.085	1.081233	1.053779	1.109402	6.99E-11	0.168	1.122	1.094	1.15	2.6297E-19	0.692	1.232	1.201	1.263	3.46E-78
natural_environment_percentage_buffer_1000m_f24506	Local Environment	0.205	1.139	1.110	1.169	5.03E-23	0.072	0.930756	0.907033	0.9551	5.28E-09	0.189	1.13	1.101	1.159	8.1266E-21	0.334	1.155	1.126	1.185	1.16E-38
neutrophil_count_f30140	Biological samples	0.207	1.140	1.111	1.169	1.88E-23	0.135	1.097434	1.069587	1.126007	2.51E-16	0.184	1.128	1.1	1.156	6.1285E-21	1.39	1.896	1.849	1.944	3.75E-142
nitrogen_dioxide_air_pollution_2007_f24018	Local Environment	0.21	1.141	1.112	1.171	2.04E-23	0.062	1.066839	1.039585	1.094808	3.64E-08	0.185	1.128	1.1	1.157	6.3362E-21	0.43	1.209	1.179	1.240	6.94E-46
number_of_daysweek_of_vigorous_physical_activity_10_minutes_f904	Lifestyle and environment	0.23	1.148	1.118	1.178	2.57E-25	0.151	0.808947	0.788173	0.830267	1.67E-17	0.179	1.126	1.098	1.155	1.5149E-20	0.279	1.548	1.510	1.587	5.07E-34
number_of_operations_selfreported_f136	Operations	0.212	1.141	1.112	1.171	6.09E-24	0.326	1.158786	1.129407	1.188929	4.51E-38	0.191	1.131	1.102	1.16	4.8634E-21	0.154	1.131	1.103	1.160	1.54E-17
number_of_selfreported_noncancer_illnesses_f135	Medical conditions	0.201	1.137	1.108	1.167	1.29E-22	1.595	1.340698	1.30661	1.375676	2E-193	0.183	1.127	1.1	1.156	5.8354E-21	0.151	0.687	0.670	0.704	5.96E-19
number_of_treatmentsmedications_taken_f137	Medications	0.214	1.142	1.113	1.172	4.55E-24	1.156	1.293116	1.260276	1.326812	5.6E-139	0.185	1.128	1.1	1.157	3.6					

recent_feelings_of_tiredness_or_low_energy_f20519	Mental health	0.173	-0.011 - 0.357	-0.013 - 0.356	0.032	0.068	-0.002 - 0.139	-0.006 - 0.135	0.029	1.127	0.99 - 1.282	0.99 - 1.282	0.035	0.060	-0.011 - 0.357	-0.013 - 0.356	0.222	0.032	-0.002 - 0.139	-0.006 - 0.135	0.220	1.072	0.99 - 1.282	0.99 - 1.282	0.226	
recent_feelings_or_nervousness_or_anxiety_f20506	Mental health	0.207	-0.004 - 0.41	0.006 - 0.412	0.023	0.081	0.005 - 0.156	0.001 - 0.152	0.018	1.152	1.004 - 1.322	1.004 - 1.322	0.022	0.102	0.004 - 0.41	0.006 - 0.412	0.216	0.055	0.005 - 0.156	0.001 - 0.152	0.207	1.134	1.004 - 1.322	1.004 - 1.322	0.212	
recent_poor_appetite_or_overeating_f20511	Mental health	0.263	0.007 - 0.519	0.012 - 0.524	0.022	0.090	0.008 - 0.172	0.002 - 0.166	0.016	1.157	1.007 - 1.33	1.007 - 1.33	0.020	0.107	-0.002 - 0.519	0.012 - 0.524	0.207	-0.001	0.008 - 0.172	0.002 - 0.166	0.493	0.998	1.007 - 1.33	1.007 - 1.33	0.507	
recent_restlessness_f20516	Mental health	0.234	-0.075 - 0.544	-0.068 - 0.552	0.069	0.078	-0.019 - 0.175	-0.027 - 0.168	0.058	1.132	0.965 - 1.328	0.965 - 1.328	0.064	0.136	-0.075 - 0.544	-0.068 - 0.552	0.031	0.087	-0.019 - 0.175	-0.027 - 0.168	0.025	1.316	0.965 - 1.328	0.965 - 1.328	0.034	
recent_thoughts_of_suicide_or_selfharm_f20513	Mental health	0.450	-0.219 - 1.118	-0.197 - 1.145	0.094	0.093	-0.036 - 0.223	-0.048 - 0.211	0.078	1.134	0.945 - 1.36	0.945 - 1.36	0.088	0.064	-0.219 - 1.118	-0.197 - 1.145	0.052	0.046	-0.036 - 0.223	-0.048 - 0.211	0.046	1.199	0.945 - 1.36	0.945 - 1.36	0.048	
recent_trouble_concentrating_on_things_f20508	Mental health	0.241	-0.034 - 0.516	-0.03 - 0.522	0.043	0.076	-0.006 - 0.158	-0.012 - 0.153	0.035	1.124	0.986 - 1.281	0.986 - 1.281	0.041	0.021	-0.034 - 0.516	-0.03 - 0.522	0.224	0.016	-0.006 - 0.158	-0.012 - 0.153	0.221	1.067	0.986 - 1.281	0.986 - 1.281	0.220	
recent_trouble_relaxing_f20515	Mental health	0.225	0.02 - 0.43	0.022 - 0.433	0.016	0.086	0.011 - 0.16	0.007 - 0.156	0.012	1.161	1.014 - 1.329	1.014 - 1.329	0.015	0.017	0.02 - 0.43	0.022 - 0.433	0.281	0.012	0.011 - 0.16	0.007 - 0.156	0.279	1.041	1.014 - 1.329	1.014 - 1.329	0.279	
recent_worrying_too_much_about_different_things_f20520	Mental health	0.268	0.08 - 0.456	0.082 - 0.458	0.003	0.110	0.038 - 0.182	0.033 - 0.178	1.45E-03	1.228	1.063 - 1.419	1.063 - 1.419	0.003	0.040	0.08 - 0.456	0.082 - 0.458	0.112	0.027	0.038 - 0.182	0.033 - 0.178	0.107	1.087	1.063 - 1.419	1.063 - 1.419	0.106	
repeated_disturbing_thoughts_of_stressful_experience_in_past_months_f2040	Mental health	0.220	0 - 0.44	0.002 - 0.443	0.025	0.077	0.004 - 0.151	-0.001 - 0.147	0.020	1.135	1.001 - 1.286	1.001 - 1.286	0.024	0.039	0 - 0.44	0.002 - 0.443	0.117	0.029	0.004 - 0.151	-0.001 - 0.147	0.111	1.134	1.001 - 1.286	1.001 - 1.286	0.111	
seen_a_psychiatrist_for_nerves_anxiety_tension_or_depression_f2100	Psychosocial fa	0.144	-0.03 - 0.318	0.028 - 0.321	0.052	0.075	-0.012 - 0.162	-0.018 - 0.156	0.045	1.186	0.966 - 1.458	0.966 - 1.458	0.052	0.041	-0.03 - 0.318	-0.028 - 0.321	0.054	0.031	-0.012 - 0.162	-0.018 - 0.156	0.050	1.148	0.966 - 1.458	0.966 - 1.458	0.050	
seen_doctor_gp_for_nerves_anxiety_tension_or_depression_f2090	Psychosocial fa	0.894	0.494 - 1.294	0.503 - 1.305	1.00E-05	0.210	0.13 - 0.29	0.125 - 0.285	<1.00E-05	1.378	1.203 - 1.58	1.203 - 1.58	<1.00E-05	0.018	0.494 - 1.294	0.503 - 1.305	0.267	0.013	0.13 - 0.29	0.125 - 0.285	0.265	1.050	1.203 - 1.58	1.203 - 1.58	0.264	
seen_doctor_gp_for_nerves_anxiety_tension_or_depression_f2090	Psychosocial fa	0.450	0.239 - 0.661	0.241 - 0.664	1.00E-05	0.152	0.087 - 0.217	0.084 - 0.214	<1.00E-05	1.299	1.149 - 1.468	1.149 - 1.468	1.00E-05	0.046	0.239 - 0.661	0.241 - 0.664	0.119	0.032	0.087 - 0.217	0.084 - 0.214	0.112	1.118	1.149 - 1.468	1.149 - 1.468	0.111	
sensitivity_hurt_feelings_f1950	Psychosocial fa	0.138	-0.006 - 0.282	0.009 - 0.281	0.031	0.079	-0.002 - 0.159	-0.006 - 0.155	0.028	1.225	0.978 - 1.535	0.978 - 1.535	0.038	0.000	-0.006 - 0.282	-0.009 - 0.281	0.504	0.000	-0.002 - 0.159	-0.006 - 0.155	0.496	0.999	0.978 - 1.535	0.978 - 1.535	0.504	
sexual_interference_by_partner_or_expartner_without_consent_as_a_child_f20490	Mental health	0.278	-0.168 - 0.725	-0.155 - 0.741	0.111	0.084	-0.043 - 0.211	-0.056 - 0.199	0.097	1.137	0.93 - 1.39	0.93 - 1.39	0.105	0.002	-0.168 - 0.725	-0.155 - 0.741	0.471	0.002	-0.043 - 0.211	-0.056 - 0.199	0.471	1.006	0.93 - 1.39	0.93 - 1.39	0.471	
sleeplessness_insomnia_f1200	Lifestyle and er	0.312	-0.019 - 0.642	-0.01 - 0.653	0.032	0.112	0.003 - 0.222	-0.008 - 0.212	0.022	1.212	0.995 - 1.478	0.995 - 1.478	0.028	0.065	-0.019 - 0.642	-0.01 - 0.653	0.044	0.044	0.003 - 0.222	-0.008 - 0.212	0.038	1.154	0.995 - 1.478	0.995 - 1.478	0.038	
snoring_f1210	Lifestyle and er	0.183	0.032 - 0.334	0.024 - 0.328	0.009	0.109	0.019 - 0.199	0.015 - 0.195	0.009	1.372	1.007 - 1.87	1.007 - 1.87	0.022	0.046	0.032 - 0.334	0.024 - 0.328	0.055	0.034	0.019 - 0.199	0.015 - 0.195	0.050	1.155	1.007 - 1.87	1.007 - 1.87	0.050	
someone_to_take_to_doctor_when_needed_as_a_child_f20491	Mental health	-0.015	-0.163 - 0.133	-0.163 - 0.134	0.580	-0.010	-0.11 - 0.09	-0.118 - 0.083	0.420	0.970	0.721 - 1.305	0.721 - 1.305	0.580	0.016	-0.163 - 0.133	-0.163 - 0.134	0.316	0.011	-0.11 - 0.09	-0.118 - 0.083	0.314	1.038	0.721 - 1.305	0.721 - 1.305	0.313	
suffer_from_nerves_f2010	Psychosocial fa	0.583	0.013 - 1.153	0.049 - 1.2	0.022	0.251	0.053 - 0.449	0.006 - 0.408	0.006	1.788	1.064 - 3.004	1.064 - 3.004	0.014	0.033	0.013 - 1.153	0.049 - 1.2	0.167	0.025	0.053 - 0.449	0.006 - 0.408	0.162	1.111	1.064 - 3.004	1.064 - 3.004	0.160	
taking_other_prescription_medications_f2492	Health and me	0.271	0.06 - 0.482	0.063 - 0.486	0.006	0.125	0.035 - 0.214	0.028 - 0.208	0.003	1.302	1.065 - 1.593	1.065 - 1.593	0.005	0.033	0.06 - 0.482	0.063 - 0.486	0.172	0.024	0.035 - 0.214	0.028 - 0.208	0.167	1.100	1.065 - 1.593	1.065 - 1.593	0.166	
tea_intake_f1488	Lifestyle and er	0.190	0.032 - 0.348	0.032 - 0.348	0.009	0.095	0.02 - 0.171	0.015 - 0.167	0.007	1.236	1.032 - 1.481	1.032 - 1.481	0.011	0.011	0.032 - 0.348	0.032 - 0.348	0.381	0.008	0.02 - 0.171	0.015 - 0.167	0.380	1.029	1.032 - 1.481	1.032 - 1.481	0.380	
tense_highly_strung_f1990	Psychosocial fa	-0.031	-0.09 - 0.028	-0.089 - 0.03	0.846	-0.025	-0.073 - 0.024	-0.076 - 0.02	-0.023 - 0.026	0.158	0.893	0.712 - 1.12	0.712 - 1.12	0.836	0.015	-0.09 - 0.028	-0.089 - 0.03	0.344	0.010	-0.073 - 0.024	-0.076 - 0.02	0.343	1.036	0.712 - 1.12	0.712 - 1.12	0.342
time_spent_using_computer_f1080	Lifestyle and er	-0.000	-0.258 - 0.198	-0.255 - 0.202	0.603	-0.014	-0.123 - 0.094	-0.132 - 0.085	0.398	0.974	0.796 - 1.19	0.796 - 1.19	0.603	0.089	-0.258 - 0.198	-0.255 - 0.202	0.018	0.053	-0.123 - 0.094	-0.132 - 0.085	0.013	1.171	0.796 - 1.19	0.796 - 1.19	0.012	
townsend_deprivation_index_at_recruitment_f189	Population cha	-0.032	-0.063 - 0.052	-0.062 - 0.054	0.573	-0.004	-0.046 - 0.038	-0.049 - 0.036	-0.02 - 0.016	0.427	0.986	0.845 - 1.15	0.845 - 1.15	0.573	0.039	-0.063 - 0.052	-0.062 - 0.054	0.134	0.029	-0.046 - 0.038	-0.049 - 0.036	0.128	1.126	0.845 - 1.15	0.845 - 1.15	0.129
triglycerides_f30870	Biological samp	0.032	-0.032 - 0.096	-0.031 - 0.098	0.165	0.022	-0.021 - 0.065	-0.024 - 0.063	-0.002 - 0.039	0.160	1.074	0.933 - 1.237	0.933 - 1.237	0.160	0.034	-0.032 - 0.096	-0.031 - 0.098	0.129	0.026	-0.021 - 0.065	-0.024 - 0.063	0.124	1.121	0.933 - 1.237	0.933 - 1.237	0.123
trouble_falling_or_staying_asleep_or_sleeping_too_much_f20517	Mental health	0.021	-0.04 - 0.083	-0.039 - 0.085	0.249	0.015	-0.028 - 0.059	-0.031 - 0.057	-0.01 - 0.031	0.246	1.058	0.902 - 1.241	0.902 - 1.241	0.245	-0.004	-0.04 - 0.083	-0.039 - 0.085	0.547	-0.003	-0.028 - 0.059	-0.031 - 0.057	0.453	0.986	0.902 - 1.241	0.902 - 1.241	0.547
trunk_fat_percentage_f23127	Physical measu	0.292	0.126 - 0.458	0.125 - 0.458	2.90E-04	0.128	0.059 - 0.197	0.055 - 0.193	1.40E-04	1.294	1.109 - 1.509	1.109 - 1.509	5.20E-04	0.049	0.126 - 0.458	0.125 - 0.458	0.062	0.036	0.059 - 0.197	0.055 - 0.193	0.057	1.161	1.109 - 1.509	1.109 - 1.509	0.057	
urate_f30880	Biological samp	0.051	-0.02 - 0.123	-0.019 - 0.125	0.080	0.035	-0.013 - 0.083	-0.016 - 0.08	-0.02 - 0.031	0.074	1.126	0.959 - 1.322	0.959 - 1.322	0.074	-0.004	-0.02 - 0.123	-0.019 - 0.125	0.553	-0.003	-0.013 - 0.083	-0.016 - 0.08	0.447	0.986	0.959 - 1.322	0.959 - 1.322	0.553
use_of_sunuv_protection_f2267	Lifestyle and er	0.099	-0.155 - 0.353	-0.149 - 0.361	0.223	0.053	-0.079 - 0.185	-0.094 - 0.17	0.215	1.130	0.83 - 1.538	0.83 - 1.538	0.219	-0.012	-0.155 - 0.353	-0.149 - 0.361	0.569	-0.009	-0.079 - 0.185	-0.094 - 0.17	0.432	0.974	0.83 - 1.538	0.83 - 1.538	0.569	
variation_in_diet_f1548	Lifestyle and er	0.031	-0.037 - 0.099	-0.035 - 0.101	0.184	0.023	-0.026 - 0.071	-0.029 - 0.067	-0.001 - 0.044	0.179	0.909	0.909 - 1.306	0.909 - 1.306	0.177	-0.029	-0.037 - 0.099	-0.035 - 0.101	0.814	-0.021	-0.026 - 0.071	-0.029 - 0.067	0.190	0.926	0.909 - 1.306	0.909 - 1.306	0.807
vascularheart_problems_diagnosed_by_doctor_f6150	Health and me	0.096	-0.043 - 0.234	-0.048 - 0.231	0.089	0.061	-0.027 - 0.15	-0.031 - 0.146	0.087	1.207	0.899 - 1.62	0.899 - 1.62	0.106	0.039	-0.043 - 0.234	-0.048 - 0.231	0.033	0.036	-0.027 - 0.15	-0.031 - 0.146	0.029	1.108	0.899 - 1.62	0.899 - 1.62	0.106	
victim_of_physically_violent_crime_f20529	Mental health	-0.001	-0.173 - 0.171	-0.171 - 0.174	0.505	-0.001	-0.106 - 0.104	-0.115 - 0.096	0.495	0.998	0.763 - 1.306	0.763 - 1.306	0.505	0.007	-0.173 - 0.171	-0.171 - 0.174	0.417	0.005	-0.106 - 0.104	-0.115 - 0.096	0.417	1.021	0.763 - 1.306	0.763 - 1.306	0.417	
victim_of_sexual_assault_f20531	Mental health	0.064	-0.155 - 0.283	-0.152 - 0.287	0.283	0.028	-0.066 - 0.121	-0.072 - 0.115	0.280	1.052	0.886 - 1.249	0.886 - 1.249	0.282	0.039	-0.155 - 0.283	-0.152 - 0.287	0.133	0.029	-0.066 - 0.121	-0.072 - 0.115	0.127	1.126	0.886 - 1.249	0.886 - 1.249	0.126	
vitamin_and_mineral_supplements_f6155	Health and me	0.102	-0.182 - 0.387	-0.177 - 0.393	0.240	0.035	-0.059 - 0.128	-0.066 - 0.122	0.235	1.055	0.91 - 1.223	0.91 - 1.223	0.238	0.040	-0.182 - 0.387	-0.177 - 0.393	0.119	0.029	-0.059 - 0.128	-0.066 - 0.122	0.113	1.120	0.91 - 1.223	0.91 - 1.223	0.113	
walst_circumference_f48	Physical measu	0.129	-0.013 - 0.271	-0.013 - 0.272	0.037	0.083	-0.005 - 0.17	-0.011 - 0.164	0.032	1.298	0.967 - 1.743	0.967 - 1.743	0.041	-0.029	-0.013 - 0.271	-0.013 - 0.272	0.834	-0.023	-0.005 - 0.17	-0.011 - 0.164	0.170	0.898	0.967 - 1.743	0.967 - 1.743	0.825	
weight_change_compared_with_1_year_ago_f2306	Health and me	-0.038	-0.112 - 0.035	-0.111 - 0.037	0.846	-0.028	-0.082 - 0.027	-0.086 - 0.023	-0.038 - 0.018	0.159	0.909	0.752 - 1.098	0.752 - 1.098	0.839												

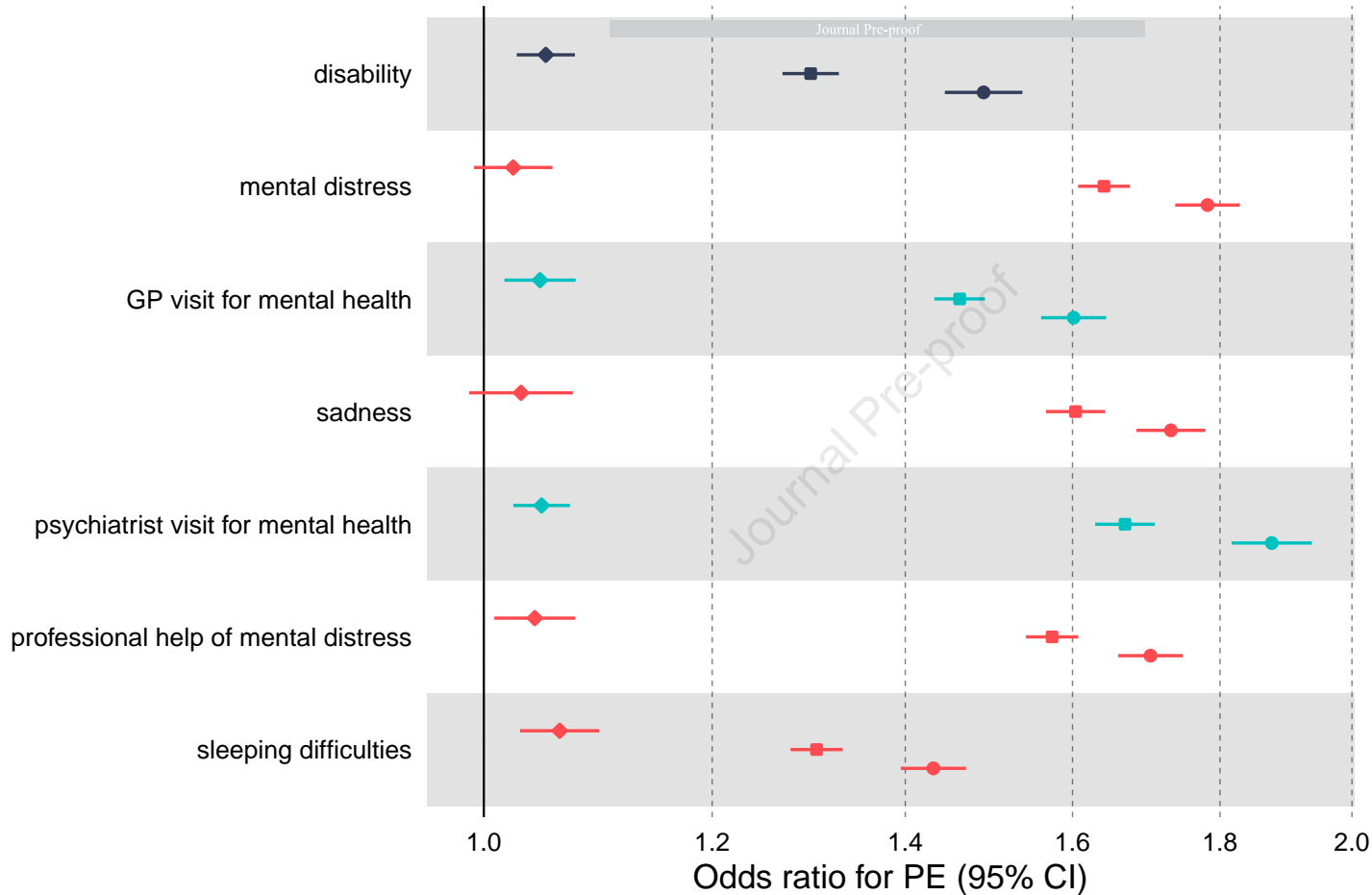
Predictors	category	PRS-cs-auto-SCZ75 (main analyses)				PRScice-SCZ75 (sensitivity analyses)			
		r	lower.CI	upper.CI	P	r	lower.CI	upper.CI	P
plays_computer_games_f2237	style and environn	-0.026	-0.031	-0.021	8.05E-24	-0.023	-0.028	-0.018	2.94E-19
hip_circumference_f49	Physical measures	-0.020	-0.025	-0.015	5.38E-15	-0.012	-0.017	-0.007	2.99E-06
impedance_of_leg_left_f23108	Physical measures	-0.020	-0.025	-0.015	9.29E-15	-0.017	-0.022	-0.012	1.15E-10
leg_fatfree_mass_right_f23113	Physical measures	-0.019	-0.025	-0.014	4.87E-14	-0.020	-0.025	-0.015	2.45E-14
weight_f21002	Physical measures	-0.019	-0.024	-0.014	4.69E-14	-0.012	-0.017	-0.007	1.44E-06
impedance_of_whole_body_f23106	Physical measures	-0.019	-0.024	-0.014	1.24E-13	-0.015	-0.020	-0.010	9.20E-09
waist_circumference_f48	Physical measures	-0.015	-0.020	-0.010	9.00E-09	-0.009	-0.014	-0.004	5.89E-04
cystatin_c_f30720	Biological samples	-0.013	-0.018	-0.008	7.17E-07	-0.011	-0.016	-0.005	5.04E-05
triglycerides_f30870	Biological samples	-0.011	-0.016	-0.006	1.70E-05	-0.008	-0.013	-0.003	1.63E-03
arm_fat_mass_left_f23124	Physical measures	-0.010	-0.015	-0.005	1.34E-04	0.002	-0.003	0.007	4.86E-01
body_mass_index_bmi_f21001	Physical measures	-0.010	-0.015	-0.005	1.42E-04	-0.002	-0.007	0.003	4.20E-01
urate_f30880	Biological samples	-0.009	-0.014	-0.004	7.87E-04	0.000	-0.006	0.005	8.89E-01
r_of_daysweek_of_vigorous_physical_activity_10_minutestyle and environn	style and environn	-0.008	-0.013	-0.003	2.19E-03	-0.003	-0.008	0.002	2.70E-01
number_of_operations_selfreported_f136	Operations	-0.008	-0.013	-0.003	2.00E-03	-0.007	-0.012	-0.002	7.13E-03
igf1_f30770	Biological samples	-0.007	-0.012	-0.001	1.18E-02	0.004	-0.001	0.009	1.04E-01
current_employment_status_f6142	sociodemographic	-0.006	-0.011	-0.001	2.63E-02	-0.001	-0.006	0.004	6.73E-01
sleeplessness_insomnia_f1200	style and environn	-0.004	-0.009	0.001	1.34E-01	0.002	-0.003	0.007	3.77E-01
number_of_treatmentsmedications_taken_f137	Medications	-0.004	-0.009	0.001	1.55E-01	0.003	-0.002	0.008	2.56E-01
hearing_difficultypblems_f2247	lth and medical his	-0.003	-0.008	0.002	2.99E-01	-0.001	-0.006	0.004	6.36E-01
snoring_f1210	style and environn	-0.003	-0.008	0.003	3.12E-01	-0.006	-0.011	-0.001	2.29E-02
ever_had_bowel_cancer_screening_f2345	lth and medical his	-0.002	-0.007	0.003	3.48E-01	-0.003	-0.008	0.002	2.95E-01
trunk_fat_percentage_f23127	Physical measures	-0.002	-0.007	0.003	4.87E-01	-0.004	-0.009	0.009	1.31E-01
ole_falling_or_staying_asleep_or_sleeping_too_much_f200	Mental health	-0.002	-0.007	0.003	5.08E-01	-0.001	-0.006	0.004	6.17E-01
fracturedbroken_bones_in_last_5_years_f2463	lth and medical his	-0.001	-0.007	0.004	5.66E-01	0.004	-0.001	0.009	1.21E-01
creactive_protein_f30710	Biological samples	-0.001	-0.007	0.004	6.03E-01	0.002	-0.004	0.007	5.32E-01
gamma_glutamyltransferase_f30730	Biological samples	-0.001	-0.006	0.004	6.10E-01	0.006	0.001	0.011	2.21E-02
medication_for_pain_relief_constipation_heartburn_f6154	lth and medical his	-0.001	-0.006	0.004	7.84E-01	0.004	-0.001	0.009	1.44E-01
number_of_selfreported_noncancer_illnesses_f135	Medical conditions	0.000	-0.005	0.005	9.78E-01	0.006	0.001	0.011	2.13E-02
taking_other_prescription_medications_f2492	lth and medical his	0.001	-0.004	0.006	7.48E-01	0.004	-0.001	0.009	1.05E-01
neutrophil_count_f30140	Biological samples	0.001	-0.004	0.006	6.29E-01	-0.003	-0.008	0.002	2.82E-01
alkaline_phosphatase_f30610	Biological samples	0.001	-0.004	0.006	6.17E-01	0.000	-0.005	0.006	8.84E-01
vascularheart_problems_diagnosed_by_doctor_f6150	lth and medical his	0.002	-0.003	0.007	3.83E-01	0.006	0.001	0.011	2.05E-02
pulse_rate_automated_reading_f102	Biological samples	0.002	-0.003	0.007	3.79E-01	0.004	-0.001	0.009	1.42E-01
fedup_feelings_f1960	'sychosocial factor	0.003	-0.002	0.008	3.20E-01	0.003	-0.002	0.008	2.93E-01
tea_intake_f1488	style and environn	0.003	-0.002	0.008	2.48E-01	0.004	-0.001	0.009	1.05E-01
diagnosed_with_lifethreatening_illness_f20528	Mental health	0.004	-0.001	0.009	1.02E-01	0.007	0.002	0.012	1.09E-02
able_to_confide_f2110	'sychosocial factor	0.004	-0.001	0.009	1.01E-01	0.006	0.001	0.011	3.09E-02
longstanding_illness_disability_or_infirmit_f2188	lth and medical his	0.005	0.000	0.010	7.62E-02	0.010	0.005	0.015	6.83E-05
leisuresocial_activities_f6160	'sychosocial factor	0.005	0.000	0.010	4.27E-02	0.006	0.001	0.011	1.92E-02
falls_in_the_last_year_f2296	lth and medical his	0.006	0.001	0.011	2.80E-02	0.008	0.003	0.013	2.90E-03
belief_that_own_life_is_meaningful_f20460	Mental health	0.006	0.001	0.011	2.86E-02	0.003	-0.002	0.008	2.82E-01
witnessed_sudden_violent_death_f20530	Mental health	0.006	0.001	0.011	2.25E-02	0.005	0.000	0.010	5.13E-02
serious_medical_conditiondisability_diagnosed_by_doctorlth and medical his	lth and medical his	0.006	0.001	0.011	2.22E-02	0.007	0.002	0.012	4.19E-03
contraindications_for_spirometry_f3088	Physical measures	0.006	0.001	0.011	1.96E-02	0.007	0.001	0.012	1.14E-02
immature_reticulocyte_fraction_f30280	Biological samples	0.006	0.001	0.011	1.87E-02	0.008	0.002	0.013	3.68E-03
high_light_scatter_reticulocyte_percentage_f30290	Biological samples	0.006	0.001	0.011	1.86E-02	0.004	-0.001	0.009	1.57E-01
in_concerned_about_or_recommmend_reduction_of_alcohol_Mental health	Mental health	0.007	0.002	0.012	7.50E-03	0.011	0.006	0.016	3.44E-05
hot_drink_temperature_f1518	style and environn	0.007	0.002	0.012	6.08E-03	0.004	-0.002	0.009	1.72E-01
general_happiness_f20458	Mental health	0.007	0.002	0.013	3.77E-03	0.007	0.002	0.012	7.94E-03
worry_too_long_after_embarrassment_f2000	'sychosocial factor	0.008	0.003	0.013	2.99E-03	0.003	-0.002	0.008	2.19E-01
itis_emphysema_asthma_rhinitis_eczema_allergy_diagnlth and medical his	lth and medical his	0.008	0.003	0.013	1.79E-03	0.007	0.002	0.012	4.59E-03
variation_in_diet_f1548	style and environn	0.008	0.003	0.013	1.57E-03	0.004	-0.001	0.009	1.21E-01
een_involved_in_combat_or_exposed_to_warzone_f2052	Mental health	0.008	0.003	0.013	1.50E-03	0.009	0.004	0.014	5.43E-04
miserableness_f1930	'sychosocial factor	0.008	0.003	0.013	1.20E-03	0.007	0.002	0.012	4.67E-03
injured_or_injured_someone_else_through_drinking_alcc_Mental health	Mental health	0.009	0.004	0.014	3.85E-04	0.015	0.010	0.020	4.02E-09
irritability_f1940	'sychosocial factor	0.009	0.004	0.014	4.58E-04	0.005	0.000	0.011	3.87E-02
weight_change_compared_with_1_year_ago_f2306	lth and medical his	0.009	0.004	0.014	2.84E-04	0.011	0.006	0.016	1.60E-05
pain_types_experienced_in_last_month_f6159	lth and medical his	0.010	0.005	0.015	1.46E-04	0.011	0.006	0.016	1.46E-05
wheeze_or_whistling_in_the_chest_in_last_year_f2310	lth and medical his	0.010	0.005	0.015	1.28E-04	0.011	0.006	0.016	1.50E-05
milk_type_used_f1418	style and environn	0.011	0.006	0.016	7.67E-05	0.011	0.006	0.016	2.81E-05
ever_smoked_f20160	style and environn	0.011	0.006	0.016	1.91E-05	0.009	0.004	0.014	5.72E-04
general_happiness_with_own_health_f20459	Mental health	0.011	0.006	0.016	1.84E-05	0.013	0.008	0.018	8.50E-07
attendancedisabilitymobility_allowance_f6146	sociodemographic	0.011	0.006	0.016	1.61E-05	0.015	0.010	0.020	5.07E-09
glycated_haemoglobin_hba1c_f30750	Biological samples	0.011	0.006	0.016	2.03E-05	0.010	0.005	0.015	2.23E-04
daytime_dozing_sleeping_narcolepsy_f1220	style and environn	0.011	0.006	0.016	8.47E-06	0.011	0.006	0.016	1.66E-05
recent_feelings_of_tiredness_or_low_energy_f20519	Mental health	0.013	0.008	0.018	3.49E-07	0.016	0.011	0.021	1.04E-09
white_blood_cell_leukocyte_count_f30000	Biological samples	0.013	0.008	0.018	4.09E-07	0.001	-0.004	0.007	5.84E-01
equency_of_tiredness_lethargy_in_last_2_weeks_f20sychosocial factor	'sychosocial factor	0.014	0.009	0.019	3.31E-08	0.015	0.010	0.020	3.27E-09
frequency_of_friendfamily_visits_f1031	'sychosocial factor	0.014	0.009	0.019	2.37E-08	0.012	0.007	0.017	2.36E-06
recent_restlessness_f20516	Mental health	0.015	0.010	0.020	5.56E-09	0.014	0.009	0.019	4.76E-08
suffer_from_nerves_f2010	'sychosocial factor	0.015	0.010	0.020	6.56E-09	0.012	0.007	0.017	2.12E-06
mouthteeth_dental_problems_f6149	lth and medical his	0.016	0.010	0.021	1.50E-09	0.016	0.011	0.021	1.16E-09
hand_grip_strength_right_f47	Physical measures	0.016	0.011	0.021	1.35E-09	0.014	0.009	0.019	4.17E-08
recent_thoughts_of_suicide_or_selfharm_f20513	Mental health	0.017	0.012	0.022	7.81E-11	0.016	0.011	0.021	2.64E-10
poultry_intake_f1359	style and environn	0.017	0.012	0.022	5.98E-11	0.007	0.002	0.012	7.02E-03
overall_health_rating_f2178	lth and medical his	0.017	0.012	0.022	5.38E-11	0.019	0.014	0.024	5.08E-14
major_dietary_changes_in_the_last_5_years_f1538	style and environn	0.017	0.012	0.022	1.97E-11	0.018	0.013	0.023	7.38E-12
recent_easy_annoyance_or_irritability_f20505	Mental health	0.017	0.012	0.022	1.36E-11	0.012	0.007	0.017	1.41E-06
nap_during_day_f1190	style and environn	0.017	0.012	0.022	1.21E-11	0.019	0.013	0.024	5.86E-13
peak_expiratory_flow_pef_f3064	Physical measures	0.018	0.012	0.023	2.81E-11	0.020	0.015	0.025	7.65E-14
time_spent_using_computer_f1080	style and environn	0.018	0.013	0.023	4.43E-12	0.013	0.008	0.018	1.77E-07
other_eye_problems_f2227	lth and medical his	0.018	0.013	0.023	8.65E-13	0.019	0.014	0.024	2.18E-13
age_first_had_sexual_intercourse_f2139	style and environn	0.019	0.013	0.024	2.82E-12	0.022	0.017	0.027	1.37E-16
chest_pain_or_discomfort_f2335	lth and medical his	0.019	0.014	0.024	3.96E-13	0.017	0.012	0.022	5.54E-11
sensitivity_hurt_feelings_f1950	'sychosocial factor	0.019	0.014	0.024	1.59E-13	0.015	0.010	0.020	1.62E-08

worrier_anxious_feelings_f1980	Psychosocial factor	0.019	0.014	0.024	1.12E-13	0.013	0.008	0.018	6.74E-07
recent_poor_appetite_or_overeating_f20511	Mental health	0.019	0.014	0.024	5.02E-14	0.020	0.015	0.025	1.48E-14
in_serious_accident_believed_to_be_lifethreatening_f1980	Mental health	0.020	0.015	0.025	1.61E-14	0.020	0.014	0.025	3.05E-14
recent_feelings_of_depression_f20510	Mental health	0.020	0.015	0.025	4.23E-15	0.018	0.013	0.023	7.16E-12
recent_trouble_concentrating_on_things_f20508	Mental health	0.021	0.016	0.026	9.76E-16	0.017	0.012	0.022	3.72E-11
changes_in_speedamount_of_moving_or_speaking_f20507	Mental health	0.021	0.016	0.026	5.94E-16	0.022	0.017	0.027	2.52E-18
mood_swings_f1920	Psychosocial factor	0.021	0.016	0.026	2.75E-16	0.017	0.012	0.022	3.62E-11
cereal_intake_f1458	style and environment	0.022	0.017	0.027	4.68E-17	0.022	0.017	0.027	1.11E-17
agency_of_tenseness_restlessness_in_last_2_weeks_f20509	Psychosocial factor	0.022	0.017	0.027	8.31E-17	0.021	0.016	0.026	1.33E-15
gone_to_take_to_doctor_when_needed_as_a_child_f20512	Mental health	0.022	0.017	0.027	8.72E-18	0.013	0.008	0.018	1.99E-07
vitamin_and_mineral_supplements_f6155	Health and medical history	0.023	0.018	0.028	5.88E-19	0.020	0.015	0.025	1.05E-14
abuse_by_partner_or_expartner_without_consent_as_a_child_f20513	Mental health	0.023	0.018	0.028	2.40E-19	0.025	0.019	0.030	1.42E-21
loss_injury_bereavement_stress_in_last_2_years_f6156	Psychosocial factor	0.023	0.018	0.028	1.02E-19	0.024	0.019	0.029	3.10E-20
getting_up_in_morning_f1170	style and environment	0.023	0.018	0.029	6.06E-20	0.022	0.017	0.027	3.82E-18
guilty_feelings_f2030	Mental health	0.024	0.019	0.029	5.72E-20	0.016	0.011	0.021	8.79E-10
loneliness_isolation_f2020	Psychosocial factor	0.025	0.020	0.030	1.53E-21	0.023	0.018	0.028	1.69E-18
recent_trouble_relaxing_f20515	Mental health	0.025	0.020	0.030	7.74E-22	0.020	0.015	0.025	2.56E-14
recent_feelings_of_inadequacy_f20507	Mental health	0.025	0.020	0.030	1.04E-22	0.024	0.019	0.029	4.93E-20
drive_faster_than_motorway_speed_limit_f1100	style and environment	0.025	0.020	0.031	2.04E-21	0.025	0.020	0.030	5.33E-21
recent_feelings_or_nervousness_or_anxiety_f20506	Mental health	0.025	0.020	0.030	6.04E-23	0.023	0.018	0.028	1.35E-18
ever_selfharm_f20480	Mental health	0.026	0.021	0.031	2.82E-24	0.024	0.019	0.029	4.20E-21
ever_taken_cannabis_f20453	Mental health	0.027	0.022	0.032	8.95E-26	0.026	0.021	0.031	2.02E-24
mean_time_to_correctly_identify_matches_f20023	Cognitive function	0.027	0.022	0.032	7.12E-26	0.023	0.018	0.028	3.19E-19
littlement_by_partner_or_expartner_as_an_adult_f20514	Mental health	0.027	0.022	0.032	2.17E-26	0.028	0.023	0.033	2.62E-27
felt_loved_as_a_child_f20489	Mental health	0.027	0.022	0.032	1.65E-26	0.021	0.016	0.026	2.20E-16
ever_addicted_to_any_substance_or_behaviour_f2040	Mental health	0.028	0.023	0.033	9.52E-27	0.027	0.022	0.032	4.52E-26
frequency_of_depressed_mood_in_last_2_weeks_f20515	Psychosocial factor	0.028	0.023	0.033	2.31E-26	0.026	0.021	0.032	3.78E-24
agency_of_unenthusiasm_disinterest_in_last_2_weeks_f20516	Psychosocial factor	0.029	0.024	0.034	1.48E-28	0.022	0.017	0.027	7.46E-18
constant_worrying_too_much_about_different_things_f20517	Mental health	0.029	0.024	0.034	1.14E-29	0.022	0.017	0.027	4.53E-18
ever_contemplated_selfharm_f20485	Mental health	0.029	0.024	0.034	1.05E-29	0.029	0.024	0.034	5.96E-29
forced_expiratory_volume_in_1second_fev1_f3063	Physical measures	0.029	0.024	0.035	1.18E-28	0.027	0.022	0.032	2.40E-24
doctor_gp_for_nerves_anxiety_tension_or_depression_f20518	Psychosocial factor	0.029	0.024	0.034	2.55E-30	0.026	0.021	0.031	1.41E-23
length_of_time_at_current_address_f699	Sociodemographic	0.030	0.025	0.035	2.29E-32	0.023	0.018	0.028	1.13E-18
recent_feelings_of_foreboding_f20512	Mental health	0.030	0.025	0.035	2.75E-32	0.027	0.022	0.032	3.59E-26
nervous_feelings_f1970	Mental health	0.030	0.025	0.036	8.18E-32	0.021	0.016	0.026	9.11E-16
help_or_received_professional_help_for_mental_distress_f20519	Mental health	0.031	0.026	0.036	3.34E-34	0.029	0.024	0.034	2.85E-30
victim_of_sexual_assault_f20531	Mental health	0.032	0.027	0.037	1.02E-34	0.028	0.023	0.033	4.38E-28
victim_of_physically_violent_crime_f20529	Mental health	0.032	0.027	0.037	4.31E-35	0.028	0.023	0.033	5.92E-27
ever_had_period_extreme_irritability_f20502	Mental health	0.032	0.027	0.037	2.11E-34	0.027	0.022	0.033	6.51E-26
alcohol_drinker_status_f20117	style and environment	0.032	0.027	0.037	1.42E-36	0.022	0.017	0.027	2.05E-17
ever_had_period_of_mania_excitability_f20501	Mental health	0.033	0.027	0.038	4.76E-36	0.029	0.024	0.035	7.09E-30
psychiatrist_for_nerves_anxiety_tension_or_depression_f20520	Psychosocial factor	0.034	0.029	0.039	1.40E-40	0.029	0.024	0.034	3.23E-30
ever_thought_that_life_not_worth_living_f20479	Mental health	0.035	0.030	0.040	1.30E-42	0.031	0.026	0.036	4.45E-34
sexually_molested_as_a_child_f20490	Mental health	0.036	0.031	0.041	3.77E-44	0.028	0.023	0.033	2.32E-27
worried_tense_or_anxious_for_most_of_a_month_or_longer_f20521	Mental health	0.036	0.031	0.042	9.79E-43	0.033	0.028	0.039	3.39E-36
had_prolonged_feelings_of_sadness_or_depression_f20522	Mental health	0.036	0.031	0.042	1.30E-45	0.033	0.028	0.038	1.63E-37
cal_violence_by_partner_or_expartner_as_an_adult_f20523	Mental health	0.037	0.032	0.042	3.44E-46	0.038	0.033	0.043	2.45E-49
experienced_mental_distress_preventing_usual_activities_f20524	Mental health	0.037	0.032	0.042	1.37E-46	0.035	0.030	0.040	3.99E-41
vitamin_d_f30890	Biological samples	0.037	0.032	0.043	2.72E-44	0.029	0.024	0.034	5.00E-27
situations_because_of_previous_stressful_experience_f20525	Mental health	0.041	0.036	0.046	2.10E-56	0.038	0.032	0.043	2.88E-48
at_when_reminde_of_stressful_experience_in_past_f20526	Mental health	0.041	0.036	0.046	6.26E-57	0.040	0.035	0.045	2.76E-55
risk_taking_f2040	Psychosocial factor	0.041	0.036	0.046	1.38E-56	0.030	0.025	0.035	5.54E-31
natural_environment_percentage_buffer_1000m_f2450	Local Environment	0.042	0.037	0.047	1.54E-59	0.031	0.026	0.036	1.81E-33
physically_abused_by_family_as_a_child_f20488	Mental health	0.043	0.038	0.048	4.75E-62	0.043	0.038	0.048	1.03E-63
turbulent_thoughts_of_stressful_experience_in_past_year_f20527	Mental health	0.043	0.038	0.048	5.91E-64	0.041	0.036	0.046	3.35E-58
type_of_accommodation_lived_in_f670	Sociodemographic	0.043	0.038	0.048	2.79E-64	0.033	0.028	0.038	5.41E-38
pork_intake_f1389	style and environment	0.044	0.039	0.049	1.61E-66	0.026	0.021	0.031	5.18E-24
tense_highly_strung_f1990	Psychosocial factor	0.046	0.041	0.051	1.34E-69	0.038	0.033	0.043	1.74E-47
townsend_deprivation_index_at_recruitment_f189	Deprivation characteristics	0.047	0.042	0.052	1.78E-73	0.039	0.034	0.044	4.71E-53
particulate_matter_air_pollution_pm10_2007_f24019	Local Environment	0.049	0.044	0.054	7.69E-80	0.035	0.030	0.040	9.04E-42
felt_hated_by_family_member_as_a_child_f20487	Mental health	0.053	0.048	0.058	1.87E-93	0.047	0.042	0.052	3.37E-74
nitrogen_dioxide_air_pollution_2007_f24018	Local Environment	0.053	0.048	0.058	7.35E-93	0.040	0.035	0.045	5.40E-54
use_of_sunuv_protection_f2267	style and environment	0.056	0.051	0.061	5.98E-105	0.040	0.035	0.045	2.73E-55

CI: upper 95% confident interval, P: P value. the variables in bold are significant results from both PRS-cs-auto-SCZ75 and PRSice-SCZ75

Predictor	protective exposure	N	multiplicative scale (Ms)				Relative excess risk due to interaction (RERI)				Attributable proportion (AP)				Synergy index (SI)			
			estimate	lower.CI	upper.CI	P	estimate	lower.CI	upper.CI	P	estimate	lower.CI	upper.CI	P	estimate	lower.CI	upper.CI	P
birth_weight	Yes	91215	0.995	0.931	1.062	0.874	-0.005	-0.080	0.070	0.550	-0.004	-0.068	0.060	0.450	0.974	0.644	1.473	0.550
maternal_	No	132602	0.942	0.837	1.061	0.325	-0.024	-0.185	0.137	0.615	-0.016	-0.124	0.092	0.386	0.954	0.697	1.307	0.615
pack_year	No	41606	1.016	0.938	1.100	0.703	0.059	-0.050	0.168	0.145	0.041	-0.032	0.114	0.137	1.153	0.894	1.488	0.136
smoking_s	No	151326	1.040	0.938	1.153	0.455	0.126	-0.014	0.266	0.038	0.076	-0.006	0.158	0.034	1.239	0.968	1.587	0.044

Note: N: sample size for interaction analyses. r²: correlation coefficient, lower.CI: lower 95% confident interval, upper.CI: upper 95% confident interval, P: P value. 95%CI is estimated by delta method.



This study explores how genetic risk for schizophrenia (PRS-SCZ) interacts with environmental factors to influence psychotic experiences (PEs). Using data from over 148,000 UK Biobank participants, researchers found that certain exposures, like mental distress and sleep problems, interact with PRS-SCZ to increase PE risk. These gene-environment interactions suggest that both genetic predisposition and environmental factors jointly contribute to the development of psychosis. The findings highlight the importance of considering both genetic and environmental influences in understanding and potentially preventing psychosis.

Journal Pre-proof