Public Health Nutrition: 24(7), 1787–1797 doi:10.1017/S1368980020002943

Associations between dietary intake of B-vitamins and psychological disorders among Iranian women: a cross-sectional study

Hadis Mozaffari[1], Manije Darooghegi Mofrad[1], Pamela J Surkan[2], Mohammadreza Askari[1] and Leila Azadbakht[1,3,4,*]

[1]Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, PO Box 1416643931, Tehran, Iran: [2]Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA: [3]Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran: [4]Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Science, Isfahan, Iran

Submitted 15 February 2020: Final revision received 9 July 2020: Accepted 27 July 2020: First published online 16 September 2020

Abstract

Objective: B-vitamins affect brain function through multiple pathways. Given limited evidence on the relationship between dietary intake of these vitamins and psychological disorders, we examined dietary intake of vitamin $B_{6\text{-}9\text{-}12}$ in relation to psychological disorders among Iranian women.

Design: Cross-sectional study. Dietary intake was assessed using a valid and reliable FFQ. To assess psychological disorders, we used a version of the Depression Anxiety Stress Scale-21 validated in Iran.

Setting: Ten public health centres in southern Tehran, Iran.

Participants: A total of 447 female participants aged 20–50 years.

Results: The median values of vitamin B_6 (pyridoxine), B_9 (folate) and B_{12} (cobalamin) were 1·30 mg/d, 313·89 μg/d and 3·99 μg/d, respectively. After adjustment for potential confounders, dietary vitamin B_6 intake was associated with lower odds of depression (OR: 0·54; 95 % CI: 0·31, 0·95; P_{trend}: 0·03). However, there was a positive association between dietary vitamin B_{12} intake with the odds of depression (OR: 2·05; 95 % CI: 1·17, 3·60; P_{trend}: 0·01) and psychological distress (OR: 2·00; 95 % CI: 1·17, 3·41; P_{trend}: 0·01). No association was found between vitamin B_9 with any psychological disorders.

Conclusions: Women with higher dietary intakes of vitamin B_6 had lower likelihood of depression. However, women with higher dietary intake of vitamin B_{12} had higher odds of depression and psychological distress. Future prospective studies in different populations are needed to clarify whether B-vitamin deficiency is a cause or consequence of psychological disorders.

Keywords
Folate
Pyridoxine
Cobalamin
Psychological disorder

Psychological disorders are considered pressing health issues, with growing numbers of people experiencing negative consequences on health and longevity[1–3]. In 2015, the global prevalence of depressive and anxiety disorders was 4·4 % (5·1 % for females, 3·6 % for males) and 3·6 % (4·6 % for females, 2·6 % for males), respectively[3]. According to national statistics, depression and anxiety affect about 21 % and 20 % of the adult population in Iran[4]. Therefore, low-cost strategies to address these mental health disorders would be valuable.

Many factors including genetic and lifestyle determinants (smoking, alcohol consumption and diet) affect the aetiology of psychological disorders[5]. Notably, the importance of food groups and dietary patterns has been recognised in the development of mental disorders[6–11]. For instance, dietary intake of whole grains, seeds, nuts, fruits and vegetable-rich sources of B-vitamins are associated with lower risk of psychological disorders[12–15]. A biological mechanism that could mediate the association between B-vitamin intake and psychological disorders is their

*Corresponding author: Email azadbakhtleila@gmail.com

involvement in single-carbon transfer reactions, which is needed for the production of monoamine neurotransmitters[16,17]. In studies among psychiatric patients, vitamin B deficiencies have been associated with severe depressive symptoms [18–20]. Folate serum level can also affect patients' responses to antidepressants[21]. It is important to note that such studies have been small and were conducted on highly selected patients, for whom folate deficiency might not be the cause but rather a consequence of depression (due to loss of appetite and poor dietary intake). Moreover, although several clinical trials have investigated the effects of vitamin B supplementation on psychological disorders[22–24], findings of such studies may not be generalisable to the whole population as they either used high dosage of B-vitamins or had short duration. To date, the few population-based studies that have focused on the association between dietary B-vitamin intake and depression have provided conflicting results. Although two studies (with Korean and Finnish participants) reported a positive link between vitamin B deficiencies[25,26] and depression, it is not clear that such results are generalisable to other settings due to geographical variation in nutrient intake. Moreover, to the best of our knowledge, no previous study has considered the association between dietary B-vitamin intake with anxiety and psychological stress, especially in women. We are only aware of one study in Iran, which assessed only vitamin B_6 in relation to depression and anxiety[27]. Investigating potential associations between dietary B-vitamin intake and psychological disorders might provide an avenue for prevention, especially in Middle East region where there is a high prevalence of psychological disorders[4,28] and consumption of whole grains, meat, fruits and vegetables as dietary sources of B-vitamins is low[29,30]. Therefore, in the present study, we examined the cross-sectional association between dietary vitamin $B_{6–9–12}$ intake with depression, anxiety and psychological distress among Iranian women.

Materials and methods

Study population

In this population-based cross-sectional study, we used clustered random sampling to recruit 455 women who were referred to ten health centres located in southern Tehran, Iran (September 2017–September 2018). To determine the number of women sampled from each health centre, the total population covered by each centre was represented proportionally in the initial estimated sample size (*n* 435). Female participants were selected if they met the following inclusion criteria: (a) were age 20–50 years old; (b) had no previous diagnosis of chronic diseases, or psychological disorders by a physician; (c) were not taking any specific medications (including those that would affect weight, lipid and/or glucose metabolism, blood pressure and mental status); (d) were not following a specific dietary pattern such as a vegetarian diet; (e) were not pregnant or lactating; (f) were not women who had immigrated to Iran and (g) did not experience emotional suffering in the preceding year (e.g. reported severe financial problems, death of close friends/relatives). Participants were not included in the analysis if they showed implausibly low or high scores for total energy intake (<3347·2 kJ/d or >17572·8 kJ/d)[31,32]. The prevalence of mental disorders among Iranian women was chosen, as a main dependent variable, to estimate sample size[4], using the following formula $\underline{N} = [(Z1 - \alpha/2)^2 P(1 - P)]/d^2$. Assuming statistical values of $P = 26$; $\alpha = 0{\cdot}05$; $d = 4{\cdot}12$, the calculated sample size was estimated to be 435. However, because of possible missing data, we interviewed 455 female participants. After removing eight participants because of unexplained energy intake, only 447 females remained in the statistical analysis. All the participants provided informed consent prior to inclusion in the study.

Dietary intake assessment

Data on individuals' dietary intakes were collected by completing a 168-item semi-quantitative FFQ through face-to-face interviews with a trained nutritionist. The validity and reliability of the FFQ have been shown to be adequate[33]. Participants were asked to report on average portion sizes and frequency of consumption of foods on a daily, weekly or monthly basis. Next, the daily intake of each food was converted from household measures into grams. An adapted version of NUTRITIONIST IV modified for Iranian foods (version 7.0; N-Squared Computing) was used to compute mean energy and nutrient intakes, especially B-vitamins[34].

Psychological profile assessment

To evaluate psychological disorders, the Iranian validated version of the Depression Anxiety Stress Scale-21 was applied[35]. This questionnaire is a 21-item self-reported structured scale that comprises three subscales: depression, anxiety and psychological distress. Each subscale contains seven items. Questions 3, 5, 10, 13, 16, 17 and 21 correspond to depression, 2, 4, 7, 9, 15, 19 and 20 correspond to anxiety and questions 1, 6, 8, 11, 12, 14 and 18 correspond to psychological distress. Answers to each item are based on a four-point Likert scale including 0 (never), 1 (little), 2 (sometimes) and 3 (always). Participants were asked to rate the extent to which they had experienced each of the states during the preceding week. To estimate the total score for each psychological disorder subscale, a bimodal scoring method (0–0 to 1–1) was used. In total, each subscale can receive a score of 0 to 21. Depression Anxiety Stress Scale-21 was developed to represent all subscales including depression, anxiety and stress; thus, it can be made equivalent to the DASS-42 by multiplying the final score of each subscale by 2. Higher scores for each subscale correspond to higher levels of depression, anxiety or psychological distress.

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

In this study, the scores of ≥10 for depression, ≥8 for anxiety and ≥15 for psychological distress were considered indicators of psychological disorders. The validity and reliability of the Iranian version of the Depression Anxiety Stress Scale-21 have been previously evaluated by Samani and Jokar[35]. The test–retest validity (depression= 0·80, anxiety = 0·76, stress = 0·77) and Cronbach's alpha coefficient (depression = 0·81, anxiety = 0·74, stress = 0·78) for each subscale of Depression Anxiety Stress Scale-21 were reported to be adequate[35].

Anthropometric assessment

Anthropometric measurements (body weight and height) were collected using the WHO standard protocol and registered by a trained assistant. Participant body weight was measured using a portable digital scale (Seca725 GmbH & Co.) after participants removed their heavy outer garments. Weight was recorded with 100 g precision. Moreover, height was measured using a stadiometer or meter while participants stood barefoot against a wall with their shoulders in a comfortable position. Height was reported within a precision of 0·5 cm. BMI was calculated as body weight in kg divided by the square of height in metres (m^2).

Assessment of other covariates

Socioeconomic status was assessed using a valid and reliable questionnaire developed for health research in Iran[36]. This questionnaire included several questions regarding level of education, participants' employment, property (car and house ownership), number of rooms in the household, electronic appliances, number of family members and number of trips abroad or within the country during the preceding year[36]. To gather data on other important covariates, a demographic questionnaire contained questions on age, body shape satisfaction and the number of hours spent sleeping and spent outside the home. A trained assistant recorded the average amount of time that each participant dedicated to different physical activities during the day. Then, the time for each activity was multiplied by the corresponding metabolic equivalent task (MET-h/week) to estimate an individual's physical activity[37].

Statistical analysis

The distribution of variables was investigated using histogram curves and the Kolmogorov–Smirnov test. Energy-adjusted dietary intake of B-vitamins was obtained using the residual method[38]. Participants were categorised based on tertiles of energy-adjusted dietary B-vitamin intake: vitamin B_6 (<1·21; 1·21–1·47; >1·47 mg/d), folate (>286·71; 286·71–354·80; >354·80 μg/d) and vitamin B_{12} (>3·66; 3·66–4·90; >4·90 μg/d). To examine continuous variables (e.g. some demographic variables and lifestyle factors) across tertiles of B-vitamin intake, one-way ANOVA was applied. The distribution of categorical variables across tertiles of B-vitamin intake was calculated using χ^2 tests. To compare participants' dietary intakes (nutrients and food groups) within tertiles of dietary B-vitamins, ANCOVA with Bonferroni correction was used to adjust for energy intake. Before conducting binary logistic regression for each psychological disorder subscale, participants were categorised based on the reported cut-offs as follows: depression ≥10, depression, anxiety ≥8 and psychological distress ≥15. Associations between dietary intake of B-vitamins and psychiatric disorders were calculated using binary logistic regression in crude models and separate multivariable models for each disorder. We adjusted for energy intake (continuous), age (continuous), socioeconomic status (weak/moderate/strong), supplement use (yes/no), satisfaction with body shape (yes/no) and BMI (continuous) as covariates. Additionally, dietary intake of fibre (continuous), *n*-3 fatty acids (continuous) and Mg (continuous) were adjusted for in the final model. All the analyses were performed using SPSS software (version 19.0; SPSS Inc.), and lowest tertiles were regarded as the reference category. *P* values were considered statistically significant at $< 0·05$.

Results

The mean age of participants (*n* 447) was 31·68 years. General participant characteristics across tertiles of dietary B-vitamin intake are displayed in Table 1. The prevalence of depression, anxiety and psychological stress was 31, 32 and 35 %, respectively. Participants in the high tertile of dietary vitamin B_6 intake were more likely to be married. However, with regard to other general characteristics, we did not observe significant differences between participants in the high tertile compared with participants in low tertile.

Participants' dietary B-vitamin intakes by tertitle are provided in Table 2.

Vitamin B_6: Participants in the high vitamin B_6 tertile had higher consumption of total protein ($P_{value} = 0·02$), fibre ($P_{value} = 0·0001$), Mg ($P_{value} = 0·0001$), fruits ($P_{value} = 0·0001$) and vegetables ($P_{value} = 0·0001$) compared with those in the low tertile. However, they showed lower intake of energy ($P_{value} = 0·001$) and grains ($P_{value} = 0·0001$).

Vitamin B_9: Participants included in the high tertile for vitamin B_9 had higher intakes of proteins ($P_{value} = 0·001$), carbohydrates ($P_{value} = 0·05$), fibre ($P_{value} = 0·0001$), Mg ($P_{value} = 0·0001$), fruits ($P_{value} = 0·005$) and vegetables ($P_{value} = 0·0001$). However, they showed lower intakes of energy ($P_{value} = 0·0001$), fat ($P_{value} = 0·003$) and grains ($P_{value} = 0·001$).

Vitamin B_{12}: Participants included in the high tertile of vitamin B_{12} had higher intakes of proteins

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

Table 1 General characteristics of Iranian women across tertiles of energy-adjusted dietary B-vitamin intake

			Vitamin B_6 (mg/d)								Vitamin B_9 (μg/d)								Vitamin B_{12} (μg/d)							
			<1·21		1·21–1·47		>1·47				<286·71		286·71–354·80		>354·80				<3·66		3·66–4·90		>4·90			
	n 447		*n* 149		*n* 149		*n* 149				*n* 149		*n* 149		*n* 149				*n* 149		*n* 149		*n* 149			
Variables	*n*	%	*n*	%	*n*	%	*n*	%	*P* value*		*n*	%	*n*	%	*n*	%	*P* value*		*n*	%	*n*	%	*n*	%	*P* value*	
Age (year)									0·18								0·51								0·41	
Mean	31·68		31·78		30·81		32·43				31·59		31·22		31·68				32·30		31·60		31·68			
SD	7·64		7·90		7·73		7·23				7·61		7·97		7·64				7·65		8·14		7·64			
Weight (kg)									0·82								0·15								0·6	
Mean	64·22		64·09		63·88		64·70				64·18		62·94		65·55				64·87		63·53		64·27			
SD	11·61		11·45		11·60		11·84				12·05		11·23		11·47				12·17		11·31		11·38			
BMI (kg/m^2)									0·78								0·12				24·17	4·11	24·21	4·27	0·73	
Mean	24·30		24·50		24·17		24·24				24·27		23·81		24·83				24·53		63·53		64·27			
SD	4·29		4·42		4·24		4·22				4·63		3·90		4·27				4·49		11·31		11·38			
Physical activity									0·19								0·07								0·49	
Mean	39·73		39·11		39·63		40·44				38·99		39·54		40·65				40·12		30·24		39·81			
SD	6·46		5·08		7·66		6·34				6·26		5·89		7·08				6·69		6·37		6·32			
Hours spent outside home									0·44								0·93								0·11	
Mean	6·10		6·37		6·11		5·82				6·05		6·19		6·06				5·95		5·74		6·61			
SD	3·73		3·89		3·54		3·75				3·57		3·83		3·80				3·73		3·60		3·82			
Sleep (hours)									0·41								0·04								0·83	
Mean	7·77		7·89		7·66		7·74				7·63		8·02		7·65				7·80		7·79		7·71			
SD	1·49		1·56		1·28		1·61				1·36		1·51		1·57				1·46		1·59		1·42			
Overweight and obesity																										
Yes	164	37	58	39	51	34	55	37	0·7		56	38	50	34	58	39	0·6		57	38	56	38	51	34	0·74	
No	283	63	91	61	98	66	94	63			93	62	99	66	91	61			92	62	93	62	98	66		
Supplement use†																										
Yes	164	37	49	33	54	36	61	41	0·35		62	42	56	38	46	31	0·15		49	33	57	38	58	39	0·49	
No	283	63	100	67	95	64	88	59			87	58	93	62	103	69			100	67	92	62	91	61		
Drug use‡																										
Yes	37	8	16	11	11	7	10	7			16	11	6	4	15	10			12	8	15	10	10	7		
No	410	92	133	89	138	93	139	93	0·4		133	89	143	96	134	90	0·06		137	92	134	90	139	93	0·57	
Marital status																										
Married	273	61	91	61	93	62	89	60	0·45		93	62	83	56	97	65	0·05		92	62	90	60	91	61	0·71	
Single/Divorced	174	39	88	12	56	38	60	40			87	38	66	44	52	35			87	38	89	40	88	39		
Body image																										
Yes	306	68	93	62	109	73	104	70	0·12		92	62	107	72	107	72	0·09		98	66	98	66	110	74	0·22	
No	141	32	56	38	40	27	45	30			57	38	42	28	42	28			51	34	51	34	39	26		
Family history of chronic diseases																										
Yes	230	51	70	47	77	52	83	56	0·32		75	50	79	53	76	51	0·89		76	51	76	51	78	52	0·96	
No	217	49	79	53	72	48	66	44			74	50	70	47	73	49			73	49	73	49	71	48		
Socio-economic status																										
Weak	174	39	63	42	59	40	52	35	0·74		65	44	54	36	55	37	0·56		59	40	54	36	61	41	0·26	
Moderate	117	26	38	26	39	26	40	27			39	26	41	28	37	25			46	31	40	27	31	21		
Strong	156	35	48	32	51	34	57	38			45	30	54	36	57	38			44	30	55	37	57	38		

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

Table 1 *Continued*

			Vitamin B_6 (mg/d)							Vitamin B_9 (μg/d)							Vitamin B_{12} (μg/d)						
			<1·21		1·21–1·47		>1·47			<286·71		286·71–354·80		>354·80			<3·66		3·66–4·90		>4·90		
	n 447		*n* 149		*n* 149		*n* 149			*n* 149		*n* 149		*n* 149			*n* 149		*n* 149		*n* 149		
Variables	*n*	%	*n*	%	*n*	%	*n*	%	*P* value*	*n*	%	*n*	%	*n*	%	*P* value*	*n*	%	*n*	%	*n*	%	*P* value*
Depression																							
Yes	137	31	60	40	42	28	35	23	0·005	54	36	49	33	34	23	0·03	37	25	50	34	50	34	0·16
No	310	69	89	60	107	72	114	77		95	64	100	67	115	77		112	75	99	66	99	66	
Anxiety																							
Yes	145	32	64	43	42	28	39	26	0·003	62	42	48	32	35	23	0·004	47	32	45	30	53	36	0·58
No	302	68	85	57	107	72	110	74		87	58	101	68	114	77		102	68	104	70	96	64	
Psychological distress																							
Yes	157	35	63	42	49	33	45	30	0·07	65	44	50	34	42	28	0·01	46	31	51	34	60	40	0·22
No	290	65	86	58	100	57	104	70		84	56	99	66	107	72		103	69	98	66	89	60	

*ANOVA was calculated for continuous variables and the χ^2 test for categorical variables.
†Multivitamin and mineral supplements, *n*-3, vitamin D, and vitamin B supplements.
‡Gastrointestinal medications.

Table 2 Energy-adjusted dietary intake across tertiles of energy-adjusted dietary B-vitamins among Iranian women*,†,‡

	Vitamin B_6 (mg/d)							Vitamin B_9 (μg/d)							Vitamin B_{12} (μg/d)						
	<1·21		1·21–1·47		>1·47			<286·71		286·71–354·80		>354·80			<3·66		3·66–4·90		>4·90		
	n 149		*n* 149		*n* 149			*n* 149		*n* 149		*n* 149			*n* 149		*n* 149		*n* 149		
Variables	Mean	SD or SE	Mean	SD or SE	Mean	SD or SE	*P* value§	Mean	SD or SE	Mean	SD or SE	Mean	SD or SE	*P* value§	Mean	SD or SE	Mean	SD or SE	Mean	SD or SE	*P* value§
Nutrients																					
Energy (kcal/d)	2219·05	602·72	1980·06	524·06	2178·07	605·98	0·001	2215·32	619·42	1971·57	531·48	2190·29	579·36	0·0001	2319·68	615·11	1924·23	503·83	2133·28	571·85	0·0001
Proteins (g/d)	74·53	1·26	77·88	1·27	79·32	1·26	0·02	73·59	1·25	77·89	1·26	80·25	1·25	0·001	68·81	1·18	78·42	1·18	84·50	1·15	0·0001
Carbohydrates (g/d)	294·01	2·75	295·91	2·77	300·86	2·74	0·19	292·65	2·74	296·16	2·76	301·97	2·74	0·05	304·19	2·75	298·29	2·75	288·30	2·69	0·0001
Fat (g/d)	78·43	1·13	77·78	1·14	76·74	1·13	0·56	79·55	1·12	78·88	1·12	74·50	1·11	0·003	78·59	1·15	76·36	1·15	77·99	1·12	0·38
Fibre (g/d)	16·14	0·35	17·86	0·35	19·35	0·35	0·0001	15·93	0·32	16·68	0·33	20·74	0·32	0·0001	17·97	0·37	17·99	0·37	17·38	0·37	0·41
n-3 Fatty acids (g/d)	0·19	0·008	0·20	0·008	0·18	0·008	0·06	0·19	0·008	0·19	0·008	0·19	0·008	0·85	0·17	0·008	0·19	0·008	0·21	0·008	0·02
Mg (g/d)	251·17	3·84	277·51	3·86	301·56	3·82	0·0001	239·02	3·29	275·23	3·32	315·97	3·29	0·0001	261·21	4·14	278·86	4·15	290·15	4·06	0·0001
Food groups																					
Grains (g/d)	396·44	9·03	364·47	9·09	334·06	9·06	0·0001	387·84	9·12	367·77	9·20	339·36	9·11	0·001	372·09	9·38	370·91	9·40	351·97	9·20	0·22
Fruits (g/d)	282·33	12·06	346·47	12·13	375·73	12·02	0·0001	311·57	12·33	326·54	12·42	366·42	12·30	0·005	355·53	12·53	344·62	12·55	304·38	12·29	0·009
Vegetables (g/d)	291·44	10·17	346·79	10·23	407·75	10·13	0·0001	285·99	9·61	326·89	9·69	433·10	9·60	0·0001	336·81	11·04	351·38	11·05	357·79	10·83	0·38
Meat (g/d)	72·75	3·80	80·38	3·83	76·03	3·79	0·37	79·48	3·81	74·16	3·84	75·51	3·80	0·59	59·98	3·73	78·75	3·73	90·42	3·66	0·0001
Dairy products (g/d)	513·98	18·27	492·00	18·38	487·74	18·22	0·55	482·22	18·26	498·06	18·40	513·44	18·22	0·47	388·83	17·23	512·58	17·25	592·32	16·90	0·0001

*Mean ± SD (only energy intake).
†Mean ± SE (other variables).
‡All the variables, except energy, were adjusted for energy intake.
§Calculated using ANOVA for energy intake and multivariate ANCOVA with Bonferroni correction for other dietary variables.

($P_{value} = 0{\cdot}0001$), *n*-3 ($P_{value} = 0{\cdot}02$), Mg ($P_{value} = 0{\cdot}0001$), meats ($P_{value} = 0{\cdot}0001$) and dairy products ($P_{value} = 0{\cdot}0001$). However, they had lower intakes of energy ($P_{value} = 0{\cdot}0001$), carbohydrates ($P_{value} = 0{\cdot}0001$) and fruits ($P_{value} = 0{\cdot}009$).

OR and 95 % CI for depression, anxiety and psychological distress by tertile of dietary B-vitamin intake are provided in Table 3.

Vitamin B_6: A significant inverse association was observed between vitamin B_6 intake and depression (OR: 0·54; 95 %CI: 0·31, 0·95; P_{trend}: 0·03), but not for anxiety (OR: 0·67; 95 %CI: 0·38, 1·16; P_{trend}: 0·14) or psychological distress (OR: 0·76; 95 %CI: 0·44, 1·31; P_{trend}: 0·32).

Vitamin B_9: No association was found between dietary intake of folate with depression (OR: 0·80; 95 %CI: 0·40, 1·60; P_{trend}: 0·56), anxiety (OR: 0·76; 95 %CI: 0·38, 1·50; P_{trend}: 0·42) or psychological distress (OR: 0·84; 95 %CI: 0·44, 1·63; P_{trend}: 0·57).

Vitamin B_{12}: A positive association was found between dietary vitamin B_{12} intake with odds of depression (OR: 2·05; 95 % CI: 1·17, 3·60; P_{trend}: 0·01) and psychological distress (OR: 2·00; 95 % CI: 1·17, 3·41; P_{trend}: 0·01), but not for anxiety (OR: 1·62; 95 %CI: 0·94, 2·79; P_{trend}: 0·07).

Discussion

Dietary pyridoxine intake was inversely associated with depression, but not anxiety and psychological distress. However, higher cobalamin intake was associated with greater odds of depression and psychological distress. No relationship was found between dietary vitamin B_9 with any of the psychological disorders studied. To the best of our knowledge, this is the first study to investigate the association between dietary B-vitamin intake and anxiety and psychological distress specifically in women.

Given that B-vitamins are essential for every aspect of normal brain function and that there are less than optimal levels of B-vitamins in many populations worldwide[39], we decided to focus on them in this study. There are also several reasons why we chose the subset of B_6, B_9 and B_{12} vitamins. The main driver of this decision was based on the 'homocysteine hypothesis'. Biochemically, vitamins B_6, B_9 and B_{12} are involved in the metabolism of adenosyl methionine and methionine which are essential compounds for the production of neurotransmitters in the brain[16]. Lower intake of these vitamins can result in homocysteine accumulation that can adversely affect vascular systems and subsequently increase the risk of depression[40,41]. Second, vitamin B_{12} deficiency is among the most prevalent nutrient deficiencies[42]. Third, vitamins B_6, B_9 and B_{12} have limited dietary sources and are more likely to be deficient compared with other B-vitamins[39].

Table 3 Psychological disorders by tertile of energy-adjusted dietary B-vitamin intake among Iranian women

Variables	Vitamin B_6 (mg/d)							Vitamin B_9 (μg/d)							Vitamin B_{12} (μg/d)						
	<1·21		1·21–1·47		>1·47			<286·71		286·71–354·80		>354·80			<3·66		3·66–4·90		>4·90		
	n 149	OR	*n* 149	95 % CI	*n* 149	OR	95 % CI	*P* trend*	*n* 149	OR	95 % CI	*n* 149	OR	95 % CI	*P* trend*	*n* 149	OR	95 % CI	*n* 149	OR	95 % CI	*P* trend*
Depression																						
Model 1†	1	0·58*	0·35, 0·94	0·45	0·27, 0·75	0·002	1	0·86	0·53, 1·39	0·52	0·31, 0·86	0·01	1	1·52	0·92, 2·53	1·51	0·90, 2·54	0·1				
Model 2‡	1	0·58	0·35, 0·96	0·44	0·26, 0·74	0·002	1	0·86	0·52, 1·43	0·53	0·31, 0·89	0·01	1	1·47	0·86, 2·50	1·64	0·97, 2·76	0·06				
Model 3§	1	0·66	0·39, 1·11	0·54	0·31, 0·95	0·03	1	1·01	0·59, 1·72	0·80	0·40, 1·60	0·56	1	1·71	0·98, 2·97	2·05	1·17, 3·60	0·01				
Anxiety																						
Model 1†	1	0·52	0·32, 0·84	0·47	0·28, 0·76	0·002	1	0·66	0·41, 1·07	0·43	0·26, 0·71	0·001	1	0·93	0·57, 1·53	1·19	0·74, 1·93	0·45				
Model 2‡	1	0·53	0·32, 0·88	0·48	0·29, 0·80	0·004	1	0·71	0·43, 1·16	0·45	0·27, 0·75	0·003	1	0·95	0·56, 1·60	1·28	0·78, 2·11	0·3				
Model 3§	1	0·64	0·38, 1·07	0·67	0·38, 1·16	0·14	1	0·86	0·51, 1·47	0·76	0·38, 1·50	0·42	1	1·11	0·64, 1·90	1·62	0·94, 2·79	0·07				
Psychological distress																						
Model 1†	1	0·66	0·41, 1·07	0·59	0·36, 0·95	0·02	1	0·65	0·40, 1·04	0·50	0·31, 0·82	0·005	1	1·16	0·71, 1·89	1·51	0·93, 2·43	0·09				
Model 2‡	1	0·70	0·43, 1·14	0·59	0·36, 0·97	0·04	1	0·71	0·43, 1·15	0·56	0·34, 0·93	0·02	1	1·18	0·70, 1·99	1·63	0·99, 2·68	0·05				
Model 3§	1	0·81	0·48, 1·35	0·76	0·44, 1·31	0·32	1	0·81	0·48, 1·37	0·84	0·44, 1·63	0·57	1	1·35	0·79, 2·30	2·00	1·17, 3·41	0·01				

*Calculated by logistic regression.
†Model 1: Crude.
‡Model 2: Adjusted for energy intake, age, socioeconomic status, supplement use, body satisfaction, BMI.
§Model 3: Adjusted for energy intake, age, socioeconomic status, supplement use, body satisfaction, BMI, *n*-3 fatty acids, fibre, Mg.

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

We found a significant inverse association between vitamin B_6 intake and depression. In line with this finding, in the Quebec Longitudinal Study, dietary intake of vitamin B_6 (>1·71 *v.* <1·33 mg/d) was negatively associated with risk of depression among Canadian elderly women (*n* 691)[43]. Moreover, a prospective study showed an inverse relationship between vitamin B_6 intake (from both diet + supplements: 2·4–207 *v.* 0·6–1·6 mg/d) and depression among US elderly (*n* 3503)[44]. In that study, for every additional 10 mg/d of vitamin B_6 intake, the risk of depression reduced by about 2 %[44]. In contrast, no association was found between dietary vitamin B_6 intake (men: 0·78 *v.* 0·47 mg/1000 kcal; women: 0·92 *v.* 0·66 mg/1000 kcal) and depression among Japanese adults (men: 309, women: 208; 21–67 years old)[45]. Moreover, there was no association between vitamin B_6 intake (>1·70 *v.* <1·46 mg/d) and depression among elderly Dutch men (*n* 332)[46]. In addition, a Finnish prospective study did not show any association between dietary vitamin B_6 intake (2·1–4·4 *v.* 0·3–1·7 mg/d) and psychological disorders among adult men (*n* 2682)[25]. A systematic review indicated no treatment effect of vitamin B_6 for depression, except for hormone-related depression in premenopausal women[47].

Various explanations may explain inconsistent findings across studies. First, some studies neglected to account for some confounding variables that are related to psychological disorders, such as satisfaction with body image, the average amount of time dedicated to sleeping and activities outside home, important dietary elements (fibre and *n*-3)[43–46,48], smoking[43,46] and physical activity[48]. Second, variability exists in fruit and vegetable consumption (as a rich source of B-vitamins) in different age groups across the globe[49]. Low fruit and vegetable consumption is more prevalent among the elderly[50]. Third, studies used different methods to estimate dietary intake and to measure psychological status. Fourth, gender differences could be another explanation since gonadal steroids can influence mood state [51,52] and the accuracy of dietary assessment differs by gender. Men and women also differ in terms of actual food choices[53,54], precision of reported dietary intakes[55] and even self-reported preferences for foods[56]. Fifth, genetic variation may play a role, as people with a specific genetic make-up might be particularly sensitive to low levels of B-vitamins[57,58].

In the current study, we observed a positive association between dietary vitamin B_{12} intake with depression and psychological distress, but not anxiety. By contrast, a cross-sectional study by Sanchez-Villegas *et al.* observed an inverse association between dietary vitamin B_{12} intake (15·7 *v.* 5·2 μg/d) and the prevalence of depression among Spanish women (*n* 5459)[16]. A prospective study of British women indicated an inverse association between dietary vitamin B_{12} (5·48 μg/d) and psychological distress[59]. The study by Skarupski *et al.* found that every additional 10 μg of vitamin B_{12} (from diet + supplement) was associated with 2 % reduced risk of depression among US elderly annually[44]. A prospective study (with 3 years of follow-up) among Canadian elderly showed that men in the lowest tertile of dietary B_{12} intake (<3·16 μg/d *v.* >4·79) had greater risk of depression[43]. Moreover, a few studies have reported null associations. For instance, no association was found between dietary cobalamin intake (men: 7 *v.* 2·6; women: 7·2 *v.* 3·8 μg/1000 kcal) and depression among Japanese adults (men: 309, women: 208; 21–67 years old)[45]. A cross-sectional study by Tolmunen *et al.* also showed no association between dietary cobalamin intake (8·7–136 *v.* 2·2–5·9 μg/d) and depression among Finnish men (*n* 2682; 42–60 years old)[48].

Incompatible results across studies could be due to various reasons. First, dietary patterns are not uniform across different cultures. To be more exact, the null finding in Tolmunen *et al.*'s study might be due to the fact that animal products such as meat and dairy (a rich source of cobalamin) play a prominent role in traditional Finnish dishes[48]. In a cohort study, about 99 % of Finnish participants received the Recommended Dietary Allowance (RDA) of cobalamin[48]. Second, another factor affecting this association could be poor absorption of cobalamin, particularly in older people[60], since most of the studies that reported a negative association between cobalamin and psychological disorders have been conducted in the elderly[43,44]. A third reason relates to the use of different methods to define and assess psychological disorders [16,43–45,48]. Dietary intake of vitamin B_{12} was above the RDA among participants in our study (mean: 4·58 μg/d). Therefore, consumption of foods that are rich in B_{12} such as meats and dairy products as well as better absorption in younger age groups might explain why we observed positive associations between this vitamin and psychological disorders in our population.

We found no relationship between dietary folate intake and psychological disorders. In line with our findings, the Chicago Health and Aging Project showed no associations between total folate intake (diet + supplement: 397–1731 *v.* 63–263 μg/d) and depression among 3503 US elderly (aged >65 years old)[44]. Moreover, a prospective study of elderly Dutch men revealed no relationship between dietary folate intake (>194 *v.* <15 μg/d) and depressive symptoms[46]. Null findings in these studies could be explained in several ways. First, the prevalence of folate deficiency has fallen in the US population (16 to 1 % since 1998) due to folic acid fortification[61]. Second, the association between dietary folate intake and psychological disorders might weaken as people advance in age. In support of the later idea, two studies showed a positive link between low plasma folate level and depression in middle-aged samples[62,63], while two other studies did not find such association in the elderly[64,65]. Although one study reported an inverse association between folate status and depression in the elderly, this finding appeared to be mainly due to CVD and comorbidities[66].

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

By contrast, a cross-sectional study by Tolmunen *et al.*, conducted with Finish adults (*n* 2682 men; 42–60 years old), revealed that participants in the lowest tertile of folate intake (45·4–226 μg/d) had about 65 % greater risk of having depression than those in the highest tertile (269·3–587·5 μg/d)[48]. Two studies conducted on Spanish[16] and Japanese[45] adults showed associations only in men (but not women). The cross-sectional study by Sanchez-Villegas *et al.* found an inverse association between dietary folate intake (569·4 *v.* 231·9 μg/d) and the prevalence of depression among Spanish men (*n* 4211), but not women[16]. Moreover, Murakami *et al.* showed that folate intake (235 *v.* 119 μg/1000 kcal) was associated with lower depression among Japanese men (*n* 309), but not women[45]. In these two studies, higher intake of folate in Spanish (618·50 *v.* 332·20 μg/d) and Japanese women (292 *v.* 155 μg/1000 kcal) might explain null findings in females compared to males[16,45].

These findings may suggest that even very low amounts of folate can aggravate psychological disorders. In support of this hypothesis, in the aforementioned Finnish study by Tolmunen *et al.*, the inverse association between dietary folate intake and depression might be due to the fact that only 24 % of the participants received the recommended daily amount of folate in Finland (300 mg/d)[48]. A higher prevalence of psychological disorders has been observed in countries where folate fortification was not compulsory, at least during the study, for instance, Japan[67], France[68], Finland[25], Norway[69], Greece[70], Singapore[71] and Australia before 2009[40]. However, once a satisfactory level is achieved, further increases in the amount of folate might not result in greater reductions in the risk of mental disorders. In support of this idea, the study by Sanchez-Villegas *et al.* found that the estimated odds of depression in the fifth quintile (OR: 1·01; median of folate: 569·4) of folate intake was not the lowest, but was higher than that of the third (OR: 0·77; median of folate: 361·7) and fourth quintiles (OR: 0·72; median of folate: 429·7)[16].

The inverse association between dietary B-vitamin intake and psychological disorders can be understood through different mechanisms. Pyridoxine and cobalamin act as cofactors in the conversion of homocysteine to cysteine and methionine, respectively[16]. Additionally, methyl folate is needed for the conversion of homocysteine to methionine as well[16]. Methionine is a precursor of S-adenosylmethionine which is responsible for methylation reactions in the production of neurotransmitters, membrane phospholipids and nucleic acids[72]. Therefore, inadequate dietary intake of B-vitamins might lead to a reduction in the production of monoamines in the brain and accumulation of homocysteine in the body, which are both likely to contribute to the development of mental disorders[41,73]. The accumulation of metabolites of homocysteine (such as cysteine sulphinic acid and homocysteinic acid) might have a large impact on psychological disorders through different pathways. First, they might inhibit one-carbon methylation reactions by S-adenosylmethionine[74]. Second, they can negatively affect N-methyl-D-aspartate glutamate receptors in the central nervous system[74]. Third, they might have negative vascular effects[75].

There were several reasons why we prioritised studying women. First, the WHO has indicated women's health to be an urgent priority and has noted that research on women is still limited and often unreliable. Second, according to international[3] and national[4] statistics, the prevalence of depression is much higher among women than men. Third, the overall mental health of women of reproductive age is also important because it may affect their fertility[76].

To the best of our knowledge, this is the first study that investigates the relationship between dietary B-vitamin intake and psychological disorders – anxiety and psychological distress – among women. Previous epidemiological studies differ in the extent to which confounding variables were controlled. The present study went beyond that of most other studies that have been conducted on the association between B-vitamins and psychological disorders by controlling for important dietary factors (fibre and *n*-3), body image, number of hours spent sleeping and spent outside the home.

Several limitations should be considered when interpreting the current findings. First, we were unable to assess causality due to the cross-sectional nature of this study. Therefore, we recommend future prospective studies be carried out to understand the casual link between B-vitamins intake and psychological disorders. Second, psychological disorders can affect food consumption in favour of high-energy and energy-dense diets rather than nutrient-dense diets[77]. Therefore, lower dietary intake of B-vitamins, which is a feature of energy-dense diet, might be a consequence rather than a cause of depression. Although such plausible sources of bias are difficult to rule out when using a cross-sectional design, participants with a previous psychiatric disorders and depressive symptoms were excluded from our study at baseline. Apart from this, energy intake was adjusted; therefore, reverse causality is unlikely. Third, due to high within-person variation and rates of turnover regarding dietary B-vitamin intake, a valid and reliable FFQ corresponding to the last 12 months was used to measure dietary intake. However, the closed-end nature of the questionnaire could increase the possibility of under- and over-reporting, leading to misclassification. Fourth, due to the aforementioned within-person variation, it would have been better to assess blood levels of B-vitamins to support our findings. Still, dietary intake of folate and cobalamin has been shown to be positively correlated with serum levels since they can be stored within body[78,79]. Fifth, although homocysteine serum level was mentioned as a possible mechanism through which low

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

levels of B-vitamins might increase the risk of psychological disorders; however, we did not evaluate if homocysteine performed as a mediator in our study Sixth, the study population was restricted to women; however, such findings may be different among men.

Conclusion

Dietary pyridoxine intake was inversely associated with depression, but not anxiety or psychological distress. However, dietary cobalamin intake was associated with higher odds of depression and psychological distress. No relationship was found between dietary vitamin B_9 intake with any of the psychological disorders studied. We recommend that future prospective studies in different populations are conducted to clarify whether B-vitamin deficiency is a cause or consequence of psychological disorders.

Acknowledgements

Acknowledgements: The authors would like to thank the participants for taking part in this study. *Financial support:* This study was supported by Tehran University of Medical Sciences (grant and ethics number: 98-01-161-42024). *Conflict of interest*: The authors declare that they have no conflict of interest. *Authorship:* L.A. and H.M. designed the study. H.M., M.D.M. and M.A. contributed in statistical analysis, data interpretation and manuscript drafting. P.J.S. reviewed and edited the manuscript. The final version of manuscript for submission was approved by all authors. *Ethics of human subject participation:* The present study was conducted in accordance with the Helsinki Declaration, and all procedures involving human subjects were approved by the ethics committee of Tehran University of Medical Sciences. All the participants gave their permission for inclusion by signing an informed consent.

References

1. Whiteford HA, Degenhardt L, Rehm J *et al.* (2010) Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study. *Lancet* **382**, 1575–1586.
2. Mojtabai R (2011) National trends in mental health disability, 1997–2009. *Am J Public Health* **101**, 2156–2163.
3. Organization WH (2017) *Depression and Other Common Mental Disorders: Global Health Estimates*. Geneva: World Health Organization.
4. Noorbala A, Yazdi SB, Yasamy M *et al.* (2004) Mental health survey of the adult population in Iran. *Br J Psychiat* **184**, 70–73.
5. Saveanu RV & Nemeroff CB (2012) Etiology of depression: genetic and environmental factors. *Psychiat Clin* **35**, 51–71.
6. Murakami K & Sasaki S (2010) Dietary intake and depressive symptoms: a systematic review of observational studies. *Mol Nutr Food Res* **54**, 471–488.
7. Azadbakht L & Esmaillzadeh A (2012) Dietary patterns and attention deficit hyperactivity disorder among Iranian children. *Nutrition* **28**, 242–249.
8. Liu Z-M, Ho SC, Xie YJ *et al.* (2016) Associations between dietary patterns and psychological factors: a cross-sectional study among Chinese postmenopausal women. *Menopause* **23**, 1294–1302.
9. Sadeghi O, Keshteli AH, Afshar H *et al.* (2019) Adherence to Mediterranean dietary pattern is inversely associated with depression, anxiety and psychological distress. *Nutr Neurosci* **22**, 1–12.
10. Abshirini M, Siassi F, Koohdani F *et al.* (2019) Dietary total antioxidant capacity is inversely associated with depression, anxiety and some oxidative stress biomarkers in postmenopausal women: a cross-sectional study. *Ann Gener Psychiat* **18**, 3.
11. Perez L (2018) The role of dietary patterns in mood disorders: prospective research in youth populations. *Am J Lifestyle Med* **12**, 286–290.
12. Su Q, Yu B, He H *et al.* (2016) Nut consumption is associated with depressive symptoms among Chinese adults. *Dep Anxiety* **33**, 1065–1072.
13. Liu X, Yan Y, Li F *et al.* (2016) Fruit and vegetable consumption and the risk of depression: a meta-analysis. *Nutrition* **32**, 296–302.
14. Sadeghi O, Hassanzadeh-Keshteli A, Afshar H *et al.* (2017) The association of whole and refined grains consumption with psychological disorders among Iranian adults. *Europ J Nutr* **58**, 211–225.
15. Anjom-Shoae J, Sadeghi O, Keshteli AH *et al.* (2020) Legume and nut consumption in relation to depression, anxiety and psychological distress in Iranian adults. *Europ J Nutr* **59**, 1–11.
16. Sánchez-Villegas A, Doreste J, Schlatter J *et al.* (2009) Association between folate, vitamin B6 and vitamin B12 intake and depression in the SUN cohort study. *J Hum Nutr Diet* **22**, 122–133.
17. Bjelland I, Ueland PM & Vollset SE (2003) Folate and depression. *Psychother Psychosom* **72**, 59–60.
18. Bell IR, Edman JS, Morrow FD *et al.* (1991) B complex vitamin patterns in geriatric and young adult inpatients with major depression. *J Am Geriatr Soc* **39**, 252–257.
19. Carney M, Chary T, Laundy M *et al.* (1990) Red cell folate concentrations in psychiatric patients. *J Affect Disord* **19**, 207–213.
20. Carney M (1967) Serum folate values in 423 psychiatric patients. *Br Med J* **4**, 512.
21. Wesson VA, Levitt AJ & Joffe RT (1994) Change in folate status with antidepressant treatment. *Psychiat Res* **53**, 313–322.
22. Bryan J, Calvaresi E & Hughes D (2002) Short-term folate, vitamin B-12 or vitamin B-6 supplementation slightly affects memory performance but not mood in women of various ages. *J Nutr* **132**, 1345–1356.
23. Hvas A-M, Juul S, Lauritzen L *et al.* (2004) No effect of vitamin B-12 treatment on cognitive function and depression: a randomized placebo controlled study. *J Affect Disord* **81**, 269–273.
24. Deijen J, Van der Beek E, Orlebeke J *et al.* (1992) Vitamin B-6 supplementation in elderly men: effects on mood, memory, performance and mental effort. *Psychopharmacology* **109**, 489–496.
25. Tolmunen T, Hintikka J, Ruusunen A *et al.* (2004) Dietary folate and the risk of depression in Finnish middle-aged men. *Psychother Psychosom* **73**, 334–339.
26. Kim J-M, Stewart R, Kim S-W *et al.* (2008) Predictive value of folate, vitamin B 12 and homocysteine levels in late-life depression. *Br J Psychiat* **192**, 268–274.

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

27. Kafeshani M, Feizi A, Esmaillzadeh A *et al.* (2019) Higher vitamin B6 intake is associated with lower depression and anxiety risk in women but not in men: a large cross-sectional study. *Int J Vitamin Nutr Res* **89**, 1–9.
28. Ferrari A, Somerville A, Baxter A *et al.* (2013) Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. *Psychol Med* **43**, 471–481.
29. Esteghamati A, Noshad S, Nazeri A *et al.* (2012) Patterns of fruit and vegetable consumption among Iranian adults: a SuRFNCD-2007 study. *Br J Nutr* **108**, 177–181.
30. Esmaillzadeh A & Azadbakht L (2008) Food intake patterns may explain the high prevalence of cardiovascular risk factors among Iranian women. *J Nutr* **138**, 1469–1475.
31. Mozaffari H, Namazi N, Larijani B *et al.* (2019) Association of dietary acid load with cardiovascular risk factors and the prevalence of metabolic syndrome in Iranian women: a cross-sectional study. *Nutrition* **110**, 570.
32. Mozaffari H, Daneshzad E, Larijani B *et al.* (2020) Association of dietary total antioxidant capacity to anthropometry in healthy women: a cross-sectional study. *Nutrition* **110**, 577.
33. Mirmiran P, Esfahani FH, Mehrabi Y *et al.* (2010) Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Health Nutr* **13**, 654–662.
34. Azadbakht L, Kimiagar M, Mehrabi Y *et al.* (2007) Dietary soya intake alters plasma antioxidant status and lipid peroxidation in postmenopausal women with the metabolic syndrome. *Br J Nutr* **98**, 807–813.
35. Samani S & Joukar B (2007) A study on the reliability and validity of the short form of the depression anxiety stress scale (DASS-21). *J Soc Hum Sci Shiraz Univ* **52**, 65–77.
36. Mozaffari H, Namazi N, Larijani B *et al.* (2019) Associations between dietary insulin load with cardiovascular risk factors and inflammatory parameters in elderly men: a cross-sectional study. *Br J Nutr* **121**, 773–781.
37. Ainsworth BE, Haskell WL, Whitt MC *et al.* (2000) Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exercise* **32**, S498–S504.
38. Brown CC, Kipnis V, Freedman LS *et al.* (1994) Energy adjustment methods for nutritional epidemiology: the effect of categorization. *Am J Epidemiol* **139**, 323–338.
39. Kennedy DO (2016) B vitamins and the brain: mechanisms, dose and efficacy: a review. *Nutrients* **8**, 68.
40. Almeida OP, Marsh K, Alfonso H *et al.* (2010) B-vitamins reduce the long-term risk of depression after stroke: the VITATOPS-DEP trial. *Ann Neurol* **68**, 503–510.
41. Bottiglieri T (2005) Homocysteine and folate metabolism in depression. *Progr Neuro-Psychopharmacol Biol Psychiat* **29**, 1103–1112.
42. Green R, Allen LH, Bjørke-Monsen A-L *et al.* (2017) Vitamin B 12 deficiency. *Nat Rev Dis Primers* **3**, 1–20.
43. Gougeon L, Payette H, Morais J *et al.* (2016) Intakes of folate, vitamin B 6 and B 12 and risk of depression in community-dwelling older adults: the Quebec Longitudinal Study on Nutrition and Aging. *Europ J Clin Nutr* **70**, 380.
44. Skarupski KA, Tangney C, Li H *et al.* (2010) Longitudinal association of vitamin B-6, folate, and vitamin B-12 with depressive symptoms among older adults over time. *Am J Clin Nutr* **92**, 330–335.
45. Murakami K, Mizoue T, Sasaki S *et al.* (2008) Dietary intake of folate, other B vitamins, and ω-3 PUFA in relation to depressive symptoms in Japanese adults. *Nutrition* **24**, 140–147.
46. Kamphuis M, Geerlings M, Grobbee D *et al.* (2008) Dietary intake of B 6–9–12 vitamins, serum homocysteine levels and their association with depressive symptoms: the Zutphen Elderly Study. *Europ J Clin Nutr* **62**, 939.
47. Williams A-L, Cotter A, Sabina A *et al.* (2005) The role for vitamin B-6 as treatment for depression: a systematic review. *Family Pract* **22**, 532–537.
48. Tolmunen T, Voutilainen S, Hintikka J *et al.* (2003) Dietary folate and depressive symptoms are associated in middle-aged Finnish men. *J Nutr* **133**, 3233–3236.
49. Chi SH, Wang JY & Tsai AC (2016) Combined association of leisure-time physical activity and fruit and vegetable consumption with depressive symptoms in older T aiwanese: results of a national cohort study. *Geriatr Gerontol Int* **16**, 244–251.
50. Hall JN, Moore S, Harper SB *et al.* (2009) Global variability in fruit and vegetable consumption. *Am J Prev Med* **36**, 402–409. e5.
51. Nolen-Hoeksema S (2012) Emotion regulation and psychopathology: the role of gender. *Ann Rev Clin Psychol* **8**, 161–187.
52. Laurin C, Lavoie KL, Bacon SL *et al.* (2007) Sex differences in the prevalence of psychiatric disorders and psychological distress in patients with COPD. *Chest* **132**, 148–155.
53. Beer-Borst S, Hercberg S, Morabia A *et al.* (2000) Dietary patterns in six European populations: results from EURALIM, a collaborative European data harmonization and information campaign. *Eur J Clin Nutr* **54**, 253.
54. Wardle J, Haase AM, Steptoe A *et al.* (2004) Gender differences in food choice: the contribution of health beliefs and dieting. *Ann Behav Med* **27**, 107–116.
55. Marks GC, Hughes MC & van der Pols JC (2006) Relative validity of food intake estimates using a food frequency questionnaire is associated with sex, age, and other personal characteristics. *J Nutr* **136**, 459–465.
56. Jensen KOD & Holm L (1999) Preferences, quantities and concerns: socio-cultural perspectives on the gendered consumption of foods. *Europ J Clin Nutr* **53**, 351.
57. Mutch DM, Wahli W & Williamson G (2005) Nutrigenomics and nutrigenetics: the emerging faces of nutrition. *FASEB J* **19**, 1602–1616.
58. Zeisel SH (2007) Nutrigenomics and metabolomics will change clinical nutrition and public health practice: insights from studies on dietary requirements for choline. *Am J Clin Nutr* **86**, 542–548.
59. Mishra GD, McNaughton SA, O'Connell MA *et al.* (2009) Intake of B vitamins in childhood and adult life in relation to psychological distress among women in a British birth cohort. *Public Health Nutr* **12**, 166–174.
60. Ho C, Kauwell GP & Bailey LB (1999) Practitioners' guide to meeting the vitamin B-12 RDA for people aged 51 years and older. *J Am Diet Assoc* **99**, 725–727.
61. Pfeiffer CM, Caudill SP, Gunter EW *et al.* (2005) Biochemical indicators of B vitamin status in the US population after folic acid fortification: results from the National Health and Nutrition Examination Survey 1999–2000. *Am J Clin Nutr* **82**, 442–450.
62. Morris MS, Fava M, Jacques PF *et al.* (2003) Depression and folate status in the US population. *Psychother Psychosom* **72**, 80–87.
63. Sachdev PS, Parslow RA, Lux O *et al.* (2005) Relationship of homocysteine, folic acid and vitamin B12 with depression in a middle-aged community sample. *Psychol Med* **35**, 529.
64. Hvas A-M, Juul S, Bech P *et al.* (2004) Vitamin B6 level is associated with symptoms of depression. *Psychother Psychosom* **73**, 340–343.
65. Penninx BW, Guralnik JM, Ferrucci L *et al.* (2000) Vitamin B12 deficiency and depression in physically disabled older women: epidemiologic evidence from the Women's Health and Aging Study. *Am J Psychiat* **157**, 715–721.
66. Tiemeier H, Van Tuijl HR, Hofman A *et al.* (2002) Vitamin B12, folate, and homocysteine in depression: the Rotterdam Study. *Am J Psychiat* **159**, 2099–2101.

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press

67. Nanri A, Mizoue T, Matsushita Y *et al.* (2010) Serum folate and homocysteine and depressive symptoms among Japanese men and women. *Europ J Clin Nutr* **64**, 289.
68. Astorg P, Couthouis A, de Courcy GP *et al.* (2008) Association of folate intake with the occurrence of depressive episodes in middle-aged French men and women. *Br J Nutr* **100**, 183–187.
69. Bjelland I, Tell GS, Vollset SE *et al.* (2003) Folate, vitamin B12, homocysteine, and the MTHFR 677C→ T polymorphism in anxiety and depression: the Hordaland Homocysteine Study. *Arch Gene Psychiat* **60**, 618–626.
70. Dimopoulos N, Piperi C, Salonicioti A *et al.* (2007) Correlation of folate, vitamin B12 and homocysteine plasma levels with depression in an elderly Greek population. *Clin Biochem* **40**, 604–608.
71. Ng TP, Niti M, Zaw MH *et al.* (2009) Depressive symptoms and incident cognitive impairment in cognitively well-functioning older men and women. *J Am Geriatr Soc* **57**, 1058–1063.
72. Lu SC (2000) S-adenosylmethionine. *Int J Biochem Cell Biol* **32**, 391–395.
73. Almeida OP, McCaul K, Hankey GJ *et al.* (2008) Homocysteine and depression in later life. *Arch Gen Psychiat* **65**, 1286–1294.
74. Parnetti L, Bottiglieri T & Lowenthal D (1997) Role of homocysteine in age-related vascular and non-vascular diseases. *Aging Clin Exp Res* **9**, 241–257.
75. Klerk M, Verhoef P, Clarke R *et al.* (2002) MTHFR 677C→ T polymorphism and risk of CHD: a meta-analysis. *JAMA* **288**, 2023–2031.
76. Rooney KL & Domar AD (2018) The relationship between stress and infertility. *Dialog Clin Neurosci* **20**, 41.
77. Gibson EL (2006) Emotional influences on food choice: sensory, physiological and psychological pathways. *Physiol Behav* **89**, 53–61.
78. Chew S-C, Khor G-L & Loh S-P (2011) Association between dietary folate intake and blood status of folate and homocysteine in Malaysian adults. *J Nutr Sci Vitaminol* **57**, 150–155.
79. Yang Q, Cogswell ME, Hamner HC *et al.* (2009) Folic acid source, usual intake, and folate and vitamin B-12 status in US adults: National Health and Nutrition Examination Survey (NHANES) 2003–2006. *Am J Clin Nutr* **91**, 64–72.

https://doi.org/10.1017/S1368980020002943 Published online by Cambridge University Press