Original Communication

Associations of dietary B vitamins intakes with depression in adults

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Abstract: *Background:* The impact of the dietary B vitamins intakes on the development of depression has been scarcely investigated. Thus, this study aimed to examine the associations of dietary B vitamins intakes with the risk of depression in American adults. *Methods:* The data we used in this study were from the National Health and Nutrition Examination Survey (NHANES) 2007-2014. We used the Logistic regression models to analyze the associations of the dietary intakes of B vitamins with the risk of depression. *Results:* 17,732 individuals (8,623 males and 9,109 females) were enrolled in the study and they were all 18 or older. Compared to the lowest quartile of dietary intake, the ORs (95%CIs) of the highest quartile were 0.64 (0.50–0.82), 0.78 (0.62–0.97), 0.60 (0.47–0.78), 0.65 (0.50–0.84), and 0.71 (0.54–0.95) for vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12, respectively. Compared to the people whose dietary intakes below the RDA in the model 2, those with intake meeting the RDA of vitamin B1 (OR: 0.68; 95%CI: 0.56–0.84), niacin (OR: 0.65; 95%CI: 0.51–0.81), B6 (OR: 0.65; 95%CI: 0.52–0.81), or B12 (OR: 0.65; 95%CI: 0.48–0.88) had a lower risk of depression, severally. We also found a nonlinear negative association between dietary vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 intakes and the risk of depression in the dose-response analyses, severally. *Conclusions:* Our results suggested that dietary vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 intakes may be inversely associated with the risk of depression.

Keywords: B vitamins, depression, dietary intake, dose-response analyses, NHANES

Introduction

Depression is a prevalent psychiatric disorder existing at all ages [1]. It is estimated that approximate 4.4% of the population was diagnosed with depression with an effect on over 300 million people, globally [2]. The quality of life of depressed people is significantly lower than that of healthy people, and depression is considered to be the major contributor to disability and suicide [3, 4]. It is predicted that, along with HIV/AIDS and ischemic heart diseases, depression will be one of three major causes of disease burden [5]. However, the number of people who take drugs for depression is low because the drugs are more expensive and have more side effects, such as dry mouth, weight gain and sexual dysfunction [6–9]. Hence, to identify the potentially modifiable risk factors for depression is indispensable.

In recent years, many epidemiology studies have revealed the roles of naturally dietary elements on depression. Studies have found that dietary fiber [1], coffee and caffeine [10], fruit and vegetable [11], and minerals (zinc, iron, copper, selenium [12] and magnesium [13]) were inversely associated with the risk of depression. B vitamins obtained mainly by diet, played a crucial role in the neurochemical pathways associated with depression, the glutamate and GABA neurotransmittory systems, as well as noradrenergic, serotonergic, dopaminergic and cholinergic systems. If neurotransmitters do not work in a normal way, it can cause depression [14, 15]. So, deficiency of either B vitamins might be associated with the development of depression.

Although some articles [14–28] have examined the relationship between dietary intakes of B vitamins (B1 [16, 25–28], B2 [14–16, 19, 20, 25, 26], niacin [16], B6 [14–24], and B12 [14–23]) and depression, the results of them were not consistent. In these studies, most of them were conducted in Asian [14, 16–20, 24–26, 28] and Europe [15, 22, 23, 27] with limited data in the North America [21], especially in American population. In this study, data from 2007 to 2014 in the National Health and Nutrition Examination Survey (NHANES) was used to estimate the associations of dietary vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 intakes with depression in US adults and to explore the dose-response relationships between variables.

Methods

Data source and study population

NHANES is a nationally representative cross-sectional research project, and aims to examine the health status

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and nutritional condition of the American civilian population using a complex, layered and multi-stage sample [29, 30]. This program is ongoing since 1999, and the data published biennially were collected by personal interviews and clinical examinations. The study protocol for the project has been approved by the National Center for Health Organization's Institutional Review Board, and all participants have signed the informed consents during the investigation [31].

This study employed publicly available data of 40,617 individuals from four NHANES two-year cycles (2007–2014). Among the 40,617 individuals, and we restricted our analyses to those aged 18 years or older (n=24,732). Then, individuals whose dietary recall information were incomplete or unreliable 24-h recall dietary information (n=5,249), pregnant women (n=206) and lactating women (n=108) were also excluded. We further excluded individuals fail to complete the depression questionnaire (n=1,243) and those with total energy intake more than mean ± 3SDs (n=194). Finally, data of 17,732 people were combined in this study (8,623 males and 9,109 females). Figure 1 summarized the detail steps.

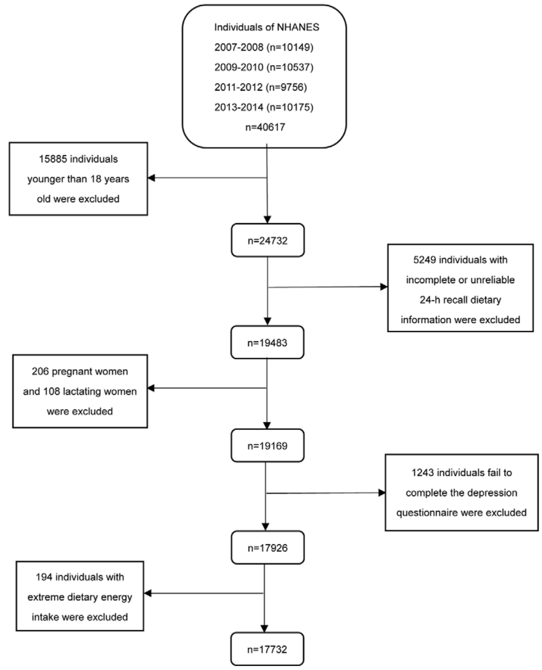

Figure 1. Flow chart of the screening process for the selection of eligible participants. NHANES: National Health and Nutrition Examination Survey.

Assessment of depressive symptoms

The outcome variable of this study was depression symptom which was evaluated by the Patient Health Questionnaire (PHQ-9) [32]. Each PHQ-9 question has four options, and is rated 0–3 score. The lowest score of the PHQ-9 scale is 0, and the highest score is 27. Individuals were diagnosed with depression when their score of PHQ-9 was greater than or equal to 10 [33].

Dietary B vitamins intakes assessment

In order to collect dietary intake information, data of individuals were collected by two 24-hour interview questionnaires during the investigation, the first by face-to-face interview at Mobile Examination Center (MEC) and the second by telephone interview 3–10 days after the first interview. During the interviews, participants were required to recall the types and quantities of foods and beverages they have eaten in the 24-h before the interviews (from midnight to midnight), as well as the use of dietary supplements. Because the B vitamins intakes of individuals were closely related to the intake of total dietary energy, we adjusted to total energy intake in this study. Each subject's daily nutrient intake was the sum of the average 24-hour dietary intake of the two groups and the average 24-hour supplement intake of the two groups.

Covariates

In order to reduce the confounding effect of other variables, this study, on the basis of reading a large number of literatures, included a series of covariates [12, 13, 34] in the Logistic regression model. The covariates were educational level, gender, age, family income, race, work activity, recreational activity, body mass index (BMI), hypertension, the smoking status, the drinking status, diabetes and total dietary energy intake (continuous, kcal).

Smokers were defined as having smoked 100 or more cigarettes in the past lifetime. Those, in past one year, who has consumed 12 or more alcohol drinks were defined as drinkers. Those with systolic blood pressure above 130 mmHg or diastolic blood pressure above 80 mmHg or who had recently taken blood pressure drugs were defined as having high blood pressure. People with diabetes were those having self-reported physician diagnosis diabetes.

Statistical analysis

In this study, Stata 15.0 software were used for all statistical analysis, and Taylor Linearization method was used to weight the data during the analysis. According to the NHANES guidelines, the new sample weight needs to be recalculated when two or more cycle data are combined. In this study, the data of eight years of NHANES (2007–2014) are combined, and the new eight-year diet weight according to the guidelines is equal to 1/4 of the 2-year diet weight [31].

When comparing the baseline data of people with PHQ-9≥10 (depression group) and those with PHQ-9<10 (non-depression group), if the characteristic variables were continuous variables and the distribution was normal, we used Student's t-tests test for comparison, if the distribution was not normal, we used Mann-Whitney *U* tests for comparison, and we used Chi-Square tests for categorical variables. To analyze the associations between B vitamins and depression, the data were first weighted and then included in three Logistic regression models respectively. The three Logistic regression models were the crude model without adjusting any confounders, model 1 adjusted for age and gender, and model 2 furtherly adjusted for multiple confounders. To investigate whether the associations were different across genders and age, we stratified the results by gender and age. Then we tested gender and age as an interaction with B vitamins intake in three model respectively. Restricted cubic spine models were used to further explore the dose-response relationships between B vitamins and depression.

Quantitative data were described as mean ± SD (standard deviation), and qualitative data were described as percentages. In the progress of assessing whether there were differences in characteristic variables between the depressed and non-depressed groups, mean values were compared by Student's t-tests, and the percentages of categorical variables were compared by Chi-Square tests. Adjusted dietary B vitamins intakes were categorized into four groups based on quartiles, and categorized into two groups based on the Recommended Dietary Allowance (RDA) [35]. The individuals with intake<25th percentile were classified into quartile 1 (Q1), with intake ≥25 to <50th percentile were classified into quartile 2 (Q2), with intake ≥50 to <75th percentile were classified into quartile 3 (Q3), and with intake ≥75th percentile were classified into quartile 4 (Q4). The associations between dietary B vitamins intakes and the risk of depression were assessed by Logistic regression using the quartile 1 as the referent group, respectively.

In multivariate Logistic regression, the covariates were gender and age in model 1, and the covariates were gender, age, education level, race, BMI, family income, smoking status, drinking status, work activity, recreational activity, hypertension and diabetes in model 2. In the model that analyzed the association between whether daily intake of vitamin met RDA and the risk of depression, we furtherly adjusted the total energy intake. In logistic regression, by changing the median value of each category of the analyzed variable to a single ordinal variable, we calculated the linear trends. In sensitive analysis, individuals with self-reported antidepressants using were excluded for testing the stability of the results. The dose-response relationship was evaluated by restricted cubic spline in fully adjusted model 2 with three knots located with 5^{th}, 50^{th}, and 95^{th} percentiles of dietary vitamin B1, B2, niacin, B6, and B12 intakes, after removing the rear 5% abnormal values. By testing the null hypothesis that the second spline coefficient is equal to zero, we calculated the *p*-values for nonlinearity.

Results

Table 1 presented the baseline characteristics of the participants included in the study. Of the 17,732 eligible individuals, the average age was about 48.72 years old, and the prevalence of depression was 9.22%. Between those with and without depression, there were statistically significant differences in age, smoking status, gender, race, education level, BMI, family income, work activity, recreational activity, hypertension status, and diabetes status. Compared to individuals without depression, those with depression had a lower education level, lower family income, higher BMI, lower level of work activity and recreational activity. Individuals were more likely to be smoker, women, hypertensive and diabetic in the depression group than in the non-depression group. The proportions of below the RDA for dietary vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 intakes in people with depression were higher than that of non-depression (30.46% VS 23.11%, 18.04% VS 15.04%, 20.06% VS 12.84%, 34.01% VS 23.17%, and 20.00% VS 14.73%).

According to quartiles of dietary B vitamins intakes, the weighted ORs (95%CIs) of depression were summarized in Table 2. The results of the univariate model were similar to that of model 1, and dietary B vitamins intakes all were inversely associated with the risk of depression. After adjusting for the potential confounding factors, the inverse associations were still stable in the model 2. Compared with the lowest quartile of dietary intake, the highest quartile of vitamin B1 was inversely associated with the depression, and the OR (95%CI) was 0.64 (0.50–0.82). The vitamin B2, B6, B12 were also inversely associated with depression. Compared with the lowest quartile of dietary intake, the ORs (95%CIs) of third and fourth quartile were 0.78 (0.61–0.99) and 0.78 (0.62–0.97) for vitamin B2, 0.54 (0.44–0.66) and 0.65 (0.50–0.84) for vitamin B6, and 0.73 (0.57–0.95) and 0.71 (0.54–0.95) for vitamin B12, respectively. For niacin, compared with the lowest quartile of dietary intake, the other three quartiles were all inversely associated with the depression, and the ORs (95%CIs) were 0.70 (0.55–0.88), 0.74 (0.58–0.94), and 0.60 (0.47–0.78), respectively.

We also conducted the stratified-analyses by gender (Table 3). A higher dietary intake of vitamin B1, B2, niacin showed statistically significant inverse associations with depressive symptoms for women but not in men. For dietary vitamin B6, the third quartile in men and the third and

Table 1. Characteristics of participants by depression status, NHANES 2007–2014

	Depression (PHQ≥10)	Non-depression (PHQ<10)	P value
Number of subjects (%)	1635 (9.22)	16097 (90.78)	
Age (%)[1]			<0.001
18–44	664 (40.61)	6913 (42.95)	
45–64	715 (43.73)	5282 (32.81)	
≥65	256 (15.66)	3902 (24.24)	
Gender (%)[1]			<0.001
Male	561 (34.31)	8062 (50.08)	
Female	1074 (65.69)	8035 (49.92)	
Race (%)[1]			<0.001
Mexican American	247 (15.11)	2327 (14.46)	
Other Hispanic	225 (13.76)	1544 (9.59)	
Non-Hispanic White	713 (43.61)	7419 (46.09)	
Non-Hispanic Black	352 (21.53)	3386 (21.03)	
Other Race	98 (6.00)	1421 (8.83)	
Educational level (%)[1]			<0.001
<High school	642 (39.27)	4297 (26.72)	
High school	373 (22.81)	3494 (21.72)	
>High school	620 (37.92)	8293 (51.56)	
Body mass index (BMI) (%)[1]			<0.001
<25 kg/m^2	388 (24.04)	4781 (30.00)	
25–30 kg/m^2	419 (25.96)	5381 (33.76)	
≥30 kg/m^2	807 (50.00)	5777 (36.24)	
Family income (%)[1]			<0.001
<$20,000	690 (44.43)	3535 (22.79)	
≥$20,000	863 (55.57)	11978 (77.21)	
Smoking status (%)[1]			<0.001
Yes	931 (58.26)	6716 (43.40)	
No	667 (41.74)	8757 (56.60)	
Drinking status (%)[1]			0.837
Yes	1159 (72.08)	11268 (71.81)	
No	449 (27.92)	4424 (28.19)	
Work activity (%)[1]			<0.001
Vigorous	281 (17.19)	2925 (18.17)	
Moderate	296 (18.10)	3552 (22.07)	
Other	1058 (64.71)	9619 (59.76)	
Recreational activities (%)[1]			<0.001
Vigorous	169 (10.34)	3703 (23.00)	
Moderate	320 (19.57)	4446 (27.62)	
Other	1146 (70.09)	7948 (49.38)	
Hypertension status (%)[1]	853 (52.92)	7795 (48.97)	0.003
Diabetes status (%)[1]	323 (19.80)	1863 (11.58)	<0.001
Below vitamin B1 RDA (%)[1]	498 (30.46)	3720 (23.11)	<0.001
Below vitamin B2 RDA (%)[1]	295 (18.04)	2421 (15.04)	0.002
Below niacin RDA (%)[1]	328 (20.06)	2067 (12.84)	<0.001
Below vitamin B6 RDA (%)[1]	556 (34.01)	3729 (23.17)	<0.001
Below vitamin B12 RDA (%)[1]	327 (20.00)	2371 (14.73)	<0.001
Total energy (kcal/day)[2]	1898.55 (750.78)	2012.13 (756.99)	<0.001

NHANES: National Health and Nutrition Examination Survey; PHQ: Patient Health Questionnaire; RDA: recommended dietary allowance.
[1]Chi-square test was used to compare the percentage between participants with and without depression. [2] Student's t-test was used to compare the mean values between participants with and without depression.

Table 2. Weighted ORs (95%CIs) for depression according to quartiles of adjusted dietary intakes of vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12, NHANES 2007–2014

Intake cutoff		Cases/participants[1]	Crude[2] OR (95%CI)	Model 1[2] OR (95%CI)	Model 2[2] OR (95%CI)
Adjusted dietary vitamin B1 intake (mg/1000 kcal/day)					
Quartile 1 (low)	<0.66	494/4435	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.66–0.87	432/4432	0.85 (0.69–1.03)	0.84 (0.68–1.03)	0.88 (0.70–1.10)
Quartile 3	0.87–1.34	388/4431	0.71 (0.57–0.88)**	0.72 (0.58–0.90)**	0.80 (0.63–1.03)
Quartile 4 (high)	≥1.34	321/4434	0.52 (0.43–0.64)**	0.50 (0.40–0.63)**	0.64 (0.50–0.82)**
p_{trend}			<0.001	<0.001	0.001
P_{value} for gender interaction			0.050	0.089	0.478
P_{value} for age interaction			0.114	0.124	0.130
Adjusted dietary vitamin B2 intake (mg/1000 kcal/day)					
Quartile 1 (low)	<0.81	481/4433	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.81–1.10	412/4433	0.93 (0.77–1.11)	0.90 (0.75–1.09)	0.96 (0.78–1.17)
Quartile 3	1.10–1.73	392/4433	0.69 (0.55–0.85)**	0.66 (0.53–0.83)**	0.78 (0.61–0.99)*
Quartile 4 (high)	≥1.73	350/4433	0.63 (0.52–0.77)**	0.60 (0.48–0.75)**	0.78 (0.62–0.97)*
p_{trend}			<0.001	<0.001	0.030
P_{value} for gender interaction			0.847	0.824	0.373
P_{value} for age interaction			0.023	0.022	0.150
Adjusted dietary niacin intake (mg/1000 kcal/day)					
Quartile 1 (low)	<10.39	534/4433	1 (ref)	1 (ref)	1 (ref)
Quartile 2	10.39–13.47	425/4433	0.65 (0.54–0.80)**	0.67 (0.55–0.82)**	0.70 (0.55–0.88)**
Quartile 3	13.47–19.53	362/4433	0.59 (0.47–0.74)**	0.63 (0.50–0.79)**	0.74 (0.58–0.94)*
Quartile 4 (high)	≥19.53	314/4433	0.47 (0.37–0.60)**	0.48 (0.37–0.62)**	0.60 (0.47–0.78)**
p_{trend}			<0.001	<0.001	0.002
P_{value} for gender interaction			0.066	0.066	0.012
P_{value} for age interaction			0.214	0.187	0.249
Adjusted dietary vitamin B6 intake (mg/1000 kcal/day)					
Quartile 1 (low)	<0.79	548/4432	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.79–1.13	436/4434	0.79 (0.66–0.95)*	0.81 (0.67–0.98)*	0.89 (0.72–1.10)
Quartile 3	1.13–2.00	333/4433	0.45 (0.37–0.54)**	0.45 (0.37–0.55)**	0.54 (0.44–0.66)**
Quartile 4 (high)	≥2.00	318/4433	0.48 (0.38–0.61)**	0.48 (0.37–0.61)**	0.65 (0.50–0.84)**
p_{trend}			<0.001	<0.001	0.007
P_{value} for gender interaction			0.736	0.740	0.130
P_{value} for age interaction			0.445	0.435	0.274
Adjusted dietary vitamin B12 intake (ug/1000 kcal/day)					
Quartile 1 (low)	<1.75	475/4433	1 (ref)	1 (ref)	1 (ref)
Quartile 2	1.75–3.25	433/4433	0.83 (0.67–1.03)	0.85 (0.69–1.05)	0.83 (0.65–1.06)
Quartile 3	3.25–7.49	387/4433	0.63 (0.49–0.80)**	0.63 (0.49–0.81)**	0.73 (0.57–0.95)*
Quartile 4 (high)	≥7.49	340/4433	0.56 (0.44–0.72)**	0.57 (0.43–0.75)**	0.71 (0.54–0.95)*
p_{trend}			<0.001	<0.001	0.063
P_{value} for gender interaction			0.399	0.392	0.974
P_{value} for age interaction			0.476	0.426	0.880

NHANES: National Health and Nutrition Examination Survey; OR: odd ratio; CI: confidence interval.
[1]Cases of depression/number of participants in quartiles. [2]Calculated using binary logistic regression.
Model 1 adjusted for age and gender. Model 2 adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status. Results were dietary-weighted. *p<0.05; **p<0.01.

fourth quartile in women were also associated with depression inversely. However, no statistically significant inverse association between vitamin B12 and depression was observed in either men or women. The results of stratified-analyses by age were shown in Table 4.

The associations between the dietary intakes of B vitamins categorized based on RDA and depression were presented in Table 5. Compared to the people whose dietary intakes below the RDA in the model 2, those with intake meeting the RDA of vitamin B1 (OR: 0.68; 95%CI:

Table 3. Weighted ORs (95%CIs) of depression according to quartiles of adjusted dietary intakes of vitamin B1, vitamin B2 niacin, vitamin B6, and vitamin B12 stratified by gender, NHANES 2007–2014

Intake cutoff		Male			Female		
		Crude[1]	Model 1[1]	Model 2[1]	Crude[1]	Model 1[1]	Model 2[1]
Adjusted dietary vitamin B1 intake (mg/1000 kcal/day)							
Quartile 1 (low)	<0.66	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.66–0.87	0.92 (0.66–1.28)	0.93 (0.67–1.30)	1.05 (0.73–1.50)	0.78 (0.61–0.99)*	0.78 (0.61–1.00)*	0.77 (0.59–1.02)
Quartile 3	0.87–1.34	0.81 (0.54–1.22)	0.83 (0.55–1.23)	0.98 (0.63–1.51)	0.66 (0.50–0.87)**	0.67 (0.50–0.89)**	0.72 (0.52–0.98)*
Quartile 4 (high)	≥1.34	0.65 (0.43–0.97)*	0.68 (0.44–1.04)	0.86 (0.54–1.38)	0.43 (0.32–0.56)**	0.44 (0.33–0.58)**	0.55 (0.40–0.75)**
p_{trend}		0.050	0.089	0.478	<0.001	<0.001	<0.001
Adjusted dietary vitamin B2 intake (mg/1000 kcal/day)							
Quartile 1 (low)	<0.81	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.81–1.10	0.90 (0.68–1.21)	0.88 (0.66–1.17)	1.02 (0.74–1.40)	0.93 (0.74–1.18)	0.92 (0.73–1.16)	0.94 (0.72–1.23)
Quartile 3	1.10–1.73	0.84 (0.55–1.28)	0.81 (0.54–1.22)	1.12 (0.75–1.70)	0.59 (0.46–0.75)**	0.58 (0.45–0.75)**	0.64 (0.47–0.87)**
Quartile 4 (high)	≥1.73	0.67 (0.43–1.04)	0.69 (0.44–1.09)	0.99 (0.64–1.55)	0.55 (0.43–0.71)**	0.56 (0.43–0.72)**	0.70 (0.53–0.92)*
p_{trend}		0.082	0.135	0.952	<0.001	<0.001	0.017
Adjusted dietary niacin intake (mg/1000 kcal/day)							
Quartile 1 (low)	<10.39	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	10.39–13.47	0.78 (0.53–1.15)	0.77 (0.52–1.14)	0.78 (0.51–1.18)	0.64 (0.49–0.83)**	0.64 (0.49–0.83)**	0.68 (0.51–0.91)*
Quartile 3	13.47–19.53	0.87 (0.56–1.34)	0.87 (0.56–1.34)	1.07 (0.68–1.68)	0.51 (0.39–0.67)**	0.51 (0.39–0.68)**	0.58 (0.44–0.78)**
Quartile 4 (high)	≥19.53	0.64 (0.41–0.99)*	0.66 (0.42–1.03)	0.86 (0.54–1.38)	0.40 (0.30–0.55)**	0.41 (0.30–0.56)**	0.51 (0.37–0.70)**
p_{trend}		0.077	0.122	0.811	<0.001	<0.001	<0.001
Adjusted dietary vitamin B6 intake (mg/1000 kcal/day)							
Quartile 1 (low)	<0.79	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.79–1.13	0.95 (0.64–1.43)	0.95 (0.63–1.41)	1.09 (0.70–1.68)	0.73 (0.56–0.94)*	0.74 (0.57–0.95)*	0.79 (0.59–1.06)
Quartile 3	1.13–2.00	0.51 (0.36–0.73)**	0.51 (0.36–0.72)**	0.66 (0.45–0.97)*	0.43 (0.33–0.55)**	0.43 (0.33–0.56)**	0.48 (0.36–0.64)**
Quartile 4 (high)	≥2.00	0.58 (0.36–0.93)*	0.59 (0.36–0.98)*	0.85 (0.51–1.41)	0.42 (0.32–0.54)**	0.42 (0.33–0.55)**	0.57 (0.43–0.76)**
p_{trend}		0.037	0.059	0.484	<0.001	<0.001	0.002
Adjusted dietary vitamin B12 intake (ug/1000 kcal/day)							
Quartile 1 (low)	<1.75	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	1.75–3.25	0.77 (0.57–1.06)	0.78 (0.57–1.06)	0.85 (0.59–1.23)	0.90 (0.68–1.19)	0.90 (0.68–1.19)	0.83 (0.59–1.18)
Quartile 3	3.25–7.49	0.58 (0.40–0.85)**	0.60 (0.41–0.87)**	0.75 (0.52–1.08)	0.65 (0.47–0.88)**	0.65 (0.48–0.90)*	0.74 (0.51–1.06)
Quartile 4 (high)	≥7.49	0.55 (0.36–0.82)**	0.56 (0.37–0.87)**	0.77 (0.50–1.19)	0.56 (0.41–0.77)**	0.58 (0.41–0.81)**	0.70 (0.48–1.02)
p_{trend}		0.023	0.039	0.400	0.001	0.002	0.098

NHANES: National Health and Nutrition Examination Survey; OR: odd ratio; CI: confidence interval.
[1]Calculated using binary logistic regression.
Model 1 adjusted for age. Model 2 adjusted for age, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status. Results were dietary-weighted. *p<0.05; **p<0.01.

Table 4. Weighted ORs (95%CIs) of depression according to quartiles of adjusted dietary intakes of vitamin B1, vitamin B2 niacin, vitamin B6, and vitamin B12 stratified by age, NHANES 2007–2014

Intake cutoff		18–44		46–64		≥65	
		Crude[1]	Model 2[1]	Crude[1]	Model 2[1]	Crude[1]	Model 2[1]
Adjusted dietary vitamin B1 intake (mg/1000 kcal/day)							
Quartile 1 (low)	<0.66	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.66–0.87	0.85 (0.62–1.17)	0.90 (0.65–1.25)	0.94 (0.66–1.35)	1.00 (0.68–1.47)	0.51 (0.23–1.12)	0.50 (0.24–1.04)
Quartile 3	0.87–1.34	0.71 (0.50–1.00)*	0.79 (0.55–1.13)	0.79 (0.57–1.09)	0.92 (0.64–1.32)	0.48 (0.22–1.04)	0.53 (0.26–1.09)
Quartile 4 (high)	≥1.34	0.56 (0.40–0.79)**	0.68 (0.45–1.01)	0.53 (0.38–0.74)**	0.64 (0.44–0.94)*	0.43 (0.19–0.98)*	0.56 (0.26–1.21)
Adjusted dietary vitamin B2 intake (mg/1000 kcal/day)							
Quartile 1 (low)	<0.81	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.81–1.10	0.71 (0.55–0.93)*	0.79 (0.58–1.09)	1.45 (1.08–1.93)*	1.36 (1.04–1.79)*	0.48 (0.20–1.14)	0.59 (0.26–1.35)
Quartile 3	1.10–1.73	0.54 (0.38–0.76)**	0.61 (0.41–0.91)*	0.97 (0.68–1.37)	1.10 (0.79–1.51)	0.49 (0.20–1.19)	0.57 (0.25–1.31)
Quartile 4 (high)	≥1.73	0.65 (0.47–0.89)**	0.80 (0.56–1.15)	0.82 (0.59–1.14)	0.95 (0.66–1.37)	0.41 (0.16–1.03)	0.55 (0.22–1.35)
Adjusted dietary niacin intake (mg/1000 kcal/day)							
Quartile 1 (low)	<10.39	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	10.39–13.47	0.61 (0.45–0.83)**	0.68 (0.49–0.94)*	0.72 (0.51–1.01)	0.72 (0.51–1.01)	0.58 (0.32–1.04)	0.60 (0.36–1.01)
Quartile 3	13.47–19.53	0.59 (0.42–0.84)**	0.77 (0.52–1.13)	0.66 (0.45–0.97)*	0.79 (0.53–1.15)	0.36 (0.21–0.62)**	0.47 (0.29–0.76)**
Quartile 4 (high)	≥ 19.53	0.56 (0.39–0.79)**	0.72 (0.48–1.06)	0.41 (0.30–0.57)**	0.49 (0.35–0.69)**	0.48 (0.26–0.90)*	0.63 (0.35–1.13)
Adjusted dietary vitamin B6 intake (mg/1000 kcal/day)							
Quartile 1 (low)	<0.79	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.79–1.13	0.84 (0.65–1.08)	0.95 (0.72–1.26)	0.80 (0.57–1.13)	0.91 (0.61–1.34)	0.56 (0.28–1.12)	0.59 (0.32–1.12)
Quartile 3	1.13–2.00	0.50 (0.37–0.68)**	0.59 (0.42–0.82)**	0.39 (0.28–0.54)**	0.49 (0.35–0.69)**	0.45 (0.21–0.98)*	0.57 (0.27–1.20)
Quartile 4 (high)	≥2.00	0.60 (0.40–0.89)*	0.78 (0.51–1.19)	0.41 (0.29–0.57)**	0.55 (0.38–0.79)**	0.47 (0.24–0.92)*	0.63 (0.34–1.19)
Adjusted dietary vitamin B12 intake (ug/1000 kcal/day)							
Quartile 1 (low)	<1.75	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Quartile 2	1.75–3.25	0.84 (0.65–1.09)	0.88 (0.66–1.16)	0.89 (0.61–1.30)	0.83 (0.53–1.31)	0.60 (0.27–1.20)	0.66 (0.33–1.35)
Quartile 3	3.25–7.49	0.68 (0.49–0.94)*	0.80 (0.55–1.16)	0.61 (0.40–0.92)*	0.66 (0.42–1.06)	0.55 (0.27–1.14)	0.76 (0.39–1.46)
Quartile 4 (high)	≥7.49	0.65 (0.47–0.90)**	0.83 (0.56–1.22)	0.55 (0.36–0.83)**	0.66 (0.42–1.03)	0.47 (0.22–1.02)	0.68 (0.32–1.44)

NHANES, National Health and Nutrition Examination Survey; OR, odd ratio; CI, confidence interval.
[1]Calculated using binary logistic regression.
Model 2 adjusted for gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status.
Results were dietary-weighted. *p<0.05; **p<0.01.

Table 5. Weighted ORs and 95%CIs for being below the RDA or meeting the RDA for total dietary intakes of vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12, NHANES 2007–2014

Intake cutoff	Cases/participants[1]	Crude[2] OR (95%CI)	Model 1[2] OR (95%CI)	Model 2[2] OR (95%CI)
Total dietary vitamin B1 intake (mg/d)				
Below the RDA	498/4218	1 (ref)	1 (ref)	1 (ref)
Met the RDA	1137/13517	0.53 (0.45–0.64)	0.57 (0.47–0.70)	0.68 (0.56–0.84)
P value		<0.001	<0.001	<0.001
Total dietary vitamin B2 intake (mg/d)				
Below the RDA	295/2716	1 (ref)	1 (ref)	1 (ref)
Met the RDA	1340/15016	0.63 (0.50–0.80)	0.64 (0.50–0.82)	0.85 (0.65–1.11)
P value		<0.001	0.001	0.233
Total dietary niacin intake (mg/d)				
Below the RDA	328/2395	1 (ref)	1 (ref)	1 (ref)
Met the RDA	1307/15337	0.47 (0.39–0.56)	0.50 (0.41–0.60)	0.65 (0.51–0.81)
P value		<0.001	<0.001	<0.001
Total dietary vitamin B6 intake (mg/d)				
Below the RDA	556/4285	1 (ref)	1 (ref)	1 (ref)
Met the RDA	1079/13447	0.48 (0.40–0.58)	0.52 (0.43–0.63)	0.65 (0.52–0.81)
P value		<0.001	<0.001	<0.001
Total dietary vitamin B12 intake (ug/d)				
Below the RDA	327/2698	1 (ref)	1 (ref)	1 (ref)
Met the RDA	1308/15034	0.50 (0.40–0.64)	0.55 (0.43–0.72)	0.65 (0.48–0.88)
P value		<0.001	<0.001	0.006

NHANES: National Health and Nutrition Examination Survey; OR: odd ratio; CI: confidence interval; RDA: recommended dietary allowance. [1]Cases of depression/number of participants in quartiles. [2]Calculated using binary logistic regression.
Model 1 adjusted for age and gender. Model 2 adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status, diabetes status and total dietary energy intake.
Results were dietary-weighted. *p<0.05; **p<0.01.

0.56–0.84), niacin (OR: 0.65; 95%CI: 0.51–0.81), B6 (OR: 0.65; 95%CI: 0.52–0.81), or B12 (OR: 0.65; 95%CI: 0.48–0.88) had a lower risk of depression, severally. However, the inverse association for vitamin B2 was not significant (OR: 0.85; 95%CI: 0.65–1.11). In sensitivity analysis, after excluding the subjects with self-reported antidepressant medication using, the results were stable (Table 6).

In the dose-response analysis, a nonlinear negative association between dietary vitamin B1 intake and depression was found ($p_{\text{for nonlinearity}}$=0.001; Figure 2), and the risk of depression no longer decreased with intake $\geq$1.90 mg/1000 kcal/day (OR: 0.41; 95%CI: 0.28–0.61). The nonlinear negative association was also found in vitamin B2 ($p_{\text{for nonlinearity}}$= 0.001; Figure 3) and niacin ($p_{\text{for nonlinearity}}$<0.001; Figure 4) with depression. The risk of depression no longer decreased with intake $\geq$2.00 mg/1000 kcal/day for vitamin B2 (OR: 0.52; 95%CI: 0.36–0.75) and $\geq$17.00 mg/1000 kcal/day for niacin (OR: 0.26; 95%CI: 0.16–0.43), however, the inverse relationship became not significant with vitamin B2 intake $\geq$4.10 mg/1000 kcal/day. Then, the dietary intakes of vitamin B6 ($p_{\text{for nonlinearity}}$<0.001; Figure 5) and B12 ($p_{\text{for nonlinearity}}$<0.001; Figure 6) were both nonlinearly associated with the risk of depression. The risk of depression no longer decreased with dietary intake $\geq$2.30 mg/1000 kcal/day for vitamin B6 (OR: 0.36; 95%CI: 0.24–0.55) and $\geq$13.00 ug/1000 kcal/day for vitamin B12 (OR: 0.55; 95%CI: 0.38–0.78). And, the inverse relationship became not significant when vitamin B6 intake $\geq$7.60 mg/1000 kcal/day, and vitamin B12 intake $\geq$31.00 ug/1000 kcal/day.

Discussion

In this study, we examined the relationship of dietary with the risk of depression in US adults. Data from 17732 individuals aged 18 years or older in NHANES was combined (from 2007 to 2014). The results of multivariate-adjusted model 2 indicated that moderate dietary vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 intakes were all inversely associated with depression. However, the inverse associations of dietary vitamin B1, B2 and niacin with depression were found only in women, not in men, and for vitamin B12 the inverse association was not found in either women or men. Compared to the people whose dietary intakes below the RDA in the model 2, those with intake meeting

Table 6. Weighted ORs (95%CIs) for depression according to quartiles of adjusted dietary intakes of vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12, NHANES 2007–2014 (Excluding participants using antidepressant medication)

Intake cutoff		Cases/participants[1]	Crude[2] OR (95%CI)	Model 1[2] OR (95%CI)	Model 2[2] OR (95%CI)
Adjusted dietary vitamin B1 intake (mg/1000 kcal/day)					
Quartile 1 (low)	<0.66	375/4084	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.66–0.87	335/4086	0.90 (0.70–1.16)	0.89 (0.69–1.15)	0.92 (0.70–1.20)
Quartile 3	0.87–1.34	296/4079	0.73 (0.56–0.95)*	0.75 (0.57–0.99)*	0.82 (0.61–1.09)
Quartile 4 (high)	≥1.34	223/3937	0.49 (0.39–0.63)**	0.48 (0.37–0.63)**	0.60 (0.45–0.82)**
p_{trend}			<0.001	<0.001	0.001
Adjusted dietary vitamin B2 intake (mg/1000 kcal/day)					
Quartile 1 (low)	<0.81	389/4158	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.81–1.10	319/4107	0.84 (0.70–1.02)	0.84 (0.69–1.02)	0.91 (0.74–1.11)
Quartile 3	1.10–1.73	281/4006	0.60 (0.47–0.76)**	0.59 (0.47–0.76)**	0.68 (0.52–0.90)**
Quartile 4 (high)	≥1.73	240/3915	0.54 (0.42–0.68)**	0.52 (0.40–0.67)**	0.69 (0.53–0.90)**
p_{trend}			<0.001	<0.001	0.009
Adjusted dietary niacin intake (mg/1000 kcal/day)					
Quartile 1 (low)	<10.39	395/4035	1 (ref)	1 (ref)	1 (ref)
Quartile 2	10.39–13.47	334/4105	0.72 (0.57–0.91)**	0.74 (0.59–0.94)*	0.76 (0.59–0.98)*
Quartile 3	13.47–19.53	282/4087	0.65 (0.49–0.86)**	0.69 (0.52–0.92)*	0.80 (0.59–1.09)
Quartile 4 (high)	≥19.53	218/3959	0.46 (0.35–0.59)**	0.47 (0.35–0.62)**	0.59 (0.44–0.79)**
p_{trend}			<0.001	<0.001	0.001
Adjusted dietary vitamin B6 intake (mg/1000 kcal/day)					
Quartile 1 (low)	<0.79	415/4046	1 (ref)	1 (ref)	1 (ref)
Quartile 2	0.79–1.13	337/4129	0.80 (0.66–0.98)*	0.82 (0.67–1.00)*	0.92 (0.73–1.16)
Quartile 3	1.13–2.00	259/4062	0.46 (0.37–0.58)**	0.48 (0.38–0.60)**	0.56 (0.44–0.71)**
Quartile 4 (high)	≥2.00	218/3949	0.44 (0.35–0.56)**	0.44 (0.34–0.57)**	0.61 (0.45–0.81)**
p_{trend}			<0.001	<0.001	0.002
Adjusted dietary vitamin B12 intake (ug/1000 kcal/day)					
Quartile 1 (low)	<1.75	369/4106	1 (ref)	1 (ref)	1 (ref)
Quartile 2	1.75–3.25	342/4127	0.81 (0.62–1.04)	0.83 (0.64–1.08)	0.81 (0.61–1.07)
Quartile 3	3.25–7.49	284/4019	0.60 (0.47–0.77)**	0.60 (0.47–0.77)**	0.70 (0.53–0.91)**
Quartile 4 (high)	≥7.49	234/3934	0.51 (0.39–0.66)**	0.53 (0.39–0.72)**	0.68 (0.49–0.93)*
p_{trend}			<0.001	<0.001	0.059

NHANES: National Health and Nutrition Examination Survey; OR: odd ratio; CI: confidence interval.
[1]Cases of depression/number of participants in quartiles. [2]Calculated using binary logistic regression.
Model 1 adjusted for age and gender. Model 2 adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status.
Results were dietary-weighted.*p<0.05; **p<0.01.

the RDA of vitamin B1, niacin, B6, or B12 had a lower risk of depression, severally. We also found a nonlinear negative association between dietary vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 intakes and the risk of depression in the dose-response analyses, respectively.

These results about the role of B vitamins (vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12) on depression are consistent with other previously published studies. Similar to us, a significantly inverse association between dietary vitamin B1 and depression was found in a Spain cohort study [27], an inverse association between dietary niacin and depression was found in a Nepal study of adult [16], and the inverse association between dietary vitamin B2 and depression were also found in other four studies [16, 19, 25, 26]. Besides, the results of some studies similarly showed that moderate increase in dietary intakes of vitamin B6 [14, 17, 18, 24] or vitamin B12 [14, 18, 20, 21, 23] might reduce the risk of depression. While, some studies failed to find a statistically significant association between vitamin B1 [16, 25, 26, 28], vitamin B2 [14, 15, 20], vitamin B6 [15, 16, 19–23], vitamin B12 [15–17, 19, 22] and the risk of depression. The inconsistent results might due to the different population background, age and gender. Furthermore, different assessment methods of depressive symptoms using in these studies might also contribute to the inconsistent results.

The negative association between B vitamins (vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12) and

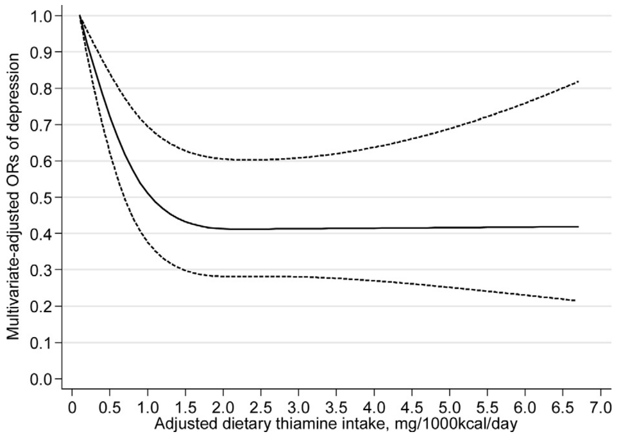

Figure 2. Dose-response relationship between dietary vitamin B1 intake and depression. The association was adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status. The solid line and dash line represent the estimated ORs and its 95% confidence intervals. (OR, odds ratio).

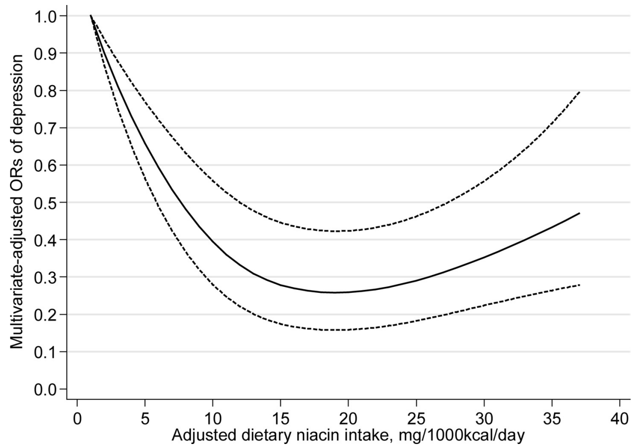

Figure 4. Dose-response relationship between dietary niacin intake and depression. The association was adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status. The solid line and dash line represent the estimated ORs and its 95% confidence intervals. (OR, odds ratio).

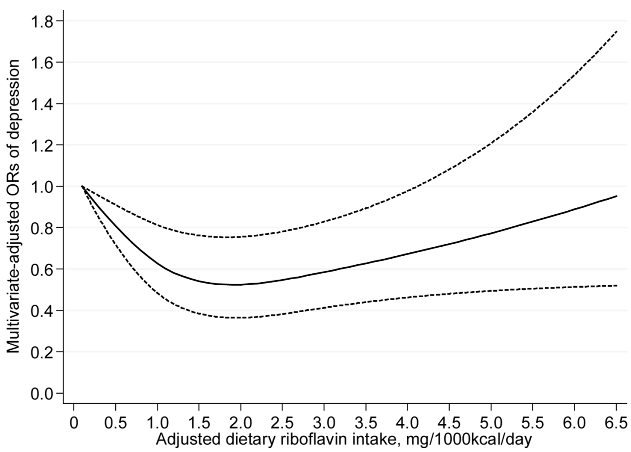

Figure 3. Dose-response relationship between dietary vitamin B2 intake and depression. The association was adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status. The solid line and dash line represent the estimated ORs and its 95% confidence intervals. (OR, odds ratio).

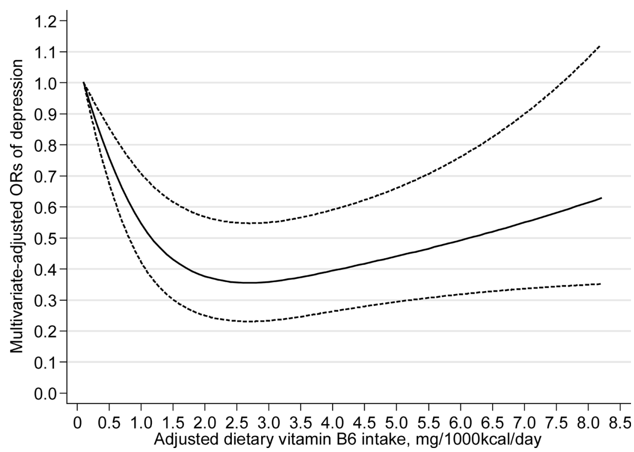

Figure 5. Dose-response relationship between dietary vitamin B6 intake and depression. The association was adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status. The solid line and dash line represent the estimated ORs and its 95% confidence intervals. (OR, odds ratio).

the risk of depression might related to its influence on the metabolism of homocysteine and the synthesis of monoamine neurotransmitters [14, 15]. Defects in vitamin B2, niacin, vitamin B6 and vitamin B12 can lead to depression-related neurochemical pathway disorders. Vitamin B6 deficiency can affect the occurrence of depression through adrengergic, serotonin, GABA, and dopamin system, and vitamin B12 through adrengergic, serotonin, glutaminergic and dopamine system. Deficiencies in vitamin B2 and niacin primarily affect the cholinergic system. As a coenzyme in the body, vitamin B1 plays an indispensable role in the glucose metabolism and the production of nerve implulses [36–38]. To active vitamin B6, vitamin B2 is needed, and vitamin B6 is an essential cofactor in the conversion of tryptophan to serotonin [39]. Vitamin B6 and vitamin B12 are associated with the formation of S-adenosyl-methionine and the metabolism of homocysteine, both are directly contributors to the development of depression [23, 40–42].

Our study has several strengths. First, we constructed a dose-response relationship model to explore the exact association between variables. Second, we got the results in this paper based on the large sample of NHANES that with well-designed and high quality, which has a good representation.

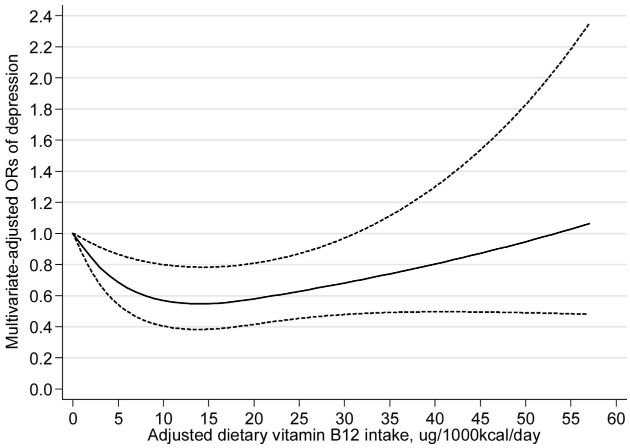

Figure 6. Dose-response relationship between dietary vitamin B12 intake and depression. The association was adjusted for age, gender, race, BMI, family income, educational level, smoking status, drinking status, work activity, recreational activity, hypertension status and diabetes status. The solid line and dash line represent the estimated ORs and its 95% confidence intervals. (OR, odds ratio).

Third, in the sensitivity analysis, we adopted a more conservative standard to define depression (subjects with self-reported antidepressant medication using were excluded), and the results remained stable. Finally, we can still observe the inverse association of dietary intakes of vitamin B1, B2, niacin, B6, and B12 with depression in multivariate analyses after adjusting for many potential confounders.

Our study also has some shortcomings. First, this study is a cross-sectional study and unable to make a causal inference, and depression can induce changes in appetite and food intake, therefore it is unclear whether depression was a result of B vitamins intakes reduced or depression, in turn, led to the intake reduced. Likewise, those with higher intakes are likely to have a better dietary patterns, therefore other components in food may contribute to a lower risk of depression. Second, although we have adjusted some factors of demographics characteristics, health behaviors, and health conditions, we cannot completely eliminate the residual confusion resulted from other unadjusted variables. Meanwhile, dietary data in this study are collected by two 24-hour recall interviews, and the values may be slightly different from the individual's actual data because of recall bias.

Conclusions

In conclusion, our results indicated that dietary intakes of vitamin B1, vitamin B2, niacin, vitamin B6, and vitamin B12 might be inversely associated with the risk of depression. Future larger prospective cohort studies are needed to confirm these findings and establish causal inference.

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Authorship
Yanjun Wu: designed the study; conducted the statistical analysis; sorting data edited the manuscript. Weijing Wang: processing data. Suyun Li: prepared and reviewed the manuscript. Dongfeng Zhang: guarantor of integrity of the entire study. All authors approved the final manuscript.

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