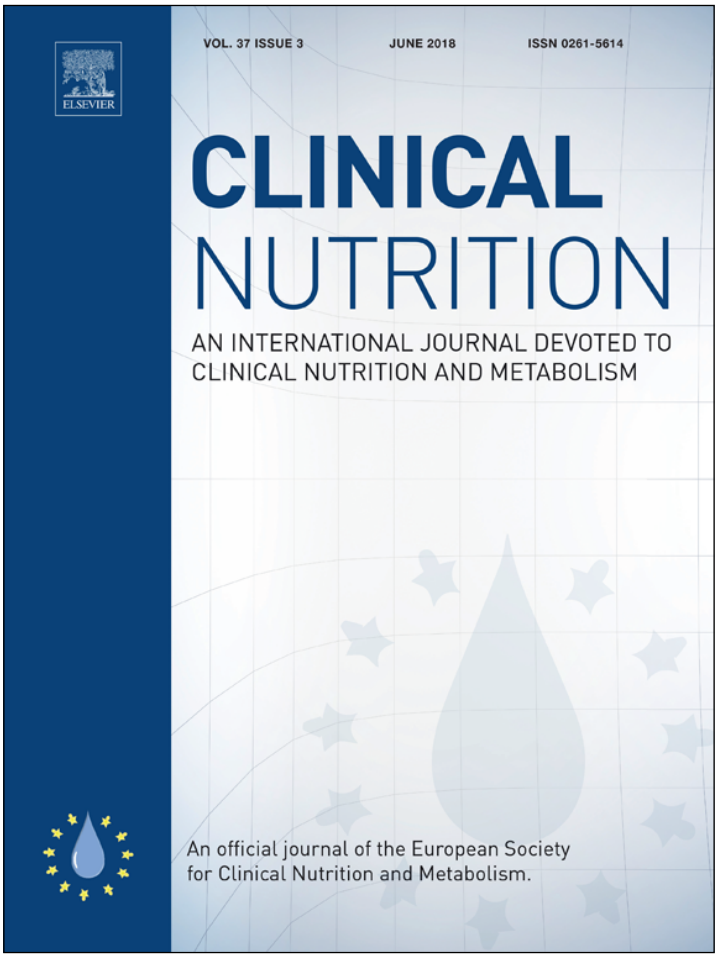

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Original article

A J-shaped association between soy food intake and depressive symptoms in Chinese adults

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SUMMARY

Background & aims: Soy food has been proven to have multiple positive effects on human health, however, no study has yet investigated the association between habitual intake of soy food and depressive symptoms in general population. The objective of this study was to examine this association.
Methods: In a cross-sectional analysis, we studied a sample of 13,760 adults (mean age 43.5 years) in Tianjin, China. The Self-Rating Depression Scale (SDS) was used to assess depressive symptoms, with four cut-off points (SDS ≥40, 45, 48 or 50) indicating increased level of depressive symptoms. Food Frequency Questionnaire (FFQ) was used to assess dietary intake.
Results: In the total population, the prevalence of increased depressive symptoms was 7.2% (SDS ≥50). Comparing to the group with lowest intake frequency of soy food (<once/week), the fully adjusted odds ratios (95% confidence intervals) of depressive symptoms were 0.80 (0.67, 0.95) for 1–3 times/week, 0.69 (0.55, 0.86) for 4–7 times/week, and 1.85 (1.21, 2.80) for ≥twice/day. Associations remained when other cut-off points (SDS ≥40, 45 or 48) were used as a definition of increased depressive symptoms.
Conclusion: Findings from this study suggested a J-shaped association between intake frequency of soy food and incidence of depressive symptoms among adults. For the first time, the study provides evidence that light-to-moderate intake of soy food may reduce the incidence of depressive symptoms, while relatively high (≥twice/day) intake may generate the opposite effect.

1. Introduction

Depression is a major public health issue with high prevalence rates all over the world [1]. Growing evidence show that lifestyle factors, particularly diet, played a role in the development of depressive disorders. Epidemiological findings have suggested that the intake of certain nutrients such as folate [2], zinc [3] and omega-3 fatty acids [4] were related to the incidence of depression. The beneficial effects of certain foods (e.g. tomato, green tea) on mental health have also been reported in recent years [5,6].

Soy food is a significant part of traditional Asian diets. Consumption of soy food in Asian are estimated to be 10–40 times higher than in Western populations [7]. Soy food is high in protein, vitamins and polyunsaturated fat. Especially, soy food is the primary sources of isoflavones in human diets [8]. Soy food intake has been shown to have beneficial effects on cardiovascular disease, osteoporosis, breast cancer and menopausal symptoms [9–12]. There are also reports about the favorable effects of soy food on human cognitive functions [13,14]. Moreover, preclinical evidence has shown that soy-derived isoflavones have an anxiolytic effect in rodents [15]. All of this evidence supports a possible beneficial effect of soy food or certain components in soy food on human mental health. However, there remains little knowledge about the association between soy food and mental health in the general population. A recent cross-sectional study in China found that

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higher frequency of soy products consumption was related to a decreased risk of depressive symptoms in rural older adults [16]. Another cross-sectional study in Japan found that a healthy dietary pattern, which was high in fruit, vegetables, and soy food, was associated with fewer depressive symptoms [17]. Several RCT studies have focused on the impact of soy isoflavones on the mental health of the climacteric women, though the results were still controversial [18,19].

For all we know, there are still no epidemiological data available on the association of habitual intake of soy food with depressive symptoms in the general population. Therefore, we turned to the comprehensive physical examination data collected in Tianjin to explore the association between soy food intake and depressive symptoms in a large population of Chinese adults.

2. Methods

2.1. Study populations

The analyses were based on the observational data from Tianjin Chronic Low-grade Systemic Inflammation and Health (TCLSIH) Cohort Study, which was designed to investigate the association between chronic low-grade systemic inflammation and the health conditions of residents living in a megacity in China [20,21]. Participants were recruited in the Health Management Center of Tianjin Medical University General Hospital. Written informed consents were obtained and the Institutional Review Board approved the study protocols.

During the research period, 16,221 adults 20 years of age and over who had received health examinations and returned the questionnaires were included in the analysis. The questionnaires were either self-administered or asked by the interviewer face to face for the participants who were unable to read the questions. We excluded participants who did not complete the depressive symptoms scale or food frequency questionnaire (n = 1265). We also excluded participants who had a history of cardiovascular disease (n = 941) or cancer (n = 255). After the exclusions, the final sample included 13,760 participants (males, 55.7%) with the age range of 20.0–90.3 years (mean = 43.5, SD = 12.4).

2.2. Measures

2.2.1. Depressive symptoms

The Chinese version of Self-Rating Depression Scale (SDS) was used to measure depressive symptoms. This scale was prepared by Zung in 1965 to evaluate the severity of depression symptoms in adults [22]. It comprises 20 four-point items with a sum score from 20 to 80. Previous studies have confirmed the reliability and validity of SDS for using in the Chinese population [23]. In order to increase the sensitivity of the detection, 4 cut-off points (40, 45, 48 and 50) were used in present study to identify the participants who have significant depressive symptoms [22,24].

2.2.2. Dietary assessment

Dietary intake was assessed using a modified version of the food frequency questionnaire (FFQ) including 98 items [20,21]. The FFQ included 7 frequencies (from hardly ever to twice or more per day) for foods and 8 frequencies (from hardly ever to four or more times per day) for beverages. The average daily consumption of nutrients was calculated with a computer program based on the Chinese food composition tables [25]. The soy food question included five commonly consumed soy foods in China and was asked like this: Please indicate the mean frequency of soy food intake (include tofu, soy drink, soy milk, tofu stick and dried soybeans). We have tested the reproducibility and validity of the FFQ on 150 participants drawn randomly from the cohort and the details were described elsewhere [26]. We were then able to calculate the isoflavones, n-3 fatty acid (EPA + DHA), total protein and energy intake of each participant based on the information obtained from the FFQ and the food composition table. Neither soy protein nor isoflavones supplements were included in our study because they are not commonly consumed in the research population.

2.2.3. Other variables

All participants received standardized physical examinations, which included a variety of physical measurements and physiological tests. The measuring protocol has been detailed elsewhere [21,26]. Body mass index (BMI) was calculated as weight (kilograms) divided by the square of height (meters). Metabolic syndrome (MetS) was defined according to the American Heart Association Statement [27]. Sociodemographic variables including sex, age, education, occupation, household income and social connections (including marital status, cohabitants, and frequency of visiting friends) were also assessed. Occupation was classified according to the Chinese Standard Classification of Occupations (CSCO) [28]. The frequency of visiting friends was assessed by the question, “do you often visit your friends?”

Previous and current smoking (and drinking) status were assessed by questionnaire. Physical activity (PA) in the previous week was assessed by the short version of International Physical Activity Questionnaire (IPAQ) [29]. Participants were asked about the type of activities (light, moderate and vigorous intensity) they performed and the frequency and duration of each activity. MET-hour-week (MET = metabolic equivalent) was calculated by multiplying the MET coefficient (3.3, 4.0 and 8.0, respectively) [29], by the mean duration (hours), by number of days.

2.3. Statistical analysis

Depressive symptoms were used as dependent variables, and soy food intake categories were used as independent variables. The differences of variables by the soy food intake frequencies were tested by variance analysis for continuous variables or by logistic regression analysis for proportional variables. Logistic regression was used for the analysis of the associations between four soy food intake categories (<once/week, 1–3 times/week, 4–7 times/week, ≥twice/day) and depressive symptoms. The <once/week group was set as the reference. Three models were fitted for the outcomes. In model 1, a crude odds ratio (ORs) was obtained by simply adding the independent variable into the equation. In model 2, potential confounding variables including age, sex, and BMI were adjusted for. In model 3, further adjustment was performed by including smoking and drinking habits, PA, education, occupation, household incomes, living alone, frequency of visiting friends, marital status, EPA + DHA intake, total protein intake, total energy intake, MetS and its components (waist, blood pressure, triglyceride, high-density lipoprotein cholesterol and fasting glucose). The interactions between sex and soy food intake for depressive symptoms were tested by adding the cross-product term in the model. All p values are two-tailed and p values for linear trends were calculated by using the categories of soy food intake. Statistical significance was accepted at $p < 0.05$. All the statistical analysis was performed by SAS v9.1.

3. Results

A total number of 13,760 participants were included in the final analysis. For all the participants, the average BMI was 24.73 kg/m^2 (SD = 3.74), and the average systolic and diastolic blood pressure were 121.2 (SD = 16.4) and 77.1 mmHg (SD = 11.4) respectively.

Among all the participants, 7.2% (11.3%, 19.1% or 38.7%) were identified with elevated depressive symptoms when the cut-off point was set as 50 (48, 45 or 40).

Table 1 shows the participant characteristics in the four groups of soy food intake frequency. Of all the participants, 58.8% reported intake of soy food 1–3 times a week, while only 17.7% reported less than once a week. Comparing to the participants who had the least frequency of soy food intake, those who had a higher frequency were more likely to be older, have higher income and higher education level, have a higher level of physical activity or employ as Professionals or Service and Sales Workers. Those participants who were current smoker consumed fewer amounts of soy food. EPA + DHA intake, mean total protein and energy intake were all significantly higher across the soy food intake quartiles.

Table 2 present the crude and adjusted associations between soy food intake categories and depressive symptoms. All the 3 models suggested a J-shaped association between depressive symptoms and categories of soy food intake. When 50 was used as the cut-off point for SDS, the crude ORs (95% CI) across soy food intake categories were 0.74 (0.63, 0.87), 0.66 (0.54, 0.81) and 2.64 (1.85, 3.71). The results were similar after multivariate adjustment. In the final regression model, the adjusted ORs for depressive symptoms were 0.80 (0.67, 0.95), 0.69 (0.55, 0.86) and 1.85 (1.21, 2.80). Participants who consumed soy food 4–7 times per week had the lowest prevalence of depressive symptoms, while those who consumed more than 2 times per day had the highest prevalence. The Fig. 1 shows the J-shaped association after the fully adjustment of confounding factors. Similar associations were obtained when male and female participants were analyzed separately (p for interaction = 0.82). Similar associations were also obtained when 40, 45 or 48 was used as cut-off point for SDS.

Additional sensitivity analyses were conducted to exclude the potential sources of bias in the association between soy food intake and depressive symptoms. We first repeated the analysis by excluding those participants with severe depressive symptoms (SDS ≥50), which did not change the J-shape association. The crude ORs (95% CI) after the exclusion were 0.87 (0.79, 0.96), 0.82 (0.72, 0.92) and 1.51 (1.12, 2.03) when 40 was set as the cut-off point. We then excluded the participant who reported the regular use of nutrition supplements such as vitamin or minerals, which did not change the association either. The crude ORs (SDS ≥50) after this exclusion were 0.74 (0.60, 0.90), 0.59 (0.45, 0.78) and 1.90 (1.05, 3.28). Since previous evidence showed that depression is associated with unhealthy eating habits [30,31], we performed a further analysis by excluding those participants with highest (upper 2.5%) or lowest (under 2.5%) total energy intake. The result did not change. The crude ORs (SDS ≥50) after this exclusion were 0.81 (0.72, 0.93), 0.67 (0.57, 0.79) and 1.56 (1.01, 2.38). Moreover, we have calculated the intake of dietary isoflavones from the FFQ and test its association with depressive symptoms. A similar J-shaped association has been found between isoflavones intake and depressive symptoms in the multivariate regression models. The ORs (SDS ≥50) for depressive symptoms across categories of isoflavones intake were 0.82 (0.69, 0.98), 0.64 (0.53, 0.77) and 1.64 (1.07, 2.47). Finally, since more frequent intake does not necessarily mean more in terms of quantity, we have also calculated the associations between amount of soy food intake categories and depressive symptoms (SDS ≥50). Comparing to the group with lowest intake amount of soy food (<14 g/day), the fully adjusted ORs (95% CI) of depressive symptoms were 0.79 (0.68, 0.92) for 14–31.9 g/day, 0.67 (0.57, 0.78) for 32–150 g/day, and 2.65 (1.85, 3.75) for >150 g/day, which implied a similar J-shaped association.

Table 1
Participant characteristics by the soy food intake frequency.[a]

	Soy food intake frequency				P values[b]
	<once/week	1–3 times/week	4–7 times/week	≥twice/day	
	(n = 2438)	(n = 8085)	(n = 3004)	(n = 233)	
Age (years)	41.5 (41, 41.9)[c]	41.3 (41.1, 41.6)	43.3 (42.9, 43.8)	42.1 (40.6, 43.6)	<0.0001
Sex (males, %)	54.3	56.6	55.3	45.1	<0.01
BMI (kg/m^2)	24.4 (24.2, 24.5)	24.5 (24.4, 24.6)	24.7 (24.6, 24.8)	24.4 (24, 24.9)	<0.001
Metabolic syndrome (yes, %)	29.5	29.6	30.9	27.7	0.54
Physical activity (Mets × hour × day)	7.8 (7.4, 8.2)	9.6 (9.3, 9.9)	11.5 (10.9, 12.1)	9.1 (7.6, 10.9)	<0.0001
Total energy intake (kcal/d)	1682.1 (1654.3, 1710.4)	2161.6 (2141.9, 2181.5)	2847.5 (2805.1, 2890.6)	3786.0 (3637.2, 3940.9)	<0.0001
EPA + DHA intake (g/d)	1.07 (1.06, 1.08)	1.09 (1.08, 1.11)	1.11 (1.10, 1.15)	1.29 (1.27, 1.3)	<0.0001
Total protein intake (g/d)	58.9 (58, 59.9)	75.2 (74.6, 75.9)	98.8 (97.4, 100.2)	217.7 (206.5, 229.4)	<0.0001
SDS score	37.3 (37, 37.7)	36.3 (36.1, 36.4)	35.7 (35.4, 36)	39.5 (38.4, 40.6)	<0.0001
Smoking status (%)					
Smoker	26.5	24.6	23.0	16.8	<0.01
Ex-smoker	6.0	6.9	7.7	7.4	0.17
Drinker (%)					
Everyday	29.7	31.9	30.6	22.8	<0.01
Sometime	59.0	60.4	58.1	53.5	0.03
Ex-drinker	8.2	7.6	7.5	5.2	0.36
Marital status (married, %)	87.7	88.2	88.7	87.6	0.75
Living alone (yes, %)	10.1	8.5	8.0	8.7	0.03
Education (≥College graduate, %)	56.8	61.6	61.5	62.6	<0.01
Working status (%)					
Managers	16.4	17.3	18.9	21.1	0.23
Professionals	18.3	20.9	18.6	13.1	<0.01
Clerk	31.2	32.5	33.6	36.4	0.23
Production, transportation and related	2.6	2.5	2.4	2.5	0.97
Service and sales	16.0	13.3	12.6	15.2	<0.01
Skilled agricultural, forestry and fishery	0.9	0.6	0.5	0.0	0.23
Others	14.7	13.1	14.0	12.6	0.24
Household income (≥10,000 Yuan, %)	33.4	37.8	37.6	29.0	<0.0001
Visiting friend (yes, %)	62.1	63.6	66.8	67.8	<0.01

[a] BMI, body mass index; SDS, self-rating depression scale.
[b] Analysis of variance or logistic regression analysis.
[c] Least square geometric mean (95% CI).

Table 2
Adjusted associations between the soy food intake frequency and depressive symptoms.[a]

	Soy food intake frequency			
	<once/week	1–3 times/week	4–7 times/week	≥twice/day
	(n = 2438)	(n = 8085)	(n = 3004)	(n = 233)
No. of depressive symptoms (SDS ≥40)	1053	3062	1078	127
Model 1[b]	1.00	0.80 (0.73, 0.88)[c]	0.74 (0.66, 0.82)	1.58 (1.20, 2.07)
Model 2[d]	1.00	0.80 (0.73, 0.88)	0.75 (0.67, 0.83)	1.56 (1.19, 2.05)
Model 3[e]	1.00	0.86 (0.78, 0.95)	0.81 (0.72, 0.92)	1.56 (1.16, 2.11)
No. of depressive symptoms (SDS ≥45)	549	1472	518	93
Model 1[b]	1.00	0.77 (0.69, 0.86)	0.72 (0.63, 0.82)	2.29 (1.73, 3.02)
Model 2[d]	1.00	0.77 (0.69, 0.86)	0.72 (0.63, 0.83)	2.27 (1.71, 3.00)
Model 3[e]	1.00	0.81 (0.72, 0.92)	0.75 (0.65, 0.87)	1.87 (1.35, 2.78)
No. of depressive symptoms (SDS ≥48)	327	866	301	66
Model 1[b]	1.00	0.77 (0.68, 0.89)	0.72 (0.61, 0.85)	2.55 (1.87, 3.46)
Model 2[d]	1.00	0.78 (0.68, 0.89)	0.72 (0.61, 0.86)	2.54 (1.86, 3.44)
Model 3[e]	1.00	0.83 (0.72, 0.96)	0.74 (0.61, 0.89).	1.94 (1.35, 2.78)
No. of depressive symptoms (SDS ≥50)	218	547	184	48
Model 1[b]	1.00	0.74 (0.63, 0.87)	0.66 (0.54, 0.81)	2.64 (1.85, 3.71)
Model 2[d]	1.00	0.74 (0.63, 0.87)	0.67 (0.55, 0.83)	2.65 (1.86, 3.72)
Model 3[e]	1.00	0.80 (0.67, 0.95)	0.69 (0.55, 0.86)	1.85 (1.21, 2.80)

[a] SDS, self-rating depression scale.
[b] Crude.
[c] Adjusted odds ratio (95% CI).
[d] Adjusted for age, sex and BMI.
[e] Adjusted for age, sex, BMI, smoking and drinking status, physical activity, marital status, EPA + DHA intake, total protein intake, total energy intake, household incomes, occupations, education, frequency of visiting friends, living alone, metabolic syndrome and its components.

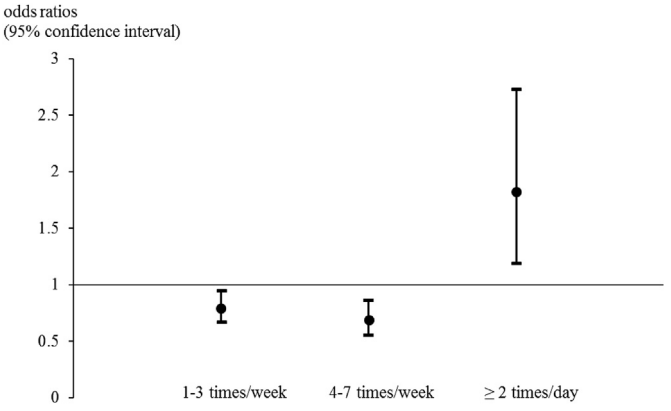

Fig. 1. Fully adjusted odds ratio (95% CI) of the relationship between frequency of soy food intake and depressive symptoms (SDS ≥50). Reference: soy food intake frequency <once/week.

4. Discussion

The aim of this study was to explore the association between soy food intake and depressive symptoms among adults in China. A J-shaped association has been found, which suggested that moderate soy intake was associated with a lower incidence of depressive symptoms. However, when the frequency was more than twice per day, soy food intake was associated with a higher incidence of depressive symptoms. This association remained after multivariate adjustment for other confounding factors.

Soy intake is extremely low in most Western countries, which might hinder epidemiologic studies of its effects on human health. The existing data are mainly focused on cardiovascular disease or breast cancer, while studies linking soy food with mental health were very limited. In a Japanese study, a dietary pattern including soy food was linked with lower depressive symptoms [17]. However, the singular impact of soy products on depressive symptoms cannot be inferred from this study. A recent study in China found an association between higher soy products consumption and lower risk of depressive symptoms in rural older adults [16]. However, the relatively small size cohort and special samples may limit the generalization of their findings. Several RCT studies, which were mainly focused on climacteric women [18,19,32], have investigated the impact of soy isoflavones on mental health, while the results were inconclusive. Chedraui et al. found no significant benefits of soy isoflavones treatment on depressive symptoms in climacteric women [19]. On the other hand, de Sousa-Munoz and Filizola found that soy isoflavones can decrease the depressive symptoms in climacteric women with increased BMI [18]. Another similar study has also shown a positive effect of soy isoflavones on the mental health of climacteric women [32].

The current findings suggested that moderate soy food intake was linked with a lower risk of depressive symptoms. Based on previous findings, this beneficial effect is quite likely due to soy isoflavones, which are well-known for their positive effects on human health. It has been hypothesized that the antioxidative and anti-inflammatory potential of isoflavones might be the explanation of the health benefits of soy food in a large portion [7,33]. Both animal and human research suggest that the isoflavones in soy are powerful antioxidants [34,35]. Soy intake has also been suggested to be linked with decreased levels of inflammatory markers [33]. Since convincing evidence support the important role of oxidative stress and inflammation in the pathology of depression [36–38], isoflavones may directly link higher soy food intake to lower depressive symptoms due to their antioxidative and anti-inflammatory potential. In addition to isoflavones, soy food is also excellent source of fiber and certain vitamins such as folate, both of which have been proven to be associated with lower level of depressive symptoms [2,39]. Further laboratory studies are required to determine which of these constituents may contribute to the mental benefits of soy food.

Interestingly, a quadratic association, meaning that when the adults in our population consumed soy food more than twice per day, was found. Where did this detrimental effect come from? Based on the previous studies, soy isoflavones are relatively safe when consumed in the soy food. Almost no evidence exists that

high consumption of isoflavones has adverse effects on human's physical or psychological health [40]. However, laboratory studies suggested that the administration of high doses of isoflavones may generate a potential adverse effect. For example, estrogen-like effects of isoflavones may increase the growth of estrogen-receptor positive tissues and tumors [41]. Isoflavones have also been found of inhibiting effect on phenol sulfotransferases, which are important for dopamine metabolism [42]. Despite these pieces of preliminary evidence, whether high doses of isoflavones have a similar detrimental effect on mental health requires further investigation. Although we have found a similar J-shaped association between isoflavones intake and depressive symptoms, this might be mainly because soy food is the primary source of isoflavones [8,25], rather than suggesting the isoflavones as the major components responsible for the mental effects of soy food. Further elaborate researches are needed to examine the exact association between isoflavones intake and mental health. Other possible explanation for the quadratic association might be that, in regard to consuming soy food more than twice a day, persons were exposed to too many other substances contained in soy food. Take the protein, which was high contained in soy food, for example. Earlier evidence showed that proteins from soy can decrease iron absorption [43]. Overconsumption of soy food may cause an iron deficiency, which has been proven to be related to depression [44].

The strengths of the present study include the large and representative samples and the multiple adjustments for a considerable number of potential confounders including socio-demographic, lifestyle and clinically relevant variables. However, the results of this study should be interpreted with caution due to some methodology limitations. First, depressive symptoms were measured by a self-administered questionnaire, which may induce recall bias. Future studies with standardized psychiatric diagnostic interview would be helpful for confirming the effect of soy food intake on depression. Second, all the five soy foods were asked in one question in the FFQ due to the space limitation of the questionnaire. It would be more accurate for the calculation if they were asked individually. However, we believe this would not substantively affect the association because the nutritional values are quite similar for these five soy foods [25]. Finally, the cross-sectional design of the study precludes a causal relation between soy food intake and depressive symptoms. Although we have adjusted for many potential confounding factors, there might be still other relevant factors (such as mental comorbidity including dementia and age-related cognitive decline) we have not fully captured. Besides, we cannot exclude the possibility that the more or less frequent soy food intake was the result of the depressive symptoms.

In brief, a J-shaped association between soy food intake and the prevalence of depressive symptoms was found in present study. These results suggest that moderate soy food intake may have a beneficial effect on human mental health, while relatively higher soy intake may generate the opposite effect. Further prospective or experimental studies are required to determine the causality of these observational results.

Conflict of interest

None.

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