

## Original Article

**Evaluation of the Relationship Between Depression, Anxiety, and Stress with Hypertension: Results of a Health Study in Yazd, Iran**Mohammad Khajeh<sup>1</sup>, Masoud Mirzaei<sup>2,\*</sup>, Azadeh Nadjarzadeh<sup>3,4</sup><sup>1</sup>Department of Biostatistics and Epidemiology, School of Public Health, Esfahan University of Medical Sciences, Esfahan- Iran.<sup>2</sup>Yazd Cardiovascular Research Centre, Shahid Sadoughi University of Medical Sciences, Yazd-Iran.<sup>3</sup>Nutrition and Food Security Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.<sup>4</sup>Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

## ARTICLE INFO

## ABSTRACT

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**Key words:**

Hypertension;

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**Background and Aim:** Over the past few decades, different epidemiological studies have been conducted on the relationship between mental disorders and hypertension. However, conflicting results have been reported. This research aimed to evaluate the relationship between symptoms of depression, anxiety and stress with hypertension in a large population.

**Materials and Methods:** This cross-sectional analytic study was conducted using the results of in Yazd Health Study, Iran (N=9340). In addition, DASS-21 questionnaire was asked from the participants to assess depression, anxiety, and stress. Moreover, logistic regression was used to evaluate the relationship between symptoms of depression, anxiety and stress with hypertension.

**Results:** A negative association was observed between systolic and diastolic blood pressure and symptoms of depression, anxiety, and stress, which were independent from other variables. Regarding systolic blood pressure, a significant and reverse relationship was found in individuals with moderate stress (OR: 0.81, 95% CI: 0.69-0.95) and mild depression (OR: 0.82, 95% CI: 0.68-0.99). In terms of diastolic blood pressure, subjects with moderate stress had a lower blood pressure, compared to healthy individuals (OR: 0.86, 95% CI: 0.75-0.99). Furthermore, participants with depression had a lower chance of being diagnosed with hypertension, compared to healthy individuals.

**Conclusion:** The present research did not confirm the previous assumptions about the relationship between depression, anxiety and stress with hypertension. Our findings showed that symptoms of depression, anxiety, and stress are correlated with a low blood pressure.

**Introduction**

Mental disorders and cardiovascular diseases are major causes of mortality and morbidity in developing countries (1). In general, mental and behavioral disorders are common diseases in societies, experienced by more than 25% of all people throughout their lives (2). According to the report by the National Survey on Drug Use and Health (NSDUH), the prevalence of 12-month mental disorders in adults has been reported at 18.5%, with the

exception of drug abuse (3). In a recent study in Iran, 23.4% of the subjects had mental disorders, which showed a significant increase compared to the year before (4).

Hypertension is one of the known risk factors for several causes of death in society, including ischemic heart disease and stroke (5). Moreover, hypertension affects around 22% of people aged 18 years and over globally (6). In a national study in Iran, the prevalence of hypertension in individuals aged >18 years was estimated 26.21% (7), which is in line

\* .Corresponding author: mmirzaei@ssu.ac.ir

with the results of other countries, including a prevalence of 28.5% in the National Health and Nutrition Examination Survey (NHANES) in the United States (8).

Since hypertension and mental disorders are one of the major challenges in public health, the relationship between these two factors has recently attracted the attention of researchers. There is a complicated relationship between mental health and physical condition. Mental disorders such as depression, stress and anxiety have adverse effects on the body function. Given the regulation of the cardiovascular system by the autonomic nervous system, the mental status of an individual may have a profound effect on the cardiovascular system, including blood pressure (9). Epidemiological studies conducted in this regard have reported conflicting results. Most of the studies conducted in this area have confirmed the hypothesis that people with mental disorders have a higher blood pressure, compared to the healthy people (10). However, the role of mental disorders in the development of hypertension has been challenged in a number of studies that have demonstrated the relationship between low blood pressure with depression, anxiety and stress (11-12). This study aimed to assess the relationship between symptoms of depression, anxiety and stress with hypertension in a large Iranian population.

## Materials and Methods

### 2.1. Study Design and Research Population

This analytical and cross-sectional research was carried out using data of Yazd Health Study (YaHS) in 2018. YaHS is largest prospective study on the health and diseases of Yazd residents, implemented in 2014. In this study, ten thousand Yazd residents were questioned about various aspects of physical and mental health. Details of the study method have been published elsewhere (13). The population frame of the study included all individuals aged 20-69 years in Yazd Greater Area, and the sample size was 10,000 people. In YaHS project, data were collected using the comprehensive questionnaire of YaHS study encompassing 300 items on various fields (e.g., demographic characteristics, physical activity, chronic diseases, nutritional habits, smoking status, and drug abuse).

Anthropometrics, blood pressure and other vital signs were also measured objectively.

### Blood Pressure Measurement

Blood pressure was measured in the sitting position and after the completion of two thirds of the interview questions. The interviewees rested for a minimum of 40 minutes during this period. Blood pressure was measured three times at a time interval of five minutes. Calibrated sphygmomanometers (Model N-Champion, Reister GMBH, Germany), were used to measure blood pressure. The mean of the second and third blood pressure levels was recorded as the blood pressure of the subjects. Classification of subjects in terms of blood pressure was carried out in accordance with the eighth committee's guidelines for the prevention, diagnosis, evaluation and treatment of blood pressure in adults. According to this report, the systolic (SBP < 120 mm Hg) and diastolic (DBP < 80 mm Hg) blood pressures were regarded as normal, whereas the systolic (SBP = 120-129 mm Hg) and diastolic (DBP < 80 mm Hg) blood pressures were considered as pre-hypertension. In addition, the systolic (SBP ≥ 130 mm Hg) and diastolic (DBP ≥ 80 mm Hg) blood pressures were recognized as hypertension (14).

According to this guideline, the study population was divided in two groups: the first group involved individuals with no hypertension, whose systolic and diastolic blood pressures were less than 130 mm Hg and 80 mm Hg, respectively. The mentioned group was regarded as the reference group. In addition, individuals with systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 80 mm Hg were considered hypertensive.

### Depression, Anxiety, and Stress Measurements

In this research, we used Depression Anxiety and Stress Scale (DASS-21) to assess the symptoms of depression, anxiety, and stress of the participants. This scale is a quantitative and self-report questionnaire used to measure the negative emotions in people, including depression, anxiety and stress. However, it should be noted that the scale is not a definitive criteria for the clinical diagnosis of individuals. Each of the three sub-scales

(depression, anxiety, and stress) has seven items scored based on a four-point Likert scale from completely disagree (zero) to completely agree (three). The total score is obtained by calculating the sum of the scores of all items of each scale. In the end, the final score is estimated by multiplying the obtained score by two (15-16). Regarding depression, individuals with scores 0-9 were regarded as healthy, whereas those obtaining the scores 10-13, 14-20, and above 20 had mild, moderate and severe depression symptoms, respectively.

In terms of anxiety, the scores 0-7 were considered normal while the scores 8-9, 10-14, and above 15 were recognized as mild, moderate and severe anxiety symptoms, respectively. Moreover, individuals with stress scores 0-14 had normal stress level, whereas those with scores 15-18, 19-25, and above 26 had mild, moderate and severe stress symptoms, respectively. In all three scales, individuals with normal scores were defined as the reference group and the rest of the groups were compared to each other.

**Statistical Analyses**

Continuous variables were reported as (mean±standard deviation) while the ordinal variables were expressed as frequency. In this research, Mann-Whitney U test was applied to evaluate the difference between the two groups in terms of mean continuous variables. In addition, Chi-square and Fisher’s exact test were exploited to compare both groups regarding ordinal variables. We have used the logistic regression model to identify the variables which have a significant relationship with the risk of developing blood pressure . In the next step, logistic regression and five

models were used to assess the hypertension odds ratio for each of the scales of depression, anxiety and stress. Then the variables in the previous step that had a significant relationship with blood pressure were entered into these models as the confounding variables . In the first model, which was a single-variable model, the crude odds ratio of hypertension was obtained for each depression, anxiety and stress scales. Following that and in order to evaluate the effect of confounding variables on the hypertension odds ratio, the second and third models were adjusted for age, gender, and age, gender, BMI, physical activity respectively. people with depression and blood pressure who take medications were also entered into the fourth model to see whether taking the antihypertensive and depression medications have any effect on the results of this study or not? .In addition, the fifth model was a complete adapted model for all confounding variables. It is notable that data analysis was performed in SPSS version 20.0, and P-value less than 0.05 was considered statistically significant.

**Results**

The basic characteristics of the study population are shown in Table 1. According to this table, a significant difference was observed between the healthy individuals and those diagnosed with hypertension in terms of age, waist circumference (WC) and BMI. Those with hypertension received higher means regarding the mentioned variables, compared to healthy individuals (P<0.001 in all cases).

Table 1. Basic characteristics of the study population categorized based on hypertension status

variable	Hypertension		
	yes	no	p-value
Age	50.2±13.72	40.1±13.4	<0.001
Body mass index(BMI)	28.5±4.9	26.3±5.1	<0.001
Waist circumference (WC)	98.5±12.5	91.5±13	<0.001
<b>Sex</b>			
Male	1781(55.5)	2780(46.5)	<0.001
Female	1429(44.5)	3200(53.5)	
<b>Education level</b>			
Less than high school	1249(39)	1135(19.1)	<0.001

High school, Diploma and Graduate Diplom	1620(50.6)	3704(62.3)	
Bachelor degree≤	332(10.4)	1108(18.6)	
<b>Smoking</b>			
Yes	357(11.4)	626(10.7)	0.36
No	2782(86.3)	5203(89.3)	
<b>physical activity per week</b>			
Twice in a week or less	2548(79.6)	4278(71.8)	<0.001
Thrice in a week or more	651(20.4)	1680(28.2)	
<b>Occupation</b>			
Employed	1168(36.9)	2476(41.9)	<0.001
Housewife	1216(38.4)	2332(39.4)	
Unemployed	758(24.8)	1107(18.7)	
<b>Hypertension</b>			
Yes	1165(36.7)	522(8.9)	<0.001
No	2009(63.3)	5362(91.1)	
<b>Depression</b>			
Yes	206(6.5)	326(5.5)	0.069
No	2968(93.5)	5550(94.5)	
<b>Symptoms of Depression</b>			
No depression	1672(53.6)	3135(53.8)	0.60
Mild	257(8.2)	547(9.4)	
Moderate	413(13.2)	798(13.7)	
Severe	779(25)	1350(23.2)	
<b>Symptoms of Anxiety</b>			
No anxiety	1359(43.3)	2730(46.5)	<0.001
Mild	336(10.7)	708(12.1)	
Moderate	294(9.4)	498(8.5)	
Severe	1152(36.7)	1930(32.9)	
<b>Symptoms of Steress</b>			
No steress	1181(38.2)	2028(35)	0.008
Mild	219(7.1)	451(7.8)	
Moderate	414(13.4)	882(15.2)	
Severe	1278(41.3)	2440(42.1)	

Moreover, a significant difference was found in diagnosis of hypertension based on gender since a higher level of male participants were diagnosed with hypertension, compared to female individuals ( $P<0.001$ ). However, no significant difference was observed between depressed and healthy subjects regarding blood pressure ( $P=0.069$ ). Similar results were obtained for individuals with depression symptoms, and no significant difference was observed between groups with mild to severe depression levels in terms of blood pressure ( $P=0.60$ ). Nonetheless, a significant difference was found between the groups with mild-severe anxiety ( $P<0.001$ ) and stress ( $P<0.001$ ) levels regarding blood pressure. The odds ratio of hypertension (systolic blood pressure) based on mild to severe depression,

anxiety and stress symptoms are presented in Table 2. In the first model (one-variable model), the crude odds ratio of hypertension in individuals with mild (OR: 0.88, 95% CI: 0.75-1.03) and

moderate (OR: 0.97, 95% CI: 0.85-1.10) depression levels was below the reference group.

After adjusting each confounders and reaching to the final model (fifth), a significant and reverse association was observed between hypertension and mild depression symptoms of the subjects (OR: 0.82, 95% CI: 0.68-0.99). In other words, the odds ratio of hypertension in individuals with mild depression symptoms was less than healthy individuals. While the same association was observed in individuals with

moderate depression symptoms, the relationship was not statistically significant. Regarding anxiety, individuals with moderate (OR: 1.18, 95% CI: 1.01-1.38) and severe (OR: 1.09, 95% CI: 1.08-1.32) anxiety symptoms had a crude odds ratio of hypertension above the reference group in the first model. Nonetheless, individuals with mild anxiety symptoms had a crude odds ratio of hypertension less than the reference group (OR: 0.95, 95% CI: 0.82-1.10). After adjusting the confounding variables in each stage, the positive relationship between moderate and severe anxiety symptoms was deteriorated. In the final model, a reverse relationship was detected between mild to severe anxiety symptoms and odds ratio of hypertension, in a way that individuals with mild-severe anxiety levels had a lower odds ratio of hypertension, compared to the reference group. Nevertheless, none of these associations between the groups were statistically significant.

Regarding stress in the first model, a significant and reverse relationship was found between all stress symptoms and crude odds ratio of hypertension. After adjusting each of the confounding variables and the final adjustment, this reverse association between mild-severe stress symptoms and the odds ratio of hypertension was maintained. However, only the relationship between the moderate stress symptoms and odds ratio of hypertension was significant (OR: 0.81, 95% CI: 0.69-0.95). In addition, individuals with

moderate stress symptoms had a lower odds ratio for hypertension compared to the reference group.

The odds ratio of hypertension (diastolic blood pressure) based on scales of depression, anxiety, and stress are shown in Table 3. Similar to Table 2, the majority of symptoms of these three scales had a reverse relationship with the odds ratio of diastolic blood pressure. However, this association was only statistically significant in individuals with moderate depression symptoms (OR:0.86, 95% CI: 0.75-0.99). In Table 4, we illustrated the odds ratio of hypertension in patients with depression. According to this table, a positive relationship was found between depression and systolic blood pressure before adjusting the confounding variables. In this regard, the crude odds ratio of hypertension was higher in depressed subjects, compared to healthy participants (OR: 1.18, 95% CI: 0.98-1.14). After adjusting the confounding variables, a reverse association was detected between patients with depression and odds ratio of systolic blood pressure. In this respect, the depressed individuals had a lower odds ratio of hypertension, compared to healthy subjects (OR: 0.94, %95 CI: 0.76-1.17). In terms of diastolic blood pressure, patients with depression had a lower odds ratio of hypertension, compared to healthy subjects, before and after adjusting the confounding variables.

**Table 2. Relationship between systolic blood pressure and mental disorders using logistic regression model**

Model	Depression		
	OR(95% CI)		
	Mild	Moderate	severe
1	0.88(0.75-1.03) 0.12	0.97(0.85-1.10) 0.97	1.08(0.97-1.20) 0.14
2	0.85(0.72-1.01) 0.07	0.99(0.85-1.14) 0.89	1.07(0.95-1.21) 0.21
3	0.84(0.7-1.006) 0.05	1.02(0.88-1.18) 0.79	1.06(0.94-1.19) 0.31
4	0.85(0.71-1.02) 0.09	0.98(0.83-1.14) 0.79	1.03(0.9-1.17) 0.65
5	0.82(0.68-0.99) 0.04	0.96(0.82-1.12) 0.62	1.01(0.89-1.15) 0.82

Continued Table 2

Anxiety			Stress		
OR(95% CI)			OR(95% CI)		
Mild	Moderate	severe	Mild	Moderate	severe
0.95(0.82-1.10) 0.51	1.18(1.01-1.38) 0.03	1.09(1.08-1.32) <0.001	0.83(0.69-0.99) 0.04	0.80(0.70-0.92) 0.002	0.89(0.81-0.99) 0.03
0.84(0.72-0.98) 0.03	1.06(0.89-1.26) 0.45	1.11(1-1.24) 0.04	0.85(0.7-1.03) 0.11	0.82(0.71-0.95) 0.01	0.98(0.88-1.10) 0.81
0.87(0.74-1.02) 0.09	1.06(0.89-1.26) 0.50	1.09(0.98-1.22) 0.09	0.86(0.71-1.05) 0.14	0.85(0.73-0.99) 0.04	1.002(0.89-1.12) 0.96
0.87(0.73-1.02) 0.10	0.98(0.81-1.18) 0.86	1.003(0.89-1.12) 0.96	0.85(0.69-1.04) 0.12	0.81(0.69-0.95) 0.009	0.94(0.83-1.05) 0.30
0.89(0.75-1.05) 0.17	0.99(0.82-1.19) 0.94	0.98(0.87-1.10) 0.76	0.87(0.7-1.06) 0.18	0.81(0.69-0.95) 0.01	0.92(0.82-1.04) 0.22

Model 1: unadjusted      Model 2: adjusted for age, sex      Model 3: adjusted for age, sex, BMI, physical activity      Model 4: adjusted for age, sex, BMI, physical activity, depression and hypertension      Model 5: fully adjusted (adjusted for age, sex, BMI, physical activity, depression and hypertension, Education level, Job status)

Table 3. Relationship between diastolic blood pressure and mental disorders using logistic regression model

Model	Depression		
	OR(95%CI)		
	Mild	Moderate	severe
1	0.89(0.76-1.04) 0.15	0.89(0.79-1.02) 0.10	0.97(0.87-1.07) 0.57
2	0.91(0.78-1.07) 0.26	0.94(0.83-1.08) 0.43	1.02(0.92-1.14) 0.59
3	0.88(0.75-1.04) 0.14	0.97(0.84-1.11) 0.66	1.01(0.91-1.13) 0.75
4	0.89(0.76-1.05) 0.19	0.95(0.82-1.09) 0.49	1.01(0.9-1.13) 0.83
5	0.89(0.75-1.05) 0.17	0.93(0.81-1.08) 0.39	0.97(0.86-1.09) 0.64

Continued Table 3

Anxiety			Stress		
OR(95% CI)			OR(95% CI)		
Mild	Moderate	severe	Mild	Moderate	severe
0.96(0.83-1.10) 0.56	1.04(0.89-1.21) 0.60	1.02(0.93-1.12) 0.62	0.99(0.84-1.17) 0.95	0.82(0.72-0.94) 0.005	0.84(0.76-0.92) <0.001
0.93(0.8-1.07) 0.34	1.03(0.88-1.21) 0.66	1.05(0.95-1.16) 0.30	1.03(0.87-1.23) 0.66	0.85(0.74-0.97) 0.02	0.91(0.83-1.01) 0.09
0.96(0.83-1.11) 0.62	1.04(0.89-1.23) 0.57	1.03(0.93-1.14) 0.56	1.04(0.87-1.25) 0.60	0.87(0.75-0.99) 0.04	0.93(0.84-1.03) 0.17
0.97(0.83-1.13) 0.73	1.02(0.86-1.20) 0.81	0.99(0.89-1.10) 0.91	1.04(0.87-1.25) 0.62	0.85(0.74-0.98) 0.03	0.91(0.82-1.02) 0.11
0.99(0.85-1.16) 0.96	1.02(0.86-1.21) 0.78	0.95(0.85-1.07) 0.45	1.06(0.88-1.27) 0.51	0.86(0.75-0.99) 0.04	0.9(0.81-1.008) 0.07

Model 1: unadjusted      Model 2: adjusted for age, sex      Model 3: adjusted for age, sex, BMI, physical activity      Model 4: adjusted for age, sex, BMI, physical activity, depression and

hypertension Model 5: fully adjusted(adjusted for age, sex, BMI, physical activity, depression and hypertension, Education level,Job status)

Table 4. Relationship between depression and odds Ratio of hypertension using logistic regression model

variable	SBP				DPB			
	Unadjusted		Adjusted*		Unadjusted		Adjusted*	
Depression	OR(95% CI)	P	OR(CI95%)	P	OR(95% CI)	P	OR(95% CI)	P
No	-	1	-	1	-	1	-	1
Yes	1.18(0.98-1.41)	0.06	0.94(0.76-1.17)	0.62	0.98(0.82-1.17)	0.85	0.82(0.68-1.01)	0.06

**Discussion**

Individuals with symptoms of depression, anxiety, and stress had a lower blood pressure. It should be noted that this association was independent of age, gender, BMI, physical activity, and other confounding variables. Among the studies conducted on the relationship between low blood pressure and mental disorders, we can cite several studies conducted on older people. In these studies, the elderly with mental disorders (e.g., depression) had a lower blood pressure too (17-18). One of the largest cross-sectional epidemiological studies in this area was conducted by Hildrum et al. on 60799 participants aged 20-89 years. According to their results, there was a relationship between stress and depression with low blood pressure (11). The present research was among the few studies that showed a reverse association between blood pressure with symptoms of depression, stress, anxiety. A majority of studies conducted on the relationship between blood pressure and mental disorders has demonstrated a positive relationship between blood pressure with depression, anxiety and stress (19-21), which is inconsistent with our findings.

The association between low blood pressure with depression, anxiety and stress has a biological rationality and there are several possible mechanisms involved in the presence of symptoms of depression, stress and anxiety with low blood pressure. Firstly, these individuals may suffer from other cardiovascular diseases or the complications of antihypertensive drugs, both of which reduce the blood pressure level of these people (22).

In the present study, no significant change was observed in the odds ratio of hypertension in the subjects consuming antihypertensive drugs. In addition, participants consuming antihypertensive drugs had a higher blood pressure, compared to the other subjects. It seems that consumption of these drugs had no effect on the association between low blood pressure and mental disorders. Therefore, the hypothesis of “consumption of anti-hypertensive drugs explains the possible relationship between low blood pressure and mental disorders” was rejected in the current research, which is in congruence with several studies in this regard (11, 22, 18).

Secondly, the chronic low blood pressure in individuals itself might be the cause of depression and other mental disorders. Various studies have been conducted in this area, reported an association between low blood pressure with depression, respiratory disorders during sleep (23), risk of dementia in the elderly (24), and increased chronic fatigue (25). Among the other reasons for decreased blood pressure could be the use of antidepressants. In the current research, a multivariate analysis was conducted on individual with depression after adjusting for the confounding factors. Those who consumed anti-depressants were less exposed to hypertension, which was similar to the association between hypertension and symptoms of depression in the total population.

In an analysis performed on the total population, a slight change occurred in the odds ratio of hypertension after entering the variable of depression in the analysis. As such, it does not seem that consumption of antidepressants could explain the association

between hypertension and symptoms of depression, anxiety, and stress. In this respect, our findings are in line with the results of other similar studies (11, 26).

Recently, it has been shown that neuropeptide Y is responsible for diseases such as depression and anxiety. Generally, neuropeptide Y is an important moderator of norepinephrine signals, changes in which may reduce sympathetic activity and decrease blood pressure (27, 28). Most of studies that have demonstrated the relationship between low blood pressure with depression, anxiety and stress have been conducted on the elderly. In a previous study on young participants, this association was reported which might be due to the young age of the participants since the prevalence of hypertension was insignificant in this age group (29).

All age groups (20-69 years) were involved in the current research, and the effect of age groups on the association between hypertension and mental disorders was considered. Therefore, it could be stated that being young or old does not justify the relationship due to low blood pressure or consumption of anti-hypertensive drugs and cardiovascular diseases, respectively. In this regard, our findings are consistent with the results obtained by Hildrum et al. (11).

One of the strengths of the current research was the large study population and random sampling, which allowed the generalization of the final results. However, one of the major limitation of the present study was the fact that while the bilateral association between low blood pressure and mental disorders has biological plausibility, the direction of this relationship cannot be determined in cross-sectional studies. Detection of the symptoms of anxiety, depression and stress based on the DASS21 form which is not regarded as a criterion for clinical diagnosis of individuals is one of the limitations of this study. In this study, we have used people with blood-pressure and depression in order to determine the effect of consumption of anti-hypertensive and anti-depressants medications on the results of the study. because there is no information available about the type, the class and the dose of the medications used in this study, therefore More detailed studies are recommended to be done. Perhaps, the reason of non-consistency between the results of this study with the

results of the previous studies, which are mostly done in European and Western countries, are the factors like alcohol drinking in those countries (as one of the main causes of blood-pressure) and religious and cultural differences in comparison with Muslim countries like Iran .It is recommended that more prospective epidemiological studies be conducted to determine whether the mentioned association is maintained after adjusting for other confounding variables such as economic and social factors, lifestyle and consumption of antidepressants and antihypertensive drugs or not.

## Conclusion

According to the results of the present study, symptoms of depression, anxiety and stress had a relationship with low blood pressure, which seems to be independent of the use anti-hypertensive and anti-depression drugs.

## Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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