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No associations between serum concentrations of 25-hydroxyvitamin D and parathyroid hormone and depression among US adults

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Although there is evidence that vitamin D deficiency may play a role in depression, studies done on the associations have yielded mixed results. The present study aimed to examine the associations between serum concentrations of 25-hydroxyvitamin D (25(OH)D) and parathyroid hormone (PTH) and the presence of depression among US adults. A cross-sectional, population-based sample (including 3916 participants aged ≥20 years) from the 2005–6 National Health and Nutrition Examination Survey was used. Participants' depressive symptoms were assessed using the Patient Health Questionnaire-9 diagnostic algorithm. The associations of 25(OH)D and PTH with depression were explored using multivariate logistic regression models. For all the participants, the age-adjusted prevalence was 5·3 (95 % CI 4·3, 6·5) % for having moderate-to-severe depression, 2·3 (95 % CI 1·7, 3·1) % for having major depression and 3·8 (95 % CI 3·0, 4·6) % for having minor depression. Although the age-adjusted prevalence and the unadjusted OR of having moderate-to-severe depression or major depression decreased linearly with increasing quartiles of 25(OH)D ($P<0·05$ for trends), no significant associations remained after adjusting for multiple potential confounders such as demographic variables, lifestyle factors and coexistence of a number of chronic conditions. Neither the age-adjusted prevalence nor the OR (unadjusted or adjusted) of having depression differed significantly by the quartiles of PTH. Thus, in contrast to some of the previous findings, the present results did not show significant associations between serum concentrations of 25(OH)D and PTH and the presence of moderate-to-severe depression, major depression or minor depression among US adults. However, these findings need to be further confirmed in future studies.

Depression: Patient health questionnaire-9 diagnostic algorithm: Vitamin D: Parathyroid hormone

The health impact of vitamin D deficiency, or hypovitaminosis D, is receiving increased attention in the literature[1]. Besides its significant associations with a broad range of physiological outcomes, including bone health, CVD (e.g. CHD and peripheral artery disease), hypertension, metabolic syndrome and diabetes, cancers and all-cause or cardiovascular mortality[1–8], vitamin D deficiency may have adverse effects on neuropsychological functions such as depression and cognitive illness because vitamin D receptors are broadly distributed in multiple neurons in the central nervous system[9–11]. However, evidence for the effects of vitamin D on mental health is limited, and controversial results obtained from the studies done on the associations between vitamin D and depression are emerging[12–15]. In addition, increased levels of serum parathyroid hormone (PTH) in primary hyperparathyroidism were reported to be associated with psychiatric symptoms varying from mild personality changes or nervousness to severe depression, obsessive–compulsive behaviour and paranoia[16–19]. A marked improvement in psychiatric symptoms was observed after surgical parathyroidectomy[18,20]. However, confirmatory evidence on the associations between PTH and depression remains insufficient to draw definitive conclusions at present. To shed light on these issues, the present study examined the relationships between serum levels of vitamin D and PTH and the presence of depressive symptoms among US adults using a nationally representative sample.

Research design and method

A cross-sectional, nationally representative sample from the 2005–6 National Health and Nutrition Examination Survey (NHANES), which was conducted on the non-institutionalised civilian US population, was obtained using a multistage stratified sampling design. Survey participants were initially interviewed at home, and were then invited to a mobile examination centre, where they underwent various examinations and provided blood samples for laboratory tests. In the 2005–6 NHANES, all procedures involving human subjects were approved by the National Center for Health Statistics Research Ethics Review Board. Written informed consent was obtained from all the participants. Details about the NHANES design and operation may be found elsewhere[21].

We examined interview and laboratory data obtained from participants who were ≥20 years of age. Participants' depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9) diagnostic algorithm, which has

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; NHANES, National Health and Nutrition Examination Survey; PHQ-9, Patient Health Questionnaire-9; PTH, parathyroid hormone.

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been described in detail elsewhere[22]. Specifically, participants were asked how often over the last 2 weeks they had experienced each of the following symptoms: (1) little interest or pleasure in doing things; (2) feeling down, depressed or hopeless; (3) trouble falling or staying asleep or sleeping too much; (4) feeling tired or having little energy; (5) having a poor appetite or overeating; (6) feeling bad as a failure or having let themselves or their family down; (7) having trouble concentrating on things such as reading the newspaper or watching TV; (8) moving or speaking so slowly that other people could have noticed, or being so fidgety or restless that they had been moving about a lot more than usual and (9) having thoughts of suicide or self-injury in some way. For each item, their responses were 'not at all' (scored as 0 point), 'having the symptoms for several days' (scored as 1 point), 'having the symptoms for more than half the days' (scored as 2 points) and 'having the symptoms nearly every day' (scored as 3 points). Their scores for each item were then added to produce a total depression severity score, and a cut-off point ≥ 10 was used to identify participants as having moderate-to-severe depression. Alternatively, a provisional diagnosis of major and minor depression was used. Participants who had at least five of the nine PHQ-9 criteria, one of which must be 'loss of interest or pleasure in doing things' or 'feeling down, depressed or hopeless', for ≥ 7 d (several days for 'having thoughts of suicide or self-injury') in the preceding 2 weeks were defined as having major depression. Participants who had two to four of the nine PHQ-9 criteria, one of which must be 'loss of interest or pleasure in doing things' or 'feeling down, depressed or hopeless', for ≥ 7 d (several days for 'having thoughts of suicide or self-injury') in the preceding 2 weeks were defined as having minor depression[23]. The PHQ-9 has been shown to provide valid measurements on major depression in the general population, and the scoring ≥ 10 on the PHQ-9 has been shown to have a sensitivity and specificity of 88 % for major depression[24–26].

Serum specimens were frozen and stored at < -70°C until analysis. Serum concentrations of 25-hydroxyvitamin D (25(OH)D) were measured using the DiaSorin RIA procedure (Diasorin Corporation, Stillwater, MN, USA). Serum concentrations of PTH were measured on an Elecsys 1010 analyser using the ECL/Origen electrochemiluminescence procedure (Roche Diagnostics Corporation, Indianapolis, IN, USA). The details of the methods are described in the laboratory procedure manuals in the NHANES web site[21]. Briefly, for assays of 25(OH)D, the hydroxylated metabolites including 25(OH)D were first extracted from serum using acetonitrile. Serum extracts, controls or the vitamin D standards were then incubated with a 25(OH)D-specific antibody and an ^{125}I-labelled 25(OH)D (used as a tracer) for 90 min at 20–25°C, followed by a continuous incubation with a secondary antibody-precipitating complex for 20 min at 20–25°C. The ^{125}I radioactivity was then counted, and the 25(OH)D concentrations of a sample were determined based on a linearised standard curve developed using the levels of ^{125}I radioactivity *v.* concentrations of vitamin D standards. The sensitivity for the 25(OH)D assay was 1·5 ng/ml, and the CV was 9·9 %. For assays of PTH, a serum sample was first incubated with a biotinylated monoclonal PTH-specific antibody and a ruthenium-labelled monoclonal PTH-specific antibody to form a sandwich complex. The complex was then immobilised to the streptavidin-labelled microparticles via biotin–streptavidin interaction. The complex-bounded microparticles were magnetically captured onto the surface of the working electrode, to which application of a voltage induced chemiluminescent emission that was measured by a photomultiplier. These light signals were used to determine the PTH concentrations of a sample based on the calibration curve generated for each instrument. The sensitivity of the PTH assay was 9·3 pg/ml, and the CV was 3·6 %. Both the 25(OH)D and PTH assay results have been shown to be acceptable based on the in-house quality control as described in the laboratory procedure manuals[21]. The quartiles of 25(OH)D and PTH were created according to their distributions in participants aged ≥ 20 years after taking the sampling weights into account.

Socio-demographic variables used in the analyses included age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black and others), educational status ($\leq$ high-school diploma and $>$ high-school diploma) and marital status (i.e. married/living with partner, divorced/widowed/separated or never married). BMI (kg/m^2) was calculated from the measured weight and height using standardised protocol and instruments. Serum concentrations of cotinine, used to evaluate smoking status, were measured using an isotope dilution-HPLC/atmospheric pressure chemical ionisation tandem MS (Perkin-Elmer Sciex Company, Norwalk, CT, USA). Physical activity was calculated as an average daily metabolic equivalent-h index that summed transportation, household and leisure-time physical activity. Alcohol consumption was calculated as the average daily number of drinks consumed. Serum concentrations of creatinine were measured using the Jaffe rate method (kinetic alkaline picrate) on a Beckman Synchron LX20 (Beckman-Coulter, Inc., Fullerton, CA, USA). The estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation[27]. Chronic conditions were assessed by asking the participants whether they had ever been told by a healthcare professional that they had the symptoms related to diabetes, CHD, stroke, arthritis and cancer, or they still had the symptoms related to asthma and chronic bronchitis. For the measurement of blood pressure, up to four readings of systolic and diastolic blood pressure were obtained from participants in the mobile examination centre. The average of the last two measurements of systolic or diastolic blood pressure for the participants for whom three or four measurements were taken, the last measurement for the participants for whom only two measurements were taken and the only measurement for the participants for whom one measurement was taken were used to establish the blood pressure status. According to the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure[28], participants who were on antihypertension medications or had systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg were defined as having hypertension.

Statistical analysis

From a total of 4773 adult participants, after excluding those who had missing values for any of the study variables, 3916 participants (1890 men and 2026 women) were included in our analyses. The prevalence of having moderate-to-severe depression (a PHQ-9 score ≥ 10) or having major or minor

depression was age standardised to the 2000 projected US population. The OR with 95 % CI were estimated by conducting logistic regression analyses to test the associations between quartiles of 25(OH)D and PTH and the presence of depression. A test for linear trends on the prevalence was conducted using orthogonal linear contrasts. A test for linear trends on the OR was conducted using the median values for the quartiles of 25(OH)D and PTH. SUDAAN (Software for the Statistical Analysis of Correlated Data, Release 9.0; Research Triangle Institute, Research Triangle Park, NC, USA) was used to account for the complex sampling design.

Results

Of all the participants, 239 had moderate-to-severe depression based on a PHQ-9 score ≥10, and 103 had major depression and 185 had minor depression based on the provisional diagnosis. The unadjusted and age-adjusted prevalence were 5·4 (95 % CI 4·3, 6·7) % and 5·3 (95 % CI 4·3, 6·5) %, respectively, for having moderate-to-severe depression, 2·4 (95 % CI 1·7, 3·3) % and 2·3 (95 % CI 1·7, 3·1) %, respectively, for having major depression, and 3·8 (95 % CI 3·1, 4·7) % and 3·8 (95 % CI 3·0, 4·6 %) % for having minor depression. Overall, the percentages of adults who reported having depression (for all three types of depression) differed significantly by socio-demographic variables, by the number of chronic conditions and by lifestyle factors including BMI, serum concentrations of cotinine and the level of physical activity except for any alcohol use (Table 1).

The mean concentrations of 25(OH)D were 19·6 and 17·8 ng/ml for participants with moderate-to-severe depression and major depression, respectively, which were significantly lower than those for participants without depression (22·0 ng/ml, $P<0·01$ for both comparisons); however, the

Table 1. Percentages of adults who reported having moderate-to-severe depression (defined as a Patient Health Questionnaire-9 score ≥10) or having major and minor depression (defined by provisional diagnosis) among participants with selected characteristics in the 2005–6 National Health and Nutrition Examination Survey

		By a PHQ-9 score ≥10			By provisional diagnosis				
		Moderate-to-severe depression			Major depression		Minor depression		
	n	%	SE	*P**	%	SE	%	SE	*P**
Total	3916	5·4	0·6		2·4	0·4	3·8	0·4	
Age (years)				<0·05					<0·01
20–< 40	1491	4·7	0·5		1·8	0·3	3·3	0·4	
40–< 60	1225	6·9	1·0		3·6	0·6	3·8	0·8	
≥ 60	1200	3·8	0·8		1·0	0·4	4·4	0·6	
Sex				<0·01					<0·01
Men	1890	4·3	0·4		1·8	0·4	3·1	0·4	
Women	2026	6·4	0·8		2·9	0·4	4·4	0·6	
Race				<0·05					0·08
Non-Hispanic white	2025	4·8	0·7		2·2	0·4	3·1	0·5	
Non-Hispanic black	840	8·5	1·4		4·0	1·0	6·7	1·2	
Other	1051	5·9	1·2		2·1	0·5	4·9	0·7	
Education				<0·01					<0·01
≤ High-school diploma	1966	7·4	0·7		3·4	0·5	5·7	0·6	
> High-school diploma	1950	3·9	0·5		1·6	0·4	2·4	0·4	
Marital status				<0·05					<0·05
Married/living together	2515	4·6	0·5		1·6	0·2	3·4	0·5	
Divorced/separated/widow	818	8·4	1·2		5·2	1·1	4·7	0·5	
Unmarried	583	5·2	1·0		2·1	0·5	4·4	0·9	
Number of chronic diseases				<0·01					<0·01
0	1839	3·4	0·6		1·3	0·4	2·6	0·3	
1	1037	5·5	0·7		2·6	0·6	2·9	0·4	
2	576	7·2	1·4		4·2	0·9	5·8	1·6	
≥ 3	464	11·8	1·7		3·9	0·9	8·8	1·7	
BMI (kg/m^2)				<0·05					<0·05
< 25·0	1173	5·1	1·0		2·2	0·6	3·6	0·4	
25·0– < 30·0	1359	3·9	0·8		1·7	0·4	2·8	0·5	
≥ 30·0	1383	7·1	0·7		3·2	0·5	4·9	0·8	
Physical activity				<0·01					<0·01
Yes (MET-h/d > 0)	3273	4·6	0·5		2·0	0·4	3·3	0·4	
No (MET-h/d = 0)	643	11·1	2·0		4·6	0·9	7·1	1·3	
Serum cotinine (ng/ml)†				<0·01					<0·01
> 0·07	1930	7·0	0·9		3·2	0·5	4·7	0·5	
≤ 0·07	1986	3·7	0·4		1·5	0·3	2·8	0·4	
Any alcohol use				0·53					0·60
Yes (daily drinks > 0)	2561	5·2	0·7		2·4	0·5	3·6	0·4	
No (daily drinks = 0)	1355	5·9	0·8		2·2	0·5	4·3	0·8	

MET, metabolic equivalent.
* χ^2 tests were used.
† The median value of serum cotinine (0·07 ng/ml) was used as a cut-off point.

British Journal of Nutrition

Table 2. Moderate-to-severe depression or having major and minor depression by quartiles of serum 25-hydroxyvitamin D (25(OH)D) among US adults in the 2005–6 National Health and Nutrition Examination Survey*
(Odds ratios and 95 % confidence intervals)

		Model 1		Model 2		Model 3	
Quartiles of serum 25(OH)D	*n*	OR	95 % CI	OR	95 % CI	OR	95 % CI
Moderate-to-severe depression (*n* 3916) (ng/ml)							
< 15	1217	1·00		1·00		1·00	
15–20	884	0·92	0·60, 1·41	1·15	0·67, 1·96	1·24	0·74, 2·10
20–26	933	0·61	0·35, 1·05	0·79	0·40, 1·58	0·92	0·45, 1·88
≥ 26	882	0·51	0·31, 0·85	0·73	0·36, 1·48	0·89	0·45, 1·79
P for trend		<0·01		0·26		0·62	
Major depression (*n* 3731) (ng/ml)							
< 15	1150	1·00		1·00		1·00	
15–20	837	0·87	0·43, 1·77	1·10	0·46, 2·62	1·23	0·51, 3·01
20–26	893	0·58	0·30, 1·10	0·71	0·32, 1·59	0·82	0·37, 1·86
≥ 26	851	0·23	0·06, 0·79	0·30	0·08, 1·22	0·37	0·09, 1·45
P for trend		<0·01		0·08		0·11	
Minor depression (*n* 3813) (ng/ml)							
< 15	1,174	1·00		1·00		1·00	
15–20	856	0·93	0·54, 1·58	1·29	0·74, 2·23	1·34	0·79, 2·28
20–26	908	0·69	0·35, 1·36	1·06	0·56, 2·02	1·17	0·60, 2·27
≥ 26	875	0·63	0·37, 1·06	1·13	0·66, 1·93	1·25	0·72, 2·16
P for trend		0·06		0·77		0·47	

* Model 1: unadjusted; model 2: adjusted for age, sex, race, education and marital status; and model 3: further adjusted for BMI, serum cotinine concentrations, physical activity, alcohol use and number of chronic diseases (i.e. hypertension, diabetes, CHD, stroke, arthritis, asthma, chronic bronchitis and cancer).

mean 25(OH)D level did not differ significantly between adults with minor depression and those without depression (21·0 *v.* 22·0 ng/ml, $P>0·05$). The mean concentrations of PTH did not differ significantly among adults with depression (44·0 pg/ml for adults with moderate-to-severe depression, 44·8 pg/ml for those with major depression and 43·0 pg/ml for those with minor depression *v.* 43·0 pg/ml for those without depression).

The age-adjusted prevalence of having moderate-to-severe depression or having major depression decreased linearly across quartiles of serum 25(OH)D ($P<0·01$ for linear trends, Fig. 1(a)); the trends for the prevalence of having minor depression were only marginally significant ($P=0·06$). Although the unadjusted OR for having moderate-to-severe depression (0·51, 95 % CI 0·31, 0·85) or for having major depression (0·23, 95 % CI 0·06, 0·79) were significantly lower in the highest quartile than in the lowest quartile of serum 25(OH)D, the relationships were no longer significant after adjusting for demographics and further adjusting for lifestyle factors (including BMI, serum cotinine, alcohol use and physical activity) and the number of chronic conditions (Table 2). Inclusion of GFR and serum PTH into the models did not affect the results (data not shown). No significant effect modifications were observed based on sex and race for all outcome measures.

Serum concentrations of PTH were non-significantly associated with depression (for all three types of depression) in the study population (Fig. 1(b) and Table 3).

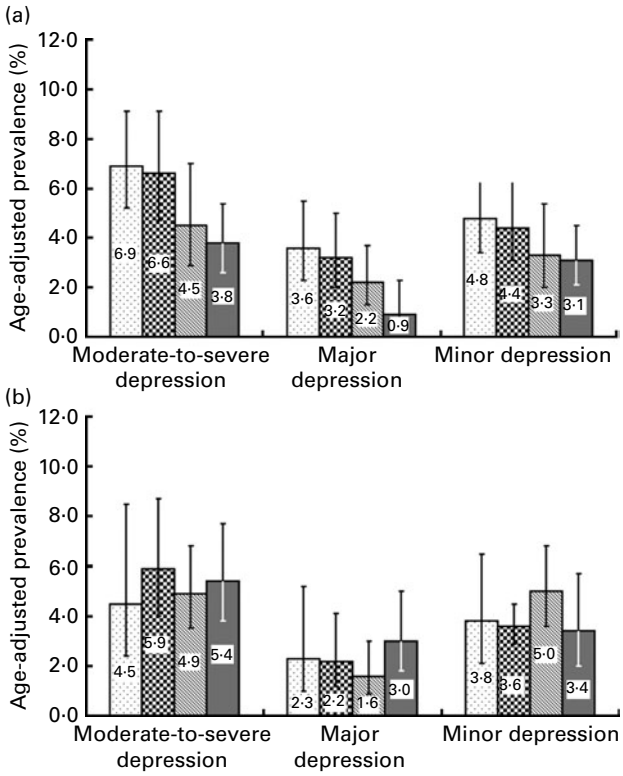

Fig. 1. Age-adjusted prevalence with 95 % CI of having moderate-to-severe depression or having major and minor depression (a) by quartiles of 25-hydroxyvitamin D (25(OH)D) and (b) by quartiles of parathyroid hormone (PTH) among US adults in the 2005–6 National Health and Nutrition Examination Survey, *n* 3916. The quartiles of 25(OH)D are □, <15 ng/ml; ▩, 15– < 20 ng/ml; ▧, 20– < 26 ng/ml; ■, ≥26 ng/ml. The quartiles of PTH are ▩, <29 pg/ml; ■, 29– < 38 pg/ml; ▧, 38– < 50 pg/ml; ■, ≥50 pg/ml.

Discussion

Using a large, population-based sample from the NHANES, we found that neither serum vitamin D nor PTH levels were associated with depression among US adults after taking the potential confounders into consideration. The inverse associations of vitamin D with moderate-to-severe depression

British Journal of Nutrition

Table 3. Moderate-to-severe depression or having major or minor depression by quartiles of serum parathyroid hormone (PTH) among US adults in the 2005–6 National Health and Nutrition Examination Survey*
(Odds ratios and 95 % confidence intervals)

		Model 1		Model 2		Model 3	
Quartiles of serum PTH	*n*	OR	95 % CI	OR	95 % CI	OR	95 % CI
Moderate-to-severe depression (*n* 3916) (pg/ml)							
< 29	955	1·00		1·00		1·00	
29–38	882	1·37	0·61, 3·08	1·40	0·63, 3·09	1·46	0·66, 3·23
38–50	969	1·09	0·54, 2·23	1·02	0·51, 2·07	1·14	0·58, 2·25
≥ 50	1110	1·24	0·68, 2·25	1·05	0·59, 1·88	1·14	0·64, 2·05
P for trend		0·61		0·75		0·96	
Major depression (*n* 3731) (pg/ml)							
<29	913	1·00		1·00		1·00	
29–38	842	0·99	0·28, 3·51	1·06	0·31, 3·63	1·08	0·33, 3·57
38–50	910	0·69	0·24, 1·96	0·66	0·25, 1·72	0·74	0·30, 1·82
≥ 50	1066	1·37	0·59, 3·18	1·21	0·54, 2·71	1·33	0·59, 2·99
P for trend		0·37		0·66		0·48	
Minor depression (*n* 3813) (pg/ml)							
<29	929	1·00		1·00		1·00	
29–38	862	1·08	0·66, 1·76	0·99	0·57, 1·72	1·05	0·59, 1·84
38–50	948	1·55	0·88, 2·73	1·32	0·70, 2·51	1·46	0·76, 2·78
≥ 50	1074	0·93	0·42, 2·03	0·67	0·27, 1·66	0·70	0·27, 1·80
P for trend		0·91		0·30		0·36	

*Model 1: unadjusted; model 2: adjusted for age, sex, race, education and marital status; and model 3: further adjusted for BMI, serum cotinine concentrations, physical activity, alcohol use and number of chronic diseases (i.e. hypertension, diabetes, CHD, stroke, arthritis, asthma, chronic bronchitis and cancer).

or with major depression observed in the unadjusted model were attenuated slightly, and remained statistically significant after adjusting for age and sex. However, the associations were attenuated to null after further adjusting for other potential confounders. Coexistence of chronic diseases appeared to be a major confounder in the present study.

Several previous studies have reported an association between vitamin D deficiency and the presence of mood disorder[15,29] or a high depression score (Beck Depression Inventory Score on items 1–13)[13], and that hypovitaminosis D occurred more frequently in patients with anxiety and depression[30,31]. These studies were conducted in adults with special conditions such as mild Alzheimer's disease[15], secondary hyperparathyroidism[13], schizophrenia, alcohol addiction or major depression[31] or fibromyalgia[30]. In addition, the sample size of these previous studies was very small (ranged from 75 to120 participants). Recently, two relatively large, population-based studies yielded different results. Hoogendijk *et al.*[12] reported that decreased vitamin D levels and increased PTH levels were significantly associated with a high depression score in 1282 older Amsterdam people (aged 65–95 years). However, Pan *et al.*[14] reported no associations between vitamin D levels and depressive symptoms in 3262 Chinese adults aged 50–70 years. Our findings obtained from a large sample (*n* 3916) that vitamin D was not associated with depression among US adults aged 20 years or older are consistent with the findings of Pan *et al.*[14]. Moreover, we conducted subanalyses on data obtained from 885 participants aged 65 years or older or from those who were non-Hispanic white (*n* 598). We could not detect significant associations between vitamin D and depression (by PHQ-9 score of ≥ 10) among these groups even though we had included a set of covariables in our analyses that were almost the same as those used in the study conducted by Hoogendijk *et al.*[12]. Thus, the present results are in conflict with the findings of Hoogendijk *et al.*[12].

In human body, about 50–90 % of vitamin D comes from the production of vitamin D_3 (cholecalciferol) in the skin from 7-dehydrocholesterol through a process that requires sunlight (UV radiation), and the remainder is obtained directly from the diet including dietary supplemental sources. The biosynthesis of vitamin D_3 in the skin depends on sunshine exposure, latitude, skin-covering clothes, skin pigmentation and the use of sun block. The dietary sources of vitamin D include cholecalciferol (animal origin – mainly in fish liver oils) and ergocalciferol (vitamin D_2, plant origin). However, in the present study, neither the data on sun exposure (such as seasonality or residential geographic regions of study participants) nor the data on dietary intake of vitamin D were available; therefore, we were unable to evaluate the possible confounding effects of these factors on the outcome measures. Nevertheless, we have conducted an additional analysis by including data on the use of any dietary supplements (in the preceding month). The results showed that although the mean concentrations of 25(OH)D were significantly higher in the participants who reported taking any dietary supplements than in those who did not (23·4 *v.* 19·9 ng/ml, $P<0·01$), the prevalence of depression (all three types of depression) did not differ significantly in these two groups (data not shown). In addition, in our fully adjusted models, further adjustment for the use of any dietary supplements did not affect the results of the present study. These results are generally in agreement with the findings of some previous studies that vitamin D supplementation did not show any improvement in depressed mood or seasonal affective disorder[29,32], although a randomised double-blind trial (*n* 441) conducted by Jorde *et al.*[33] reported that in overweight and obese adults, high-dose vitamin D supplementation (0·5–1 mg; 20 000–40 000 IU) reduced serum PTH levels and improved the Beck Depression Inventory scores after 1 year. Obviously, the controversial results of the clinical trials done on vitamin D supplementations deserve further

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investigation. Taken together, although vitamin D elicits benefits for general health including bone health and reduction in metabolic syndrome and diabetes, CVD and mortality[1–8], the real functional role of vitamin D in promoting mental health remains to be investigated further before any suggestions/recommendations are made for increasing vitamin D to improve the mental health.

The present results further demonstrated that serum PTH was not associated with depression either in unadjusted or in multivariate-adjusted analyses. The subanalyses on data obtained from 885 participants aged 65 years or older or from those who were non-Hispanic white (*n* 598) yielded similar results. This finding is in conflict with those of several other studies[12,13,20]. At present, we are unable to provide reasonable explanations for the conflicting results. Apparently, the three population-based studies including the present study have used different measures for depression (The Center for Epidemiologic Studies-Depression scale was used in the studies conducted by Hoogendijk *et al.*[12] and Pan *et al.*[14], and the PHQ-9 diagnostic algorithm was used in the present study.), and were conducted in different populations. The measures of depression obtained using both the The Center for Epidemiologic Studies-Depression and the PHQ-9 have been validated and used widely in the general population; therefore, the bias resulting from these measures should not contribute much to the differences in the findings of these studies. In addition, although no significant interactions between serum levels of vitamin D and PTH and race/ethnicity were observed in the present study, whether or not racial/ethnic and other cultural differences contributed to the different results of these studies need to be investigated further.

The present study is subject to at least two limitations. First, depressive symptoms were evaluated based on self-reports (not clinically diagnosed depression), and thus were subject to recall bias. Secondly, as noted herein, we were unable to adjust for dietary intake of vitamin D as well as seasonality or residential geographic regions because the data were not available in the present study. However, this may not have affected the present results because they are explanatory factors that should drive the associations further towards null if included.

In summary, the present study results obtained from a large population-based survey sample did not show significant associations between serum concentrations of vitamin D and PTH and depression among US adults, which is in contrast to some of the previous findings. More evidence from future prospective studies or randomised clinical trials may be needed to disentangle the conflicting results on the relationship of vitamin D and PTH with depression and other mental disorders.

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