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Title: Neuroticism polygenic risk score predicts 20-year burden of depressive symptoms for Whites but not Blacks

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Abstract:

Background. Black-White differences are reported in social, psychological, behavioral, medical, and biological correlates of depression. This study was conducted to compare Black and White older adults for the association between neuroticism polygenic risk score (N-PRS) and chronicity of depressive symptoms over 20 years.

Methods. Data came from the Health and Retirement Study (HRS), 1990 – 2012, a nationally representative sample of Americans above age 50. Current analysis followed 9,249 individuals (7,924 Whites and 1,325 Blacks) for up to 22 years. Depressive symptoms were measured every two years between 1992 and 2012 using the 8-item Center for Epidemiological Studies-Depression Scale (CES-D-8). The independent variable was N-PRS. The dependent variable was average depressive symptoms between 1992 and 2012. Linear regression was used for data analysis.

Results. In the pooled sample, higher N-PRS was associated with higher average depressive symptoms over the 20-year follow up period [b=0.01, 95%CI=0.00 to 0.04], net of all covariates. We also found an interaction between race and N-PRS [b=-0.02, 95%CI=-0.03 to 0.00], suggesting a stronger effect of N-PRS on 20-year average depressive symptoms for Whites than Blacks. Based on our race-specific linear regression models, higher N-PRS was associated with higher depressive symptoms from 1992 to 2012 for Whites [b=0.01, 95%CI=0.01 to 0.02] but not Blacks [b=0.00, 95%CI=-0.02 to 0.02].

Conclusion. Black and White older adults may differ in the salience of the existing N-PRS for depressive symptoms, which better reflects the burden of depression for Whites than Blacks. This may be because the existing PRSs are derived from mostly or exclusively White samples, limiting their applicability in other race groups. Racial variation in psychosocial, clinical, and biological correlates of depression needs further research.

Keywords: African Americans; Whites; Ethnic groups; Neuroticism; Depression, Genetics, Polygenic Risk Score

1. Background

Neuroticism (N), a relatively stable personality trait with major public health significance (1), reflects some of the between-individual variation in the tendency to respond to threats with negative emotion. N is of high public health significance because it is a strong predictor of a wide range of undesired physical health outcomes such as heart disease, stroke, hypertension, diabetes, and obesity (2,3). N is also associated with an increased risk of premature mortality (3). N predicts quality of life, health service use, and mental disorders including depression (1-3).

N is believed to reflect vulnerability to anxiety and depression (4-8). Higher scores of N predict more frequency and intensity of negative emotional reactions in response to stress (2). Individuals with a higher N score are also more sensitive to negative emotional information (9,10). Therefore, individuals with higher N frequently experience emotional arousal which is a well-accepted risk factor for a wide range of negatively charged emotions (e.g. sadness, anger, anxiety, fear, worry, frustration, distress, loneliness, and depression) (11-13).

N, however, may not be universally harmful. The health consequences of N may depend on the context, culture, and health outcome, probably through differential behavioral and physiological consequences of N trait across sub-populations (14-17). At high-risk environments, high N may help individuals avoid exposures (18). In such contexts, N may become protective, as individuals with high N may have a higher tendency to avoid risks due to their higher sensitivity to the potential costs associated with environmental exposures (19). In this view, contextual factors such as culture and environment should be regarded as moderating factors that alter the health effects of N (18). In a study, N was a risk and protective factor for cardiovascular mortality in women with low and high socioeconomic status (SES) respectively (20). N differently moderates the effect of social support on health across cultures (19). Thus, the health effects of N may depend on sociodemographic factors.

A recent study suggested that N may better reflect the future risk of depression for Whites than Blacks (21). In the Americans' Changing Lives (ACL) data that included 847 Whites and 372 Blacks higher N at baseline was associated with higher risk major depressive disorder (MDD) 25 years later (OR=2.23) in the pooled sample. The study showed an interaction between race and baseline N on subsequent risk of MDD (OR=0.37), suggesting a weaker effect for Blacks compared to Whites. Race-specific models showed an effect for Whites (OR=2.55) but not Blacks (OR=0.90) (21).

According to the "cultural moderation" hypothesis, correlates of N and other domains of negative affectivity depend on culture, race, and ethnicity (22). As proposed by the "differential effects hypothesis" (23), psychosocial mechanisms that shape populations' health and illness are group-specific and not universal. As suggested by this hypothesis, such mechanisms vary across race and ethnic groups. These hypotheses conceptualize race and ethnicity as potential effect modifiers that may alter the effects of the very same risk factors on the very same health outcomes (24). Considerable empirical data support these hypothesis (25), as multiple Black-White differences have been found in correlates of psychosocial constructs such as negative affect, anger, and N (22,27).

Race, ethnicity, culture, and SES may alter the salience of N as a psychological risk factor for depression (19,20). N may not have the same salience for the majority as the minority groups (21,28). To better understand racial and ethnic differences in the association between N polygenetic risk (N-PGS) on depressive symptoms, the current study compared Blacks and Whites aged 50 or older for the association between N-PGS and average

depressive symptoms over a 20 year follow up period, using a national sample of older adults in the United States.

2- Methods

Study design

Data were from the Health and Retirement Study (HRS), 1990-2012. HRS is an ongoing state of the art longitudinal cohort study with a nationally representative sample of U.S. adults over the age of 50. The HRS has collected extensive data on SES, psychological factors, health behaviors, physical health, mental health, and health care utilization, with the primary goal of understanding the healthy transition of populations into retirement.

The baseline HRS interview was conducted in 1992. Follow-up interviews are conducted every two years, using alternating face-to-face and telephone interviews. Probability sampling was used to select households in all 50 states, and primary respondents were selected from age-eligible household members. Spouses or partners of primary respondents were also enrolled in the study. The core sample in the HRS was comprised of people who were born between 1931 and 1941 and were 51-61 years of age at the time of enrollment. To maintain the sample size (due to attrition) and the representative nature of the data to U.S. adults older than 50 years, HRS has recruited additional participants over time and now includes over 37,000 respondents. More information on the HRS study design, measures, and methodology are available elsewhere (29-31).

Analytic sample

This study included only White or Black individuals from the HRS core sample with data on N-PRS and depressive symptoms. The White analytic sample consisted of respondents who self-reported being White and met criteria for genetically-determined White ancestry (see HRS QC report for additional details) (48); the same procedure was used to create the Black analytic sample. The current analysis included 9,249 individuals (7,924 Whites and 1,325 Blacks).

Ethics

The University of Michigan Institutional Review Board (IRB) approved the HRS study protocol. All participants signed written informed consent documents. All study procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national), as determined by the Helsinki Declaration of 1975, and revised in the year 2000. Participants received financial compensation for their participating in the study.

Measures

Demographics. All demographics were taken from the baseline interview (1992). Demographic factors included sex (1 for female, 0 for male), age (continuous measure in years), and race (a dichotomous variable, Whites=0, Blacks=1).

Socio-economic status (SES). We took SES measures including education and income from the 1992 survey. We used continuous variables for years of education as well as household income.

Depressive symptoms. An eight -item version of the Center for Epidemiologic Studies Depression Scale (CES-D) (33) was applied to measure frequency of depressive symptoms (32,33). This CES-D, applied at each wave, asked respondents about the extent to which they felt depressed, lonely, sad, and happy in past week. All of the item responses were dichotomous. An average score was calculated with a potential range from 0 to 8. A higher score indicated more depressive symptoms.

Chronic medical conditions (CMC). The HRS obtained self-reported information on respondents' CMC at all waves. Respondents were asked whether a physician has ever diagnosed them with each condition. The following seven conditions were evaluated: high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, and arthritis.

Self-rated health (SRH). HRS asked respondents' overall health using a 5-point scale. Responses were excellent, very good, fair, good, and poor. SRH was treated as a continuous variable, with a potential range from 1 to 5, with a higher score indicating worse SRH (34,35).

Body mass index (BMI). From 1992 to 2004, BMI was calculated based on self-reported weight and height. BMI was then directly measured starting in 2006, during face to face interviews. Weight and height were originally collected in pounds (1 pound = 0.453 kilograms), and feet (1 foot = 0.3048 meters) / inches (1 inch = 0.0254 meters). As people have a tendency to overestimate their height and underestimate their weight, BMI based on self-reported data is on average an underestimation of actual BMI, particularly for women. However, BMI based on self-reported weight and height strongly correlates with directly measured BMI (36,37).

Neuroticism PRSs (*N-PRS).* Using the llumina HumanOmni2.5 BeadChips (HumanOmni2.5-4v1, HumanOmni2.5-8v1), genotype data was obtained from the HRS participants, based on about 2.4 million SNPs. Individuals were removed if they had first-degree relatives in the HRS or missing call rates more than 2%. SNPs with call rates less than 98% or Hardy-Weinberg p-value less than 0.0001 were removed. Individuals were evaluated for chromosomal anomalies, and all affected SNPs were removed from the analysis if an anomaly was detected. Genotype data was based on saliva samples (DNA) that were collected in 2006, 2008, or 2010.

The N-PRS was created using beta coefficients from a GWAS meta-analysis for neuroticism conducted on approximately 171,000 participants (38), with the HRS sample removed. The Whites' PRS contains 1,152,920 SNPs that overlapped between the HRS genotype data and the GWAS meta-analysis; Blacks' PRS contains 1,148,174 SNPs. The N-PRSs were standardized within racial groups (mean=0, standard deviation=1) (39,40,74).

2.7. *Statistical Analysis*

We used SPSS for Windows 21.0 (IBM Inc. Armonk, NY) for data analysis. Descriptive and frequency tables were used for univariate analysis. Four linear regression models were used for multivariable analysis. In all models, N-PRS was the main independent variable, average depressive symptoms over 20 years from 1992 to 2012 was the main outcome, and demographics (age and sex), SES (education and income), and health (CMC, SRH, and BMI), and baseline depressive symptoms were covariates. First, we ran two models in the pooled sample. *Model 1* tested the main effects of N, race, and covariates. *Model 2* also included an interaction term between race and N. Then we conducted separate race-specific models for Whites (*Model 3*) and Blacks (*Model 4*). We reported unstandardized regression coefficients (b), their 95% CI, and p values for each variable. P-values <0.05 were considered significant.

3. Results

Current analysis included 9,249 individuals who were either Whites (n=7,924, 85.7%) or Blacks (n=1,325, 14.3%). **Table 1** summarizes the descriptive statistics of the pooled sample and for each racial group. Blacks had lower education and income and worse physical health status (i.e. CMC, SRH, and BMI). Blacks also had higher average depressive symptoms over time compared to Whites (**Table 1**).

Table 1 about here.

Table 2 shows correlation coefficients for the study variables in the pooled sample and based on race. In the pooled sample and in Whites, N-PRS was negatively correlated with education and income and positively correlated with CMC, SRH, BMI, and average depressive symptoms over time. In Blacks, N-PRS was negatively correlated with education and income and positively correlated with CMC, SRH, and BMI, but not with average depressive symptoms over time (**Table 2**).

Table 2 about here.

Table 3 shows two linear regression models in overall sample. These models have the N-PRS as the independent variable (predictor) and mean depressive symptoms over time as the dependent variable (outcome). The first model only included main effects. Second models also included an interaction term between race and N-PRS. According to the first model, in the pooled sample, a higher N-PRS was associated with a higher average of depressive symptoms over the follow up time [b=0.01, 95%CI=0.00 to 0.04], net of all covariates. According to the second model, we found a significant interaction between race and N-PRS on average depressive symptoms [b=-0.02, 95%CI=-0.03 to 0.00], suggesting that the association between N-PRS and average depressive symptoms is smaller for Blacks than Whites (**Table 3**).

Table 3 about here.

Table 4 reports the results of linear regressions with N-PRS as the independent variable and average depressive symptoms over time as the dependent variable based on race. Based on these linear regression models, in Whites, higher N-PRS was associated with higher average depressive symptoms over the follow up time [b=0.01, 95%CI=0.01 to 0.02]. In Blacks, however, N-PRS was not associated with average depressive symptoms over the follow up time [b=0.00, 95%CI=-0.02 to 0.02]

Table 4 about here.

4. Discussion

We found that N-PRS is associated with average depressive symptoms for Whites but not Blacks ages 50 or older. This finding is in line with previous research that bio-psycho-social correlates of negative affect, MDD, and depressive symptoms are stronger for Whites than Blacks (36,41-47). We provide four potential explanations for the current finding. The first three explanations are not specific to N. The last explanation suggests that high N may not similarly indicate depressive symptom risk for sociodemographic groups.

Our first explanation is based on how PRSs are developed and validated. As currently available PRSs are developed and validated in exclusively or almost exclusively White samples, PRSs typically explain more outcome variability in Whites. This is partially due to the discordant patterns of linkage disequilibrium (LD) across diverse populations (48). As a result, the existing PRSs better reflect the pertaining phenotypes for Whites than other minority groups (39,40,49,50). N-PRS is no exception to this rule. Research into the development and validation PRSs in non-White populations will show whether the same percentage of the variance of phenotypes can be explained by PRSs for Whites and racial and ethnic minorities (40). Similar results are reported for other PRSs (51,52).

The second explanation is a measurement argument. Many psychosocial measures show better psychometric properties in Whites compared to Blacks as they have been developed in studies that have mostly enrolled Whites. The same is true for psychometric properties of the existing N and depression measures that better operate in Whites compared to any minority groups including Blacks. The result is systematically weaker correlates of psychosocial factors for Blacks in comparison with Whites (41-43,53,54). There is also some specific evidence showing that CES-D measure may not provide identical results for Whites and Blacks (57-60). Relevance of DSM criteria may differ for depression of Blacks and Whites (55,56), resulting in different nature of depression based on race and ethnic group. Racial and ethnic groups may also differ in what constructs that are designed to capture personality traits such as N reflect (56). This problem is not specific to N and depression, as race and ethnicity alter the meaning of almost all psychosocial measures (61,62). Race and ethnicity alter how personality traits and psychological distress covary with particular psychiatric disorders such as MDD (63). Psychiatric disorders better impact perceived mental health and perceived need to health care in Whites than Blacks (64,65). Concordance between CES-D score and clinical depression also depends on contextual factors such as race and ethnicity (66,67). Stressful life events may also better reflect risk of MDD in Whites than Blacks (45,46). The link between depressive symptoms and MDD also varies by race (90). As mentioned, the stronger associations between subjective and objective health outcomes in Whites than Blacks extends to a wide range of psychosocial and health measures (53,63,64,68).

The associations between race, SES, personality traits such as N, and health are very complex. From one side, research has shown that personality traits such as N may partially mediate the effects of SES and health. N explains some between-SES strata differences in mortality risk, as well as some individual risk heterogeneity within each SES strata. As a result, N may be shaped by individual predispositions as well as social and structural inequalities (69). At the same time, SES alters the effects of N on health. One study showed a significant interaction between sex, N, and SES on CVD mortality, so the effects of N was stronger in women with low SES, whereas the effects of N was smaller among high SES women (70). Race also changes the health effects of N (21). However, the direction of the moderation of race and low SES seems counterintuitive. One explanation is that race and SES differently engage behavioral and biological mechanisms that reflect the effects of N on physical and mental health. More research is needed in these complex patterns.

The third explanation, again not specific to N, is the unequal effects of potentials to actual outcomes due to racism in the United States. In the presence of racism, resources and assets better translate to their pertaining outcomes in Whites than Blacks. In this view, presence or absence of risk and protective factors have more consequences for the privileged than the minority group. A similar pattern is documented for several economic resources such as education, employment, neighborhood quality, and size of social network on risk of mortality (25,71-73). Similar patterns are also shown for psychological assets such as affect, anger control, self-efficacy, and perceived control over life (70,74-76).

The forth explanation is specific to N. Previous empirical research has suggested that N (19,20) and other negative affectivity measures (77-80) may have group-specific rather than universal health effects. In a recent study using American Changing Lives (ACL) data, high N at baseline predicted subsequent risk of clinical MDD 25 years later for Whites but not Blacks (21). Depressive symptoms predicted all-cause (77) and cause-specific (78) mortality for Whites but not Blacks. Hostility and anger have also predicted cardiovascular mortality for Whites but not Blacks (79). Park et al., found that N altered the link between social support and health in Japanese but not American individuals (19) and anger may even be linked to better health in some cultures (80). Park et al., showed that for White Americans, lower social standing was associated with greater expression of anger, but for Japanese individuals, high social status was associated with more anger expression. While for White Americans, anger expression was predicted by subjective social status, for Japanese, objective social status predicted anger expression (22). These racial differences are important as both current and historical racism and discrimination may have altered social and behavioral implications for N, vigilance, and sensitivity to threats for Blacks.

In line with the last explanation, Kitayama et al., have argued that N becomes a protective factor in some and a risk factor in other contexts, depending on the level of risk in the environment. As N reflects sensitivity to potential costs associated with environmental exposures, high N may be associated with avoiding exposures through vigilance (19). At least in some contexts, high N may mean less exposure, which has health implications (18,81). Blacks and Whites also differ in the effect of stress on chronic disease and depression, possibly due to their differential behavioral coping strategies (82-86). Moderating effects of context, race, and ethnicity holds for a wide range of psychosocial domains and health (26,27,77,78). This is in part because race, ethnicity and culture shape experiences and expression of emotions (87,89). More research is still needed to discern the exact mechanisms by which race, ethnicity, sex, and culture influence health outcomes such as depression.

There are limitations to this study. First, this study did not measure N. Second, we measured depressive symptoms using a self-report measure rather than risk of clinical MDD diagnosis based on structural interviews. Third, this study used an eight-item CES-D measure that may have differential validity across ethnic groups. As a result, there is a need for replication of these findings using standardized measures of depression and N. Fourth, we conceptualized N, SES, and health as fixed factors; however, all of these constructs are subject to change over time. Fifth, the sample size was not balanced between Whites and Blacks resulting in lower statistical power for Blacks. Sixth, we did not control for mental health care use, anti-depressant prescription, or access to care. Seventh, due to the higher mortality of Blacks, race is not independent of attrition in this study. This has implications for the calculation of 20-year average of depressive symptoms. Eighth, it is not clear that the results are solely due to the interaction of N-PRS with race. Future research should test the interactions between N-PRS and SES. More research is needed on validation of these findings using a wide range of data

sets. Although these limitations exist, our study was one of the first attempts to explore Black-White variation in the link between N-PGS and depression.

In conclusion, Black and White older adults differ in the salience of currently accepted genetic predisposition for N on severity of depressive symptoms. The N-PRS does not operate well for Blacks, which may be because the PRS was developed and validated in Whites. This finding is in line with other previously reported Black - White differences in social, psychological, clinical, and biological correlates of depression. Other explanations may be structural racism and the cultural moderation hypothesis.

Ethics: The University of Michigan IRB approved the study protocol. Written informed consent was obtained from all participants included in the study.

Conflict of Interest: Author declares no conflicts of interest.

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Animal Study: None

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Table 1: Descriptive statistics in the pooled sample and stratified by race

	All (n=9249)		Whites (n=7924)		Blacks (n=1325)	
	n	%	n	%	n	%
Sex						
Male	3857	41.70	3374	42.58	483	36.45
Female	5392	58.30	4550	57.42	842	63.55
	Mean	SD	Mean	SD	Mean	SD
Age (Years)	56.33	3.96	56.38	3.99	56.17	3.85
Education (Years)*	12.19	3.24	12.42	3.12	11.30	3.19
Income, (Thousands of USD)*	225.80	485.73	265.94	525.73	70.45	136.96
Chronic Medical Conditions (Baseline)*	0.92	1.00	0.89	0.98	1.16	1.07
Self-Rated Health (Baseline)*	2.44	1.13	2.35	1.11	2.88	1.12
Body Mass Index (Baseline)*	27.17	4.90	26.87	4.64	28.87	5.86
N-PRS	0.01	1.01	0.01	1.01	0.03	1.01
Depressive Symptoms (20 Year-Average)*	0.14	0.25	0.13	0.24	0.18	0.28

Neuroticism Polygenic Risk Score (N-PRS)

* $p<0.05$ for test of difference in means (t-test) between Whites and Blacks

Table 2. Correlation matrix in the pooled sample and based on race

	2	3	4	5	6	7	8	9	10
Pooled sample									
1 Race (Black)	.068**	-0.019	-.129**	-.137**	.099**	.168**	.147**	.005	.074**
2 Sex (Female)	1	.132**	.040**	.047**	.081**	.054**	-.019	-.001	.137**
3 Age (Years)		1	-.068**	.045**	.083**	.048**	-.023	0.02	-.001
4 Education (Years)			1	.214**	.123**	.352**	.117**	.071**	.253**
5 Income (USD)				1	-.096**	.167**	.074**	-.033**	.112**
6 Chronic Medical Conditions (Baseline)					1	.458**	.256**	.047**	.251**
7 Self-Rated Health (Baseline)						1	.218**	.058**	.337**
8 Body Mass Index (Baseline)							1	-.001	.102**
9 Depressive Symptoms (20 Year Average)								1	.081**
10 N-PRS									1
Racial groups									
1 Race (Black)	-	-	-	-	-	-	-	-	-
2 Sex (Female)	1	-.131**	-.064**	-.039**	-.061**	.033**	-.078**	-0.004	-.130**
3 Age (Years)	-.137**	1	-.057**	-.044**	-.096**	-.061**	-0.012	0.028	0.006
4 Education (Years)	.142**	.188**	1	.205**	.111**	.350**	.122**	.077**	.251**
5 Income (USD)	-.070**	.022	.256**	1	-.087**	.155**	.063**	-.036**	.109**
6 Chronic Medical Conditions (Baseline)	.151**	.051	-.125**	-.131**	1	.447**	.231**	.039**	.236**

7 Self-Rated Health (Baseline)	.085**	-.009	-.259**	-.111**	.474**	1	.201**	.058**	.325**
8 Body Mass Index (Baseline)	.176**	-.053	.009	.021	.285**	.171**	1	.009	.080**
9 Depressive Symptoms (20 Year Average)	.017	-.02	-.05	.013	.083*	.056	-.043	1	.096**
10 N-PRS	.150**	-0.034	-.216**	-.097**	.285**	.342**	.113**	.021	1

Neuroticism Polygenic Risk Score (N-PRS)

In the lower panel, Whites are the upper diagonal, and Blacks are the lower diagonal

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 3: Effect of neuroticism polygenic risk score (N-PRS) on average of depressive symptoms over 20 years of follow up in the pooled sample (n=9249)

	Model 1 Main Effects		Model 2 Model 1 + Race × N-PRS	
	b	95% CI	b	95% CI
Race (Black)	0.02*	0.00 to 0.04	0.02*	0.00 to 0.04
Sex (Female)	0.04***	0.03 to 0.06	0.04***	0.03 to 0.06
Age (Years)	0.00	0.00 to 0.00	0.00	0.00 to 0.00
Education (Years)	-0.01***	-0.01 to -0.01	-0.01***	-0.01 to -0.01
Income (USD)	0.00	0.00 to 0.00	0.00	0.00 to 0.00
CMC	0.03***	0.02 to 0.04	0.03***	0.02 to 0.04
SRH	0.04***	0.04 to 0.05	0.04***	0.04 to 0.05
BMI	0.00	0.00 to 0.00	0.00	0.00 to 0.00
N-PRS	0.01***	0.01 to 0.02	0.01***	0.01 to 0.02
N-PRS × Race			-0.02*	-0.03 to 0.00
Intercept	0.10#	-0.01 to 0.21	0.10#	-0.01 to 0.22

Chronic medical conditions (CMC), Body Mass Index (BMI), Self-Rated Health (SRH), Neuroticism Polygenic Risk Score (N-PGS)

# $p < 0.1$ * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 4: Effect of neuroticism- polygenic risk score (N-PRS) on average depressive symptoms over 20 years of follow up by race.

	Whites (n=7924)		**Blacks (n=1325)**	
	b	**95% CI**	**b**	**95% CI**
Sex (Female)	0.04***	0.03 to 0.05	0.06**	0.02 to 0.10
Age (Years)	0.00	0.00 to 0.00	0.00	-0.01 to 0.00
Education (Years)	-0.01***	-0.01 to -0.01	-0.02***	-0.02 to -0.01
Income (USD)	0.00*	0.00 to 0.00	0.00	0.00 to 0.00
CMC	0.03***	0.02 to 0.04	0.03**	0.01 to 0.06
SRH	0.04***	0.03 to 0.05	0.06***	0.04 to 0.08
BMI	0.00	0.00 to 0.00	0.00	0.00 to 0.00
N-PRS	0.01***	0.01 to 0.02	0.00	-0.02 to 0.02
Intercept	0.09	-0.02 to 0.21	0.23	-0.15 to 0.60

Chronic medical conditions (CMC), Body Mass Index (BMI), Self-Rated Health (SRH), Neuroticism Polygenic Risk Score (N-PGS)

# $p < 0.1$ * $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$