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## Quantification of diet quality utilizing the rapid eating assessment for participants-shortened version in bipolar disorder: Implications for prospective depression and cardiometabolic studies

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### Conflict of interest

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### CRedit authorship contribution statement

Writing – Original draft preparation: MGR, and MAF. Critical revision of the article contributing with ideas related to their area of expertise: All authors. Statistical analysis: SJW, JMB, CC, RSP. Analysis interpretation: MGR, MAF, SJW, JMB. Contribution to conceptualization: MGR, MAF, ABCB, FRN. All authors contributed to and have approved the final manuscript.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jad.2022.05.037>.

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## Abstract

**Objectives:** Recognizing bipolar disorder as a multi-system metabolic condition driven, in part, by binge eating behavior and atypical depressive symptoms, this study aimed to quantify diet quality and evaluate clinical correlates in a bipolar disorder cohort.

**Methods:** Participants from the Mayo Clinic Bipolar Disorder Biobank (n = 734) completed the Rapid Eating Assessment for Participants – Shortened version (REAP-S) to determine diet quality. The average REAP-S score for a U.S. omnivorous diet is 32 (range 13 to 39) with higher scores indicating healthier diet. Demographic variables were collected in a standardized clinical questionnaire. Depressive symptoms were assessed by the Bipolar Inventory of Symptoms Scale. Cardiometabolic variables were retrieved from the electronic health record. Associations between continuous variables and REAP-S scores (total, ‘healthy foods’ and ‘avoidance of unhealthy foods’) were assessed using linear regression.

**Results:** Overall, our sample had a mean REAP-S score of 27.6 (4.9), suggestive of a lower diet quality than the average general population in the US. There was a significant inverse relationship between mean REAP-S lower scores with increased BMI, waist circumference, disordered eating and depression. All these associations were significantly stronger in female participants.

**Limitations:** EHR cross-sectional data.

**Conclusions:** Our data suggest unhealthy diet quality in bipolar disorder is associated with depression, obesity and cardiometabolic abnormalities. Additional work is encouraged to prospectively track mood and diet quality to further understand the bidirectional relationship and clarify if dietary interventions can positively impact mood. Further delineating potential sex differences in diet quality and depression may provide greater appreciation of modifiable risk factors for future cardiometabolic burden.

## Keywords

Bipolar disorder; Diet quality; Cardiometabolic markers; Obesity; Bipolar depression

## 1. Introduction

Bipolar disorder (BD) is increasingly recognized as a multi-system metabolic condition mediated by genetic, biological and environmental factors (Leboyer et al., 2012; Goldstein et al., 2020). BD is highly comorbid with disordered eating behaviors, obesity, and metabolic disturbances, which all are thought to contribute to the increased risk for major adverse cardiovascular events and all-cause mortality in bipolar disorder (Prieto et al., 2016; Cuellar-Barboza et al., 2020; Foroughi et al., 2021). Obesity and central adiposity, which

highly correlate with insulin resistance, have been associated with worse illness trajectory and impaired treatment response in bipolar patients (McElroy et al., 2016a; Bentham et al., 2017). Additionally, rates of metabolic syndrome are increased in patients with BD compared to the general population with differential risk based on mood stabilizing treatment (Bly et al., 2014; Vancampfort et al., 2015; Cardenas et al., 2008).

Diet is a multidimensional concept that encompasses caloric intake, nutritional value, and diversity of food choices, all of which can be further influenced by social determinants of health and culture (Miller et al., 2020). Unhealthy dietary patterns are known to include high consumption of processed and/or fried/refined foods, sweets and sweetened beverages and corresponding low consumption of fruits, vegetables, whole grains and fish (Rahe et al., 2014). Dietary metrics have been increasingly used to assess diet patterns as potential independent predictors of depressive symptoms in major depressive disorder (MDD) (Korczak et al., 2021). Current evidence suggest an inverse bidirectional relationship between depressed mood and diet quality, where depression worsens dietary patterns and an unhealthy diet increases the risk for depressed mood, negatively affecting depressive illness progression (Lassale et al., 2019; Painold et al., 2019; Kuczmarski et al., 2010). This relationship has been consistent across different age groups, including children with MDD (Korczak et al., 2021; Manosso et al., 2021). Dietary patterns and course of illness have not been systematically investigated in bipolar disorder (Łojko et al., 2019; Elmslie et al., 2001; McAulay et al., 2019). Early studies suggest that BD patients, in comparison to the general population, have a higher caloric, sodium, and processed foods intake, increased carbohydrate craving and glycemic load, as well as lower adherence to a Mediterranean diet (Łojko et al., 2019; Teasdale et al., 2019; Jacka et al., 2011). Pathological contributions to diet in BD may further include comorbid binge eating behavior, with prevalence ranging from 8.8 to 28%, atypical symptoms of depression (i.e. increased appetite and hyperphagia) and adverse psychotropic drugs associated weight gain (McElroy et al., 2016b; Dent et al., 2012; Frye, 2011; Elstgeest et al., 2019).

In this study, our aim was to evaluate the relationship among diet quality, body mass index, depressive symptoms, and cardiometabolic disturbances in patients with BD from the Mayo Clinic Bipolar Disorder Biobank (Frye et al., 2015a).

## 2. Materials and methods

### 2.1. Study population

The study protocol was approved by the institutional research review board at each study site, and every participant provided written informed consent. Participants were enrolled in the Mayo Clinic Bipolar Biobank at the Mayo Clinic, Rochester, MN, the Lindner Center of Hope/University of Cincinnati, OH, the University of Minnesota, Minneapolis, MN, Universidad Autónoma de Nuevo León, Mexico and Universidad de los Andes, Chile (Frye et al., 2015b). A subset of the total sample completed self-report measures to assess diet quality and, for participants from Mayo Clinic site, complementary metabolic data was acquired through review of electronic health records (EHR) (Supplementary Table 1) (Cuellar-Barboza et al., 2020; Frye et al., 2015a; Romo-Nava et al., 2020). Criteria for participation in the Bipolar Biobank included: a) a diagnosis of types I and II bipolar

disorder or schizoaffective disorder, bipolar type confirmed with the Structured Clinical Interview for DSM-IV (SCID-IV); b) no current suicidal ideation or psychosis; and c) age 18 through 80 years (Frye et al., 2015a).

## 2.2. Study methods

The Rapid Eating Assessment for Participants (REAP) was developed to promote dietary counseling in clinical settings based on the assessment of patients' baseline diet related to the Food Guide Pyramid and the 2000 U.S. Dietary Guidelines (Gans et al., 2003; Gans et al., 2000). This dietary assessment tool has been validated with medical students and consumers and has undergone feasibility/acceptability testing with practicing physicians (Gans et al., 2006). Further development and validation of a 16-item self-report shortened version of the original REAP (REAP-S) aimed to rapidly assess diet content and intake in primary care settings, facilitating an accurate appraisal of dietary information (Segal-Isaacson et al., 2004; Johnston et al., 2018). The use of REAP-S, piloted in a medical student population, has been previously used in a cross-sectional study of patients with bipolar disorder, longitudinal studies of disadvantaged women with HIV/AIDS and individuals with uncontrolled type 2 diabetes and depression (Romo-Nava et al., 2020; Segal-Isaacson et al., 2004; Tobin et al., 2006; Lutes et al., 2018). The first 13 items of this tool assess relative intake of fat, sugar, fiber and selected food groups, with 3 additional questions, which were not included in this study, evaluating cooking practice and willingness to improve eating habits (Gans et al., 2003; Segal-Isaacson et al., 2004). Quantification of response is anchored to the response of 'usually/often' (1 point), 'sometimes' (2 points), and 'rarely/never or does not apply to me' (3 points). REAP-S scores for the first thirteen items range from 13 to 39 and significantly correlate to the Healthy Eating Index-2010, a measure of diet quality that includes recommendations from the Dietary Guidelines for Americans (Johnston et al., 2018; Guenther et al., 2014). The total score estimates diet quality, with a higher score indicating a healthier diet. The estimated mean score for a typical U.S. omnivorous adult diet is 32 (Johnston et al., 2018). In addition to the total score, based on our previous study using REAP-S, items were grouped into what nutritionally constitutes healthy and unhealthy food choices for further testing for associations: "healthy foods" (items 3, 4 and 5: whole grains, fruit and vegetable intake, respectively) and "avoidance of unhealthy foods" (items 8, 9, 10 and 11, which assess for processed meats, fried foods, snacks and butter/oil intake, respectively) (Romo-Nava et al., 2020).

Depressive symptoms were assessed using the Bipolar Inventory of Symptoms Scale (BISS), a 41-item survey that discriminates between bipolar clinical states (depressed, manic/hypomanic, mixed episodes and recovered status) (Bowden et al., 2007). Specifically, the BISS-Depression subscale (including reported/observed sadness, depressed mood, depressed cognition, diminished energy and anxiety) was used to identify the participants with active depressive symptoms and a score of  $\geq 24$  was used as a cut-off point to classify a depressive episode (Gonzalez et al., 2008).

The Eating Disorder Diagnostic Scale (EDDS), a 22-item self-report questionnaire to screen for eating disorders providing a continuous composite score, was used to assess binge-eating behavior and disorder, bulimia nervosa and anorexia nervosa (Stice et al.,

2000). We calculated an EDDS overall symptom composite z-score, which assesses overall eating disorder symptomatology as a continuous measure, by standardizing all items and subsequently averaging across all items for each participant, excluding the height and birth control pill items (Romo-Nava et al., 2020). The symptom composite z-score provides an evidence on the individual's level of eating pathology, including dietary restraint, eating and hunger, weight and shape concerns, eating preoccupations, rituals, and disinhibition. Positive z-scores indicate a more disordered eating behavior than the mean (Stice et al., 2000).

### 2.3. Cardiometabolic markers and weight-labile psychotropic drugs

Cardiometabolic markers previously studied in our cohort were selected based on current cardiometabolic literature, including: BMI, waist circumference, fasting plasma glucose, triglycerides, high-density lipoproteins (HDL), low-density lipoproteins (LDL), total cholesterol, thyroid-stimulating hormone (TSH), glycated hemoglobin (HbA1c) and systolic and diastolic blood pressures (SBP and DBP) (Cuellar-Barboza et al., 2020). Cardiometabolic abnormalities were determined according to previously published cut-off points and based on international guidelines (Supplementary Table 1) (Cuellar-Barboza et al., 2020). Cardiometabolic markers data was collected from EHRs, within  $\pm 1$  year of enrollment to the Bipolar Biobank. Use of psychotropics with weight-gain potential was collected only from the clinical interview at study enrollment and not from EHR and reported for statistical analysis as a categorical variable indicating the presence/absence at time of enrollment. Psychotropics included in this list are shown in Supplementary Table 3 and were selected based on their association with weight gain.

### 2.4. Statistical analysis

Based on the typical score for an average omnivorous U.S. diet, an initial analysis focused on REAP-S total score and grouping based on 'healthier diet', defined as REAP-S total score  $\geq 32$ , and 'less healthy diet', defined as REAP-S total score  $< 32$  (Johnston et al., 2018).

Cardiometabolic markers, BISS-Depression scores and EDDS composite were treated both as continuous and binary variables based on clinical cutoff values (Supplementary Table 1). Use of weight-labile psychotropics at time of enrollment into the Biobank (dichotomous yes/no) were analyzed as categorical variable only. Continuous variables were summarized as mean  $\pm$  SD and categorical variables were summarized as N, %. For both continuous and categorical markers, associations with REAP-S total scores and subscores were tested with linear regression, adjusted for age and sex, where REAP-S scores were treated as the independent variable. To assess potential sex differences across the different variables, analyses were conducted in the overall sample, as well as separately in males and females. All statistical analyses were conducted using RStudio.

## 3. Results

A total of 734 BD participants with available REAP-S scores were included in this study; mean values  $\pm$  SD and sample sizes for each of the assessed markers are presented in Supplementary Table 1. The mean age was  $39.6 \pm 14.7$  and the group was predominantly

female (n = 471; 64.2%) and white (n = 512; 69.8%). The mean REAP-S total score was  $27.6 \pm 4.9$ .

For continuous variables, there was a significant negative relationship between the REAP-S total, 'healthy foods' and 'avoidance of unhealthy foods' scores with BMI ( $b = -0.16$ ,  $p < 0.001$ ;  $b = -0.04$ ,  $p = 0.001$ ;  $b = -0.05$ ,  $p < 0.001$ ) and waist circumference ( $b = -0.2$ ,  $p < 0.001$ ;  $b = -0.05$ ,  $p = 0.001$ ;  $b = -0.06$ ,  $p = 0.007$ ). There was also a significant association between REAP-S total and 'healthy foods' scores with depressive symptoms ( $b = -0.05$ ,  $p < 0.001$ ;  $b = -0.01$ ,  $p = 0.005$ ) and EDDS composite z-scores ( $b = -1.6$ ,  $p < 0.001$ ;  $b = -0.51$ ,  $p < 0.001$ ). A similar negative association was found between 'healthy foods' scores with triglycerides ( $b = -0.01$ ,  $p = 0.04$ ). Complete results are displayed in Table 1.

Sex differences across different variables and REAP-S scores were observed. In female participants, lower diet quality was significantly associated with, both, higher BMI ( $b = -0.199$ ,  $p = 0.0001$ ) and waist circumference ( $b = -0.22$ ,  $p = 0.002$ ). Likewise, in women, low REAP-S scores were significantly associated with more severe depressive and manic symptoms ( $b = -0.05$ ,  $p = 0.003$  and  $b = -0.08$ ,  $p = 0.015$ , respectively) and worse bipolar illness ( $b = -0.04$ ,  $p = 0.001$ ). Statistically significant inverse associations were also observed between REAP-S scores and EDDS composite z-scores in the overall sample and women, suggesting that disordered eating might have a worse impact in women's diet quality. Interestingly, no significant associations between diet scores and cardiometabolic and mood markers were observed in male participants. Results are shown in Table 2.

For dichotomized characterization of the variables (abnormal markers), there were statistically significant associations between lower total REAP-S scores and obesity ( $p < 0.001$ ), abdominal obesity ( $p = 0.014$ ), hyperglycemia ( $p = 0.04$ ), depression ( $p = 0.001$ ) and binge eating behavior ( $p < 0.001$ ). Similarly, lower scores in 'healthy foods' and 'ability to avoid unhealthy foods' were significantly associated with increased BMI ( $p = 0.03$  and  $p = 0.002$ ) and waist circumference ( $p = 0.002$  and  $p = 0.05$ ). Hypertriglyceridemia was associated with lower 'healthy foods' scores ( $p = 0.03$ ). Use of weight-labile psychotropics was not associated with REAP-S scores (total score,  $p = 0.21$ ; 'healthy foods' score,  $p = 0.14$ ; 'avoidance of unhealthy foods' score,  $p = 0.42$ ). See Supplementary Table 2.

#### 4. Discussion

To our knowledge, this is the first cross-sectional study to conduct a comprehensive nutritional assessment in BD and to explore the relationship between diet quality, depressive symptoms and cardiometabolic markers. Utilizing the REAP-S, unhealthy diet quality was consistently associated with increased depressive symptoms, BMI and waist circumference and disordered eating. An inverse association was also observed between healthy food intake and hypertriglyceridemia, a frequent clinical marker of metabolic syndrome (Dregan et al., 2020; Alberti et al., 2009). The strengths of this study include the large sample of well-characterized patients with BD, use of a validated dietary screening tool, evaluation of multiple metabolic outcomes and anthropometric and laboratory measures. Moreover, to our knowledge, this is the first and largest cross-sectional study (n = 734) to use the

REAP-S scale, an operationalized and validated instrument, to assess diet quality among BD individuals.

Overall, our sample had a mean REAP-S score of 27.6 (4.9), suggestive of a lower diet quality than the average general population in the US, as defined by REAP-S total scores <32. Unhealthy diet is usually rich in pro-inflammatory foods (i.e. processed foods, refined carbohydrates, sweetened beverages) which have been associated with higher cardiovascular disease risk burden, including metabolic syndrome, and increased risk for MDD and BD (Lassale et al., 2019; Jacka et al., 2011; Neufcourt et al., 2015; Li et al., 2020). Diets with low intake of fruits, vegetables and whole-grain products and higher intake of refined carbohydrates and fried foods, favor a proinflammatory state and pose an increased risk for metabolic syndrome (Khan et al., 2020). In contrast, dietary patterns with low inflammatory potential, such as the Mediterranean diet which is rich in fruits, vegetables, monounsaturated fats and whole grains, have been linked to decreased risk of depression and reduced odds for BD (Akbaraly et al., 2009; Parletta et al., 2019). To date, most studies have focused on the relationship between diet and MDD, however, despite the known obesity-BD link and metabolic risk, the potential influence of diet quality in BD has been significantly understudied.

Obesity in BD has been associated with greater illness burden including suicidality, worse treatment response, greater mood symptom burden, increased relapse risk, and increased risk for cardiovascular mortality (Goldstein et al., 2020; McElroy et al., 2016a). It is important to highlight the latter, since, in women with BD and an unhealthy diet, in our sex-stratified analysis, compared to men, had a statistically significant increase in BMI, waist circumference, bipolar symptoms and disordered eating. These findings suggest that diet quality may be an important contributing factor mediating the risk of obesity and severity of bipolar illness in women. This association is in accordance with previous data suggesting that women with BD are at increased risk of developing obesity, metabolic syndrome and adverse cardiovascular events as well as a trend towards having higher glycemic load and consumption of processed foods (Goldstein et al., 2020; Jacka et al., 2011). Similarly, we have previously reported concordant evidence from a large case-controlled study suggesting that obesity was associated with BD in women and this same metabolic finding has been reported in women with MDD (Cuellar-Barboza et al., 2020; Dregan et al., 2020; Ma and Xiao, 2010; Appelhans et al., 2012). Changes in feeding patterns and food preferences during depressive episodes, especially in episodes with atypical features, may explain the significant association between unhealthy diet and disordered eating behavior but also the inverse association between depressive symptoms with overall REAP-S scores, avoidance of unhealthy foods and healthy food intake. The observed gender-specific differences in our study are in line with the limited emerging evidence suggesting a specific bidirectional relationship between obesity and bipolar disorder in women, in addition to the known increased cardiovascular risk (Łojko et al., 2019; Jacka et al., 2011). Within our female sample, increased BMI and central adiposity and a low diet quality were associated with increased depressive symptoms. The absence of significant associations in men between diet quality and cardiometabolic and mood markers suggests that diet may not be the main driver of the increased risk for metabolic syndrome and adverse cardiovascular events (Foroughi et al., 2021).

Potential limitations should be considered when interpreting these findings. First, the cross-sectional design does not permit determination of causality for the associations. Second, analysis of associations between some cardiometabolic markers was limited by small sample sizes, however, these values were obtained from electronic health records, hence measured in clinical settings. Third, while there were no differences between participants with and without weight-labile psychotropics, this was only assessed by looking at current medications. Evaluation of lifetime psychotropic use might provide more evidence on the contributing effect on the obesity-BD link of psychotropics with weight-gain potential. Fourth, we acknowledge the risk for reporting and recall biases as a limitation of retrospective diet assessment tools and the need for larger studies using REAP-S to increase the validity of this tool. Fifth, most of the study population was white and of European ancestry which may limit the generalizability of our findings to the general population. Finally, socioeconomic status, a major influence of diet quality, was not assessed (Darmon and Drewnowski, 2015).

Considering the existing evidence suggesting a direct impact of metabolic disturbances, including obesity and increased waist circumference, in bipolar disorder, it is worth considering that low diet quality alone may have a negative impact on bipolar course of illness, severity of depressive episodes and treatment response (McElroy et al., 2016a; Steardo et al., 2018). In light of our findings, we propose the inclusion of routine assessment of diet quality and metabolic health in bipolar disorder treatment and the development of dietary interventions that take into account metabolic sex differences, such as a tendency to increased central adiposity, that might put women with BD at higher risk of metabolic disturbances (Cuellar-Barboza et al., 2020; Jacka et al., 2011; Aronica et al., 2021).

In conclusion, in our study, diet quality inversely correlated to increased cardiometabolic measures associated with metabolic syndrome, including BMI, waist circumference and, less consistently, triglycerides. Likewise, overall bipolar illness, depressive symptoms and disordered eating behaviors were also associated with low diet quality. All these associations were significantly stronger in female participants. Although there is an increasing recognition of the metabolic influence in bipolar disorder, what is less well appreciated and not reliably followed is the influence of diet. In this line, REAP-S may be a reliable tool for longitudinal assessment of diet interventions in research and clinical settings. While the exact interrelation remains unclear, our data suggests that diet quality has a direct influence on depressive symptoms and cardiometabolic markers in BD. Considering the high risk of cardiovascular and metabolic diseases in bipolar disorder, with the consequential increased risk for mortality, studies examining the impact of diet and dietary interventions in bipolar illness course are needed.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Further Reading

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**Table 1**

Age- and sex-adjusted associations between REAP-S scores and continuous markers.

Variable	N	REAP-S total			Healthy foods			Avoidance of unhealthy foods		
		Estimate	SE	P-value	Estimate	SE	P-value	Estimate	SE	P-value
BMI	706	-0.161	0.026	<0.001 <sup>a</sup>	-0.037	0.01	<0.001 <sup>b</sup>	-0.053	0.012	<0.001 <sup>c</sup>
Waist circumference	29	-0.197	0.048	<0.001	-0.051	0.014	0.001	-0.058	0.02	0.007
Fasting plasma glucose	76	-0.021	0.027	0.437	-0.003	0.009	0.762	-0.005	0.011	0.667
Triglycerides	72	-0.009	0.009	0.319	-0.006	0.003	0.037	-0.001	0.004	0.873
High-density lipoproteins	76	0.02	0.032	0.542	0.003	0.011	0.795	0.003	0.013	0.791
Thyroid-stimulating hormones	103	0.039	0.192	0.838	0.005	0.066	0.938	0.114	0.08	0.157
Glycosylated hemoglobin	35	-0.488	0.836	0.564	-0.286	0.305	0.356	-0.25	0.291	0.397
Low-density lipoproteins	73	0.013	0.018	0.472	-0.005	0.006	0.435	0.006	0.007	0.36
Total cholesterol	72	0.015	0.016	0.338	-0.004	0.005	0.499	0.01	0.006	0.119
Systolic blood pressure	65	0.027	0.043	0.534	0.013	0.015	0.389	0.015	0.017	0.391
Diastolic blood pressure	59	0.067	0.062	0.29	-0.014	0.021	0.527	0.038	0.024	0.12
BISS - depression	467	-0.046	0.014	<0.001	-0.01	0.006	0.078	-0.01	0.006	0.109
BISS - mania	467	-0.045	0.026	0.082	-0.003	0.011	0.799	-0.003	0.012	0.807
BISS - total	461	-0.036	0.011	0.001	-0.007	0.004	0.133	-0.006	0.005	0.218
EDDS composite	727	-1.6	0.304	<0.001	-0.51	0.117	<0.001	-0.186	0.139	0.18

<sup>a</sup> Lower scores indicative of worse diet quality is associated with more altered markers.

<sup>b</sup> Lower scores indicate low intake of healthy foods.

<sup>c</sup> Lower scores indicate increased consumption of unhealthy foods.

**Table 2**

Associations between REAP-S and continuous markers, overall and stratified by sex.

Variable	REAP-S total, overall				REAP-S total, males				REAP-S total, females			
	N	Estimate	SE	P-value	N	Estimate	SE	P-value	N	Estimate	SE	P-value
BMI	706	-0.161	0.026	<0.001	254	-0.043	0.054	0.424	452	-0.199	0.03	0.0001
Waist circumference	29	-0.197	0.048	<0.001	12	-0.127	0.062	0.072	17	-0.224	0.06	0.002
Fasting plasma glucose	76	-0.021	0.027	0.437	35	-0.013	0.037	0.728	41	-0.022	0.038	0.566
Triglycerides	72	-0.009	0.009	0.319	32	-0.004	0.011	0.703	40	-0.012	0.014	0.368
High-density lipoproteins	76	0.020	0.032	0.542	33	0.046	0.066	0.493	43	0.026	0.04	0.514
Thyroid-stimulating hormones	103	0.039	0.192	0.838	48	0.065	0.188	0.729	55	-0.121	0.444	0.786
Glycosylated hemoglobin	35	-0.488	0.836	0.564	18	0.233	1.109	0.836	17	-1.59	1.294	0.239
Low-density lipoproteins	73	0.013	0.018	0.472	31	0.006	0.023	0.796	42	0.022	0.026	0.404
Total cholesterol	72	0.015	0.016	0.338	32	0.007	0.019	0.704	40	0.027	0.024	0.279
Systolic blood pressure	65	0.027	0.043	0.534	26	0.065	0.051	0.217	39	0.001	0.063	0.987
Diastolic blood pressure	59	0.067	0.062	0.29	23	0.066	0.088	0.463	36	0.051	0.083	0.549
BISS - depression	467	-0.046	0.014	<0.001	169	-0.036	0.023	0.125	298	-0.051	0.017	0.003
BISS - mania	467	-0.045	0.026	0.082	169	0.018	0.039	0.641	298	-0.083	0.034	0.015
BISS - total	461	-0.036	0.011	0.001	167	-0.017	0.018	0.335	294	-0.044	0.014	0.001
EDDS composite	727	-1.600	0.304	<0.001	261	-1.054	0.548	0.055	466	-1.826	0.367	0.0001