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Original article

Vitamin and mineral supplements: Are they associated with fatigue?

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SUMMARY

Background and aims: Vitamin/mineral supplements (VMS) and vitamin/mineral and/or dietary supplements (VMDS) are commonly consumed, based on the belief of their invigorating properties. Still, the association of VMS/VMDS with fatigue in the general population remains sparse and conclusions are mixed. This study aimed to understand the association between VMS/VMDS and fatigue.

Methods: Two cross-sectional studies (2014–2017 and 2018–2021) conducted on a population-based cohort. Participants were divided into VMS/VMDS users and non-users. Fatigue levels were assessed using the Fatigue Severity Scale (FSS) and the 14-item version of the Chalder Fatigue Scale (CFS).

Results: Overall, 2084 (50.8 % female, 61.7 ± 9.8 years) and 1728 (51.0 % female, 64.1 ± 9.3 years) were included in the first and second surveys, respectively. In the first survey, after multivariable analysis, no association was found between VMS use and FSS: adjusted mean ± sem 3.04 ± 0.13 vs. 2.82 ± 0.03 for users and non-users, respectively, $p = 0.083$, while users scored higher in the CFS: 6.17 ± 0.22 vs. 5.72 ± 0.06 for users and non-users, respectively, $p = 0.048$. In the second survey, no association was found between VMS use and FSS (2.83 ± 0.19 vs. 2.84 ± 0.03, $p = 0.952$) and CFS (5.38 ± 0.33 vs. 5.61 ± 0.06, $p = 0.504$). In the first survey, VMDS users scored higher in both FSS (3.03 ± 0.06 vs. 2.76 ± 0.04, $p < 0.001$) and CFS (6.19 ± 0.11 vs. 5.58 ± 0.06, $p < 0.001$) while no differences were found in the second survey in both FSS (2.93 ± 0.07 vs. 2.81 ± 0.04, $p = 0.161$) and CFS (5.78 ± 0.12 vs. 5.54 ± 0.07, $p = 0.088$).

Conclusion: In this population-based cross-sectional study, the authors found no consistent association between VMS consumption and fatigue. Participants taking VMDS tended to present with higher fatigue scores.

1. Introduction

Fatigue is a common symptom in primary care, usually characterized by low energy, mental exhaustion, and poor muscle endurance. It can have a negative impact on work, family, and society [1]. In healthy people, fatigue is a physiological response to prolonged strenuous physical or mental exertion. It is short-lived and predictable, decreases with rest, and usually does not interfere with daily activities [2]. However, fatigue in sick people has different characteristics and is described as an overwhelming tiredness, lack of energy, and feeling of exhaustion that cannot be compared with physiological fatigue after physical or mental exertion and cannot be recovered by sleep [3]. For ill people to improve fatigue symptoms, the underlying disease should be treated actively. However, in healthy individuals, the underlying reason for symptoms is often unknown, and treatment options are scarce; thus, nutritional supplements have become a common response, despite lack of scientific evidence [4].

Vitamin/mineral supplements (VMS) are common nutritional supplements that provide essential elements for humans. According to the 2011–2014 National Health and Nutrition Examination Survey, half (52 %) of U.S. adults reported using at least one dietary supplement, and nearly one-third (31 %) reported using a VMS [5]. On the one hand, vitamins and minerals are involved in important physiological functions such as energy-producing metabolism, DNA synthesis, oxygen transport, and neuronal function. Their

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deficiency can directly cause diseases in the body, leading to fatigue symptoms. On the other hand, vitamin and mineral deficiencies can cause mental fatigue by translating into effects on cognitive and mental processes [6].

Therefore, fatigue symptoms caused by insufficient vitamins and minerals can usually be treated through active supplementation. However, research on the potential association of VMS with fatigue in the general population remains sparse and conclusions are mixed. Hence, given the lack of scientific evidence, this study focused on the association between VMS and/or dietary (VMDS) supplements and fatigue in the general population.

2. Participants and methods

2.1. Population and study design

This study used data from CoLaus|PsyCoLaus (www.colauspsycolaus.ch). CoLaus|PsyCoLaus study is a population-based study initiated in 2003 with 6733 middle-aged participants from Lausanne, Switzerland, to investigate the epidemiology and genetic determinants of cardiovascular risk factors [7]. Recruitment began in 2003 and ended in 2006. The first follow-up was performed between 2009 and 2012, the second between 2014 and 2017 and the third between 2018 and 2021. In this study, the authors used the 2nd and 3rd follow-up data for cross-sectional analysis, as they contained the necessary variables.

2.2. Vitamin/mineral/dietary supplements consumption

Participants were asked to report all prescribed and over-the-counter medications and supplements taken regularly over the last six months. Vitamin and mineral supplements were defined according to the Swiss compendium (compendium.ch/home/fr, assessed June 2017). When the supplements were not listed in the Swiss compendium, further searches were conducted on the internet. Due to wide differences in the composition of Swiss VMS [8] and to inaccurate reporting (i.e., reporting “multivitamins from producer X″ that manufactures six different types of multivitamins), it was not possible to assess the amounts of vitamins and minerals consumed by participants. Dietary supplements were defined as any other supplement that could not be considered as a VMS, such as plant extracts not considered as phytotherapy by the Swiss compendium, cod liver oil, shark cartilage or amino acids.

2.3. Assessment of fatigue

Fatigue levels were assessed using the Fatigue Severity Scale (FSS) and the 14-item version of the Chalder Fatigue Scale (CFS), which were filled by the participants.

Fatigue over the previous week was assessed by the 9 items FSS [9]. This questionnaire has been validated for a general healthy population in the Swiss setting [10] and has a high test-retest reliability [11]. The questionnaire is composed of nine questions; responses are graded using a Likert scale from 1 to 7, where 1 indicates strong disagreement and 7 strong agreement. The final score is the mean value of the 9 responses, and a score $\geq$4 is considered as severe fatigue. Fatigue was also assessed using the 14-item CFS [12]. In this study, a binary coding (presence/absence) to the items was applied, as it has been shown that near-maximal scoring of the 14 items constituting the Chalder fatigue scale supports the validity of a two-point scoring rather than the four-point Likert scoring [13].

Cronbach α coefficient was used to evaluate internal consistency and reliability, and the results indicated that the internal reliability of both FSS and CFS was very good (Cronbach's alpha were 0.918 and 0.866 respectively). While the CFS has good internal consistency [14,15] and convergent validity [16], it also presents ceiling effects [17], as most fatigued patients score the highest value.

2.4. Relevant covariates

This study selected potential confounding factors based on the literature on the relationship between VMS and Fatigue. Authors selected age (years), sex (male/female), education, marital status, weekly alcohol consumption (units), smoking, hypertension (yes/no), diabetes (yes/no), body mass index (BMI) categories, total energy intake (kcal/day), and Alternate Healthy Eating Index (AHEI).

Education was categorized into high (university), middle (high school) and low (apprenticeship + mandatory). Marital status was defined as living alone (single, divorced, widowed) or living with a partner. Usual alcohol consumption during the week was self-reported as number of units (glasses of wine, bottles or cans of beer, and shots of spirits) per week. Smoking was self-reported and categorized as never, former (irrespective of the time since quitting smoking) and current.

Body weight and height were measured with participants barefoot and in light indoor clothes. Body weight was measured in kilograms to the nearest 100 g using a Seca® scale (Hamburg, Germany). Height was measured to the nearest 5 mm using a Seca® (Hamburg, Germany) height gauge. BMI was calculated and categorized as normal (<25 kg/m^2), overweight $\geq$25 and <30 kg/m^2) and obese $\geq$30 kg/m^2).

Blood pressure (BP) was measured using an Omron® HEM-907 automated oscillometric sphygmomanometer after at least a 10-min rest in a seated position, and the average of the last two measurements was used. Hypertension was defined by a SBP $\geq$140 mm Hg or a DBP $\geq$90 mm Hg or presence of antihypertensive drug treatment.

Glucose was assessed by glucose dehydrogenase. Diabetes mellitus (DM) was defined as fasting plasma glucose $\geq$7.0 mmol/L and/or presence of oral hypoglycaemic or insulin treatment.

The AHEI was adapted from McCullough et al. [18]. In our study, the amount of trans fat could not be assessed, and in a first analysis, the authors considered all participants taking multivitamins as taking them for a duration $\geq$5 years. Thus, the modified AHEI score ranged between 2.5 and 77.5 instead of 2.5 and 87.5 for the original AHEI score. As it was not possible to assess whether participants were taking multivitamins for the last 5 years, a second AHEI was computed after removing the multivitamin component. This vitamin-free AHEI ranged between 2.5 and 70.0. The Spearman correlation between the vitamin-free and the modified AHEI was 0.984. For both AHEIs, higher values represented a healthier diet.

2.5. Exclusion criteria

This study excluded participants with missing data for 1) fatigue; 2) covariates.

2.6. Ethical statement

The institutional Ethics Committee of the University of Lausanne, which afterwards became the Ethics Commission of Canton Vaud (www.cer-vd.ch) approved the CoLaus-PsyCoLaus study (project number PB_2018–00038, reference 239/09). All participants gave their signed informed consent before entering the study.

2.7. Statistical analysis

Statistical analyses were conducted using Stata v.18 (Stata Corp, College Station, TX, USA). Descriptive results were expressed as

number of participants (percentage) for categorical variables and as average ± standard deviation for continuous variables. Between-group comparisons were conducted using chi-square for categorical variables and student's t-test for continuous variables. Multivariable analyses were conducted using logistic regression for categorical variables, and results were expressed as odds ratio and (95 % confidence interval). Multivariable analyses were conducted using analysis of variance (ANOVA) for quantitative variables and results were expressed as adjusted mean ± standard error. Multivariable analyses were adjusted for the covariates defined previously. Statistical significance was considered for a two-sided test with $p < 0.05$.

3. Results

3.1. Selection of participants

Of the initial 4881 participants in the 2nd follow-up, 2084 (42.7 %) were included in the analyses. Of the initial 3482 in the 3rd follow-up, 1728 (49.6 %) were included in the analyses. The reasons for exclusion are indicated in Figure 1 and the comparison between included and excluded participants is provided in Supplementary Table 1. In both follow-ups, excluded participants were older, more frequently female, with lower education level, living alone, abstainers from alcohol, hypertensive or diabetic, and had lower total energy intake. Excluded participants scored higher than included participants regarding FSS and CFS at the 2nd follow-up, but there was no difference upon 3rd follow-up.

3.2. Association between VMS and VMDS consumption and fatigue

Among participants enrolled in the study at the 2nd follow-up, 129 (6.2 %) consumed VMS and 563 (27.0 %) consumed VMDS. The corresponding numbers for the 3rd follow-up were 55 (3.2 %) and 262 (23.4 %). Tables 1 and 2 summarize the characteristics of participants according to VMS and VMDS consumption in the 2nd and 3rd follow-ups, respectively. In the 2nd follow-up, compared with participants who did not consume VMS, participants who consumed VMS were more frequently female, lived alone, and had a higher AHEI (Table 1). Compared with participants who did not consume VMDS, participants who consumed VMDS were older, more frequently female, highly educated, non-obese, lived alone and had a higher AHEI (Table 1). In the 3rd follow-up, compared with participants who did not consume VMS, participants who consumed VMS presented less frequently with hypertension, and had a higher AHEI (Table 2). Compared with participants who did not consume VMDS, participants who consumed VMDS were older, more frequently female, non-obese, less often current smokers, lived alone, and had a higher AHEI (Table 2).

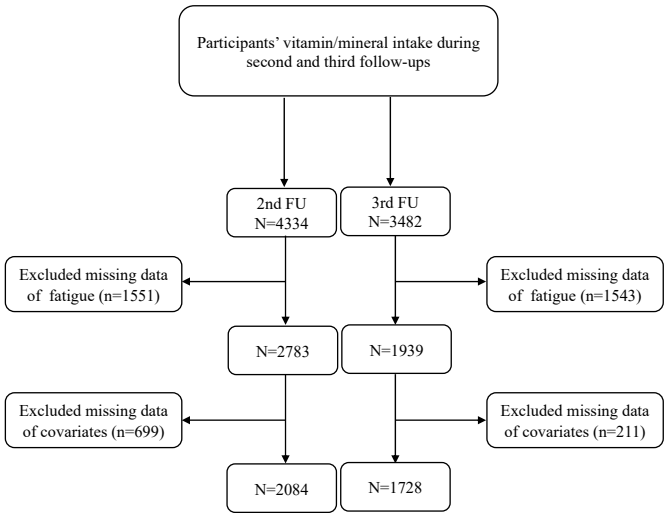

Fig. 1. Selection of participants from the second and third follow-ups. CoLaus study, Lausanne, Switzerland.

For the 2nd follow-up, a summary of the association between VMS consumption and fatigue is shown in Table 3. In bivariate and multivariable analyses, there was no association between VMS consumption and FSS and prevalence of clinical fatigue. However, participants consuming VMS had higher scores for CFS (Table 3). A summary of the association between VMDS consumption and fatigue is shown in Table 4. In bivariate and multivariable analyses, participants consuming VMDS at second follow-up had higher scores for FSS and CFS, and more frequently had clinical fatigue (Table 4). To examine the robustness of the results, when the authors adjusted the multivariable analysis using the vitamin-free AHEI, the results were completely consistent for VMDS, whereas for VMS, the association between VMS consumption and higher CFS scores disappeared (Supplementary Table 2 and Supplementary Table 3).

For the 3rd follow-up, a summary of the association between VMS consumption and fatigue is shown in Table 3. In bivariate and multivariable analyses, there was no association between VMS consumption upon 3rd follow-up and FSS, CFS or prevalence of clinical fatigue (Table 4). A summary of the association between VMDS consumption upon 3rd follow-up and fatigue is shown in Table 4. In bivariate and multivariable analyses, there was no association between VMDS consumption and FSS. In bivariate analyses, participants consuming VMDS had higher scores for CFS, but the association was not significant in multivariable analysis. However, in bivariate and multivariable analyses, participants consuming VMDS more frequently had clinical fatigue (Table 4). To examine the robustness of the results, when the authors adjusted the multivariable analysis using the vitamin-free AHEI, the results were completely consistent (Supplementary Tables 2 and 3).

4. Discussion

In this study, the authors found no consistent association between VMS consumption and fatigue after adjusting for potential confounders. However, participants taking VMDS tended to present with higher fatigue scores.

4.1. Association between VMS consumption and fatigue

Research on the potential association between VMS, dietary supplements, and fatigue in the general population remains sparse and conclusions are mixed. A study conducted by Suzuki et al. showed that supplementing 16 young athletes with high-dose thiamine (vitamin B_1) for 3 days after cycling exercise increased blood thiamine levels and reduced the number of fatigue complaints [19]. A double-blind randomized controlled trial showed that intravenous vitamin C reduced fatigue within 2 h and the effects lasted for a day [20]. In another study that included 290 women, 1g intravenous iron reduced fatigue in 65.3 % of the intervention group, compared to 52.7 % in the placebo group, a significant difference [21]. Among healthy elderly people with low physical activity levels, vitamin D and calcium might prevent muscle fatigue by regulation of the biosynthesis of creatine kinase, lactic acid dehydrogenase, and troponin I [22]. In addition, vitamin D treatment significantly improved fatigue in healthy people deficient in vitamin D [23,24]. Finally, vitamin E supplementation also

Table 1
Characteristics of the participants, according to VMS and VMDS consumption, second follow-up of the CoLaus|PsyColaus study, Lausanne, Switzerland.

	VMS Non-users	VMS Users	*P*-value	VMDS Non-users	VMDS Users	*P*-value
Sample size (%)	1955 (93.8)	129 (6.2)		1521 (73.0)	563 (27.0)	
Age (years)	61.6 ± 9.8	62.8 ± 9.7	0.197	61.2 ± 9.6	63.1 ± 10	**<0.001**
Women (%)	974 (49.8)	84 (65.1)	**0.001**	689 (45.3)	369 (65.5)	**<0.001**
Educational level (%)			0.180			**0.009**
Low	905 (46.3)	52 (40.3)		728 (47.9)	229 (40.7)	
Middle	581 (29.7)	37 (28.7)		442 (29.1)	176 (31.3)	
High	469 (24.0)	40 (31.0)		351 (23.1)	158 (28.1)	
Marital status, %			**<0.001**			**<0.001**
Living alone	615 (31.5)	65 (50.4)		449 (29.5)	231 (41.0)	
Living in couple	1340 (68.5)	64 (49.6)		1072 (70.5)	332 (59.0)	
Alcohol consumption, %			0.791			**0.023**
None	407 (20.8)	31 (24)		297 (19.5)	141 (25.1)	
1–13/week	1255 (64.2)	79 (61.2)		990 (65.1)	344 (61.1)	
14–27/week	245 (12.5)	15 (11.6)		199 (13.1)	61 (10.8)	
28+/week	48 (2.5)	4 (3.1)		35 (2.3)	17 (3.0)	
Smoking categories (%)			0.827			0.105
Never	795 (40.7)	53 (41.1)		636 (41.8)	212 (37.6)	
Former	802 (41)	50 (38.8)		601 (39.5)	251 (44.6)	
Current	358 (18.3)	26 (20.2)		284 (18.7)	100 (17.8)	
BMI categories (%)			0.326			**0.002**
Normal	840 (43)	54 (41.9)		620 (40.8)	274 (48.7)	
Overweight	789 (40.4)	59 (45.7)		632 (41.5)	216 (38.3)	
Obese	326 (16.7)	16 (12.4)		269 (17.7)	73 (13.0)	
Hypertension (%)	862 (44.1)	51 (39.5)	0.312	673 (44.3)	240 (42.6)	0.508
Diabetes (%)	166 (8.5)	7 (5.4)	0.222	128 (8.4)	45 (8.0)	0.756
Total energy intake (kcal/d)	1735 ± 631	1688 ± 570	0.412	1733 ± 637	1729.7 ± 601.6	0.915
AHEI	32 ± 10	35.8 ± 10.3	**<0.001**	31.3 ± 9.8	34.7 ± 10.3	**<0.001**

Results are expressed as number of participants (column percentage) for categorical variables and as average ± standard deviation for continuous variables. Between-group comparisons performed using chi-square for categorical variables and student's t-test for continuous variables. Abbreviations: VMS: Vitamin/mineral supplements; VMDS: Vitamin/mineral and/or dietary supplements; AHEI: Alternate Healthy Eating Index.

Table 2
Characteristics of the participants, according to VMS and VMDS consumption, third follow-up of the CoLaus|PsyColaus study, Lausanne, Switzerland.

	VMS Non-users	VMS Users	*P*-value	VMDS Non-users	VMDS Users	*P*-value
Sample size (%)	1673 (96.8)	55 (3.2)		858 (76.6)	262 (23.4)	
Age (years)	64.0 ± 9.3	64.9 ± 9.0	0.486	63.6 ± 9.2	65.6 ± 9.5	**<0.001**
Women (%)	849 (50.8)	33 (60.0)	0.177	613 (46.3)	269 (66.6)	**<0.001**
Educational level (%)			0.195			0.236
Low	766 (45.8)	20 (36.4)		617 (46.6)	169 (41.8)	
Middle	498 (29.8)	16 (29.1)		386 (29.2)	128 (31.7)	
High	408 (24.4)	19 (34.6)		320 (24.2)	107 (26.5)	
Marital status, %			0.520			**0.001**
Living alone	748 (44.7)	27 (49.1)		564 (42.6)	211 (52.2)	
Living in couple	925 (55.3)	28 (50.9)		760 (57.4)	193 (47.8)	
Alcohol consumption, %			0.053			0.133
None	416 (24.9)	7 (12.7)		323 (24.4)	100 (24.8)	
1–13/week	998 (59.6)	43 (78.2)		784 (59.2)	257 (63.6)	
14–27/week	209 (12.5)	4 (7.3)		175 (13.2)	38 (9.4)	
28+/week	50 (3.0)	1 (1.8)		42 (3.2)	9 (2.2)	
Smoking categories (%)			0.191			**0.015**
Never	723 (43.2)	20 (36.4)		581 (43.9)	162 (40.1)	
Former	682 (40.8)	29 (52.7)		521 (39.3)	190 (47.0)	
Current	268 (16.0)	6 (10.9)		222 (16.8)	52 (12.9)	
BMI categories (%)			0.074			**0.012**
Normal	717 (42.8)	22 (40.0)		544 (41.1)	195 (48.3)	
Overweight	637 (38.1)	28 (50.9)		515 (38.9)	150 (37.1)	
Obese	319 (19.1)	5 (9.1)		265 (20.0)	59 (14.6)	
Hypertension (%)	826 (49.4)	17 (30.9)	**0.007**	663 (50.1)	180 (44.6)	**0.052**
Diabetes (%)	144 (8.6)	4 (7.3)	0.728	115 (8.7)	33 (8.2)	0.745
Total energy intake (kcal/d)	1634 ± 656	1717 ± 5545	0.358	1641 ± 672.6	1623.3 ± 586	0.633
AHEI	31.3 ± 9.9	38.7 ± 8.8	**<0.001**	31 ± 9.9	33.4 ± 10	**<0.001**

Results are expressed as number of participants (column percentage) for categorical variables and as average ± standard deviation for continuous variables. Between-group comparisons were performed using chi-square for categorical variables and student's t-test for continuous variables. Abbreviations: VMS: Vitamin/mineral supplements; VMDS: Vitamin/mineral and/or dietary supplements; AHEI: Alternate Healthy Eating Index.

improved subjective status and antioxidant capacity in healthy people with daily fatigue [25].

Regarding multivitamins or minerals, research by Lee et al. found that supplementing vitamin B complex for 28 consecutive days improved the exercise endurance performance of non-athletes and reduced fatigue-related biochemical metabolites [26]. A placebo-controlled, double-blind, randomized, parallel-group trial by Haskell et al. showed that participants in the vitamin/mineral group exhibited an attenuation of the negative effects of extended task completion on mood/fatigue [27]. A prospective study by

Table 3
Bivariate and multivariable association VMS consumption and fatigue, CoLaus|PsyColaus study, Lausanne, Switzerland.

	Bivariate			Multivariable		
	VMS Non-users	VMS Users	*P*-value	VMS Non-users	VMS Users	*P*-value
2nd **FU**						
Fatigue score	2.82 ± 0.03	3.06 ± 0.13	0.064	2.82 ± 0.03	3.04 ± 0.13	0.083
Chalder score	5.70 ± 0.06	6.33 ± 0.23	**0.008**	5.72 ± 0.06	6.17 ± 0.22	**0.048**
Clinical fatigue (%)	402 (20.6)	32 (24.8)	0.250	1 (ref.)	1.33 (0.87–2.05)	0.191
3rd **FU**						
Fatigue score	2.84 ± 0.03	2.83 ± 0.19	0.948	2.84 ± 0.03	2.83 ± 0.19	0.952
Chalder score	5.61 ± 0.06	5.49 ± 0.33	0.732	5.61 ± 0.06	5.38 ± 0.33	0.504
Clinical fatigue (%)	335 (20.0)	12 (21.8)	0.744	1 (ref.)	1.30 (0.67–2.55)	0.440

Results are expressed as average ± standard deviation or number of participants (column percentage) for bivariate analysis and as multivariable-adjusted average ± standard error or odds ratio and 95 % confidence interval. Between group comparison using ANOVA or t-test for bivariate analyses and ANOVA or logistic regression for multivariable analyses, adjusting for age, sex, BMI categories (normal, overweight, obese), education (low/medium/high), marital status (alone, in couple), smoking (never, former, current), alcohol consumption (none, 1–13, 14–27 and 28+ per week), hypertension (yes, no), diabetes (yes, no), total energy intake (continuous), Alternate Healthy Eating Index (continuous). Abbreviations: VMS: Vitamin/mineral supplements; 2nd FU: second follow-up; 3rd FU: third follow-up.

Table 4
Bivariate and multivariable association between VMDS consumption and fatigue, CoLaus|PsyColaus study, Lausanne, Switzerland.

	Bivariate			Multivariable		
	VMDS Non-users	VMDS Users	*P*-value	VMDS Non-users	VMDS Users	*P*-value
2nd **FU**						
Fatigue_score	2.76 ± 0.04	3.03 ± 0.06	**<0.001**	2.76 ± 0.04	3.03 ± 0.06	**<0.001**
Chalder_score	5.53 ± 0.07	6.31 ± 0.11	**<0.001**	5.58 ± 0.06	6.19 ± 0.11	**<0.001**
Clinical fatigue (%)	293 (19.3)	141 (25.0)	**0.004**	1 (ref.)	1.44 (1.13–1.85)	**0.004**
3rd **FU**						
Fatigue_score	2.81 ± 0.04	2.95 ± 0.07	0.083	2.81 ± 0.04	2.93 ± 0.07	0.161
Chalder_score	5.51 ± 0.07	5.93 ± 0.12	**0.003**	5.54 ± 0.07	5.78 ± 0.12	0.088
Clinical fatigue (%)	249 (18.8)	98 (24.3)	**0.017**	1 (ref.)	1.40 (1.06–1.86)	**0.019**

Results are expressed as average ± standard deviation or number of participants (column percentage) for bivariate analysis and as multivariable-adjusted average ± standard error or odds ratio and 95 % confidence interval. Between group comparison using ANOVA or t-test for bivariate analyses and ANOVA or logistic regression for multivariable analyses, adjusting for age, sex, BMI categories (normal, overweight, obese), education(low/medium/high), marital status (alone, in couple), smoking (never, former, current), alcohol consumption (none, 1–13, 14–27 and 28+ per week), hypertension (yes, no), diabetes (yes, no), total energy intake (continuous), Alternate Healthy Eating Index (continuous). Abbreviations: VMDS: Vitamin/mineral and/or dietary supplements; 2nd FU: second follow-up; 3rd FU: third follow-up.

Maric et al. showed that multivitamin and mineral supplementation decreased fatigue in patients with chronic fatigue syndrome [28].

However, unlike the above positive results, a randomized controlled trial showed that oral vitamin D3 did not improve markers of vascular health or fatigue in patients with chronic fatigue syndrome [29]. Data from Brouwers et al. showed no statistically significant relationship between symptoms of chronic fatigue syndrome and multivitamins and mineral supplementation[30]. Also, a meta-analysis showed that vitamin and mineral status did not lead to clinical improvement in chronic fatigue syndrome [31]. Hence, our results confirm the negative findings of the previous studies [29–31], suggesting that VMS is not associated with a lower fatigue level.

4.2. Association between VMDS consumption and fatigue

In addition to the vitamin and mineral supplements mentioned above, some dietary supplements such as dietary polysaccharides, coenzyme Q_{10}, octacosanol, and omega-3 poly-unsaturated fatty acids have also been suggested to reduce the burden of fatigue [32–35]. However, a systematic review found limited evidence that dietary supplements can help relieve symptoms of chronic fatigue syndrome, findings being inconsistent across studies [36]. Another study showed no significant association between dietary supplement intake and fatigue severity or functional impairment [37].

In our study, participants taking VMDS tended to present with higher fatigue scores. Our results thus partially confirm the lack of beneficial effect of VMDS on fatigue as suggested previously [36,37]. Still, a reverse causation bias cannot be excluded, participants with higher fatigue score consuming more VMDS in the hope of decreasing fatigue levels.

4.3. Strengths and limitations

This study has several strengths. First, the authors studied two separate periods to assess the associations between consumption of vitamins/minerals and dietary supplements with fatigue. Second, the relatively large sample size allowed an adequate statistical power. Third, it was conducted on a population-based sample, not on specific populations such as athletes [19] or people with chronic fatigue syndrome [28]. Hence, the results of our study might be more generalizable than others [19,28].

However, our study also has some limitations. First, its cross-sectional setting does not allow inferring causal relationships; a prospective study will be needed. Second, large variations and inaccurate reporting of VMS composition prevented us from assessing the amount of vitamins and minerals consumed by participants. Finally, when computing the AHEI, it was not possible to establish if participants took multivitamins regularly for five years. Hence, two extreme approaches were applied, one by considering all multivitamin users as taking them regularly for at least five years, and another by excluding the multivitamin component from the AHEI calculation, however, in both approaches, the results were similar. Future studies should attempt to collect more detailed information on vitamin supplements so that exact intakes can be estimated.

5. Conclusion

In this population-based cross-sectional study, the authors found no consistent association between VMS consumption and fatigue. Participants taking VMDS tended to present with higher fatigue scores.

Disclosure

The authors report no conflict of interest.

Data availability statement

The data of CoLaus|PsyCoLaus study used in this article cannot be fully shared as they contain potentially sensitive personal information on participants. According to the Ethics Committee for Research of the Canton of Vaud, sharing these data would be a violation of the Swiss legislation with respect to privacy protection. However, coded individual-level data that do not allow researchers to identify participants are available upon request to researchers who meet the criteria for data sharing of the CoLaus|PsyCoLaus Datacenter (CHUV, Lausanne, Switzerland). Any researcher affiliated to a public or private research institution who complies with the CoLaus|PsyCoLaus standards can submit a research application to research.colaus@chuv.ch or research.psycolaus@chuv.ch. Proposals requiring baseline data only, will be evaluated by the baseline (local) Scientific Committee (SC) of the CoLaus and PsyCoLaus studies. Proposals requiring follow-up data will be evaluated by the follow-up (multicentric) SC of the CoLaus|PsyCoLaus cohort study. Detailed instructions for gaining access to the CoLaus|PsyCoLaus data used in this study are available at www.colaus-psycolaus.ch/professionals/how-to-collaborate/

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Credit author statement

Sisi Xie: formal analysis, investigation, visualization, writing-original draft. Vanessa Kraege and Pedro Marques-Vidal: conceptualization, supervision, validation, writing-review & editing.

Declaration of generative AI and AI-assisted technologies in the writing process

No generative AI technology was used to write this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2024.10.170.

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