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Vitamin supplements: Are they associated with immune status?

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SUMMARY

Background & aims: Vitamins are essential nutrients, taken in very small amounts (0.01–100 mg a day). Associations between vitamin supplement intake or status and the immune system are far from consensual. Our aim was to understand the association between vitamin supplements and the immune system, namely regarding lymphocyte count and immunoglobulin levels against infectious pathogens.
Methods: Cross-sectional study using data from the first follow-up of the CoLaus|PsyCoLaus study (April 2009 to September 2012). Participants were categorized as vitamin users and non-users. Serostatus for 15 viruses, six bacteria, and one parasite was assessed. Data for inflammatory markers (hs-CRP, IL-1β, IL-6, and TNF-α) and blood elements were also collected.
Results: Of the initial 5064 participants, 3769 (74.5 %, mean age 58.3 ± 10.5 years, 53.6 % women) were retained for serostatus. On bivariate analysis, participants taking vitamins presented with higher positivity levels in three markers and lower positivity levels in two, but those differences were no longer statistically significant after multivariable analysis. 4489 participants (88.6 %, mean age 57.7 ± 10.5 years, 53.2 % women) had data for inflammatory markers; no association was found between vitamin supplement use and inflammatory markers both on bivariate and multivariable analysis. Finally, 3349 participants (66.1 %, mean age 57.3 ± 10.3 years, 53.1 % women) had data for blood elements; on bivariate analysis, vitamin supplement users had lower levels of haemoglobin and lymphocytes, but those differences were no longer significant after multivariable adjustment.
Conclusion: In this cross-sectional, population-based study, we found no association between vitamin supplement use and markers of immune status.

1. Introduction

Vitamins are essential nutrients in very small amounts (0.01–100 mg/day) and are divided into two classes: water-soluble (vitamins B and C) and fat-soluble (vitamins A, D, E and K) [1].

The immune system protects the host against pathogens such as bacteria, viruses, fungi, and tumours. Innate immunity is an immediate, non-host-specific response. Adaptive immunity, typical of more evolved animals, has a much more specific answer, developing in days to weeks; it involves the production of specific cells such as T- and B-lymphocytes that have a memory, allowing stronger and faster response to the next exposition [2].

Both inflammation [3] and infection [4–6] have been suggested to facilitate the occurrence of cardiovascular disease (CVD). The mechanism by which infection promotes CVD could be due to increased production of inflammatory markers, in turn promoting atherosclerosis [7]. Thus, reducing infection and inflammation could prevent atherosclerosis and CVD.

Associations between vitamin intake or status and immunity are far from consensual. A meta-analysis found no association between vitamin D deficiency and immunogenic response to influenza vaccination [8], nor did a population-based study between vitamin D levels or deficiency and serologic response to influenza vaccination in older adults [9]. A randomized controlled trial (RCT)

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reported that vitamin D supplementation (VDS) did not reduce influenza infection risk among vaccinated elderly [10] and another concluded that VDS promoted a higher TGF-β plasma level in response to influenza vaccination without improving antibody production [11]. Similarly, no association was found between vitamin D levels and antibody titres directed against COVID-19 after infection [12], nor between VDS and response to COVID-19 vaccination [13]. Finally, no effect of vitamin D on immune responses to hepatitis B or pneumococcal vaccination in HIV-infected patients was found [14].

Supplementation of vitamin C (SVC) with zinc has been suggested to improve neutrophil and lymphocyte function in elderly people [15] and spike and neutralising antibody production following COVID-19 infection [15], but a recent review concluded to the lack of SVC effect regarding prophylaxis or treatment against COVID-19 [16]. An RCT including vitamin C and zinc supplementation also showed no effect on immune response in malaria patients [17].

In kidney transplantation recipients, an inverse correlation was found between vitamin B_6 levels and CD28 (+) lymphocyte subsets, and the proliferative response of peripheral blood mononuclear cells [18]. An RCT concluded that large doses of vitamin B_6 could increase immune response in critically ill subjects [19]. Overall, vitamins and minerals with the highest potential of modulating immune response would be vitamins C, D, and zinc [20], but it is unclear if taking vitamin and mineral supplements (VMS) with such micronutrients improves immune response.

Our aim was to study the association between VMS and immune system, namely regarding lymphocyte count and immunoglobulin levels against infectious pathogens.

2. Materials and methods

2.1. Population and study design

We used data from CoLaus|PsyCoLaus (https://www.colaus-psycolaus.ch/professionals/colaus/), a population-based prospective study assessing the clinical, biological, and genetic determinants of cardiovascular disease in subjects aged 35–75 years living in the city of Lausanne, Switzerland [21]. 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 each survey, participants answered questionnaires, underwent a clinical examination and had blood samples drawn for analysis. For more details, see www.colaus-psycolaus.ch. As serology was only assessed upon first follow-up, only data from that survey was used.

2.2. Vitamin supplement consumption

Participants were asked to report all prescribed and over-the-counter medications and supplements taken during the last six months. Vitamin and mineral supplements were defined according to the Swiss compendium (https://compendium.ch/home/fr, assessed June 2017). When the supplements were not listed in the Swiss compendium, further searches on the internet were conducted. Due to wide differences in the composition of Swiss VMS [22] and to inaccurate reporting (i.e., reporting "multivitamins from producer X" that actually 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. Positivity for different viruses/bacteria

Serostatus for 22 human pathogens was assessed. This included 15 viruses [human polyomaviruses BK (BKV), JC (JCV), 6 (HPyV6), and WU (WUPyV), herpes simplex virus (HSV)-1, HSV-2, varicella zoster virus (VZV), Epstein–Barr virus (EBV), cytomegalovirus (CMV), human herpes virus 6A (HHV-6A), HHV-6B, HHV-7, Kaposi's sarcoma-associated herpes virus (KSHV), parvovirus B19 (PVB-19), and rubella virus]; six bacteria [*Chlamydia trachomatis* (*C. trachomatis*), *Clostridium tetani* (*C. tetani*), *Cornybacterium diphteriae* (*C. diphteriae*), *Fusobacterium nucleatum* (*F. nucleatum*), *Helicobacter pylori* (*H. pylori*), and *Streptococcus gallolyticus* (*S. gallolyticus*)]; and one parasite, *Toxoplasma gondii* (*T. gondii*). The overall seropositivity ranged from 3.99 % (*S. gallolyticus*) to 96.80 % (EBV). The techniques used to assess serostatus are detailed elsewhere [5].

2.4. Blood elements or inflammatory markers

Venous blood samples were drawn in the fasting state. The measurements of hs-CRP, IL-1β, IL-6, and TNF-α cytokine levels were described in detail previously [23]. Briefly, hs-CRP levels were assessed by immunoassay and latex HS (IMMULITE 1000-High, Diagnostic Products Corporation, Los Angeles, CA, USA). Cytokine levels were measured using a multiplexed particle-based flow cytometric cytokine assay (FC500 MPL, BeckmanCoulter, Nyon, Switzerland). The lower limits of detection for IL-1β, IL-6, and TNF-α were 0.2 pg/mL. Intra- and inter-assay coefficients of variation were, respectively, 15.0 % and 16.7 % for IL-1β, 16.9 % and 16.1 % for IL-6, and 12.5 % and 13.5 % for TNF-α. As a sizable fraction of participants had IL-1β levels below detection level, IL-1β levels were categorized in quartiles, the first corresponding to values below detection.

2.5. Other covariates

Participants self-filled questionnaires on socio-economic and health data. Educational level was categorized as low (primary or apprenticeship), middle (high school), and high (university) for the highest completed level of education. Smoking status was self-reported and categorized as never, former, and current. Alcohol consumption was categorized as yes or no.

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. Body mass index (BMI) was computed and categorized into normal (BMI<25 kg/m^2), overweight (25 ≤ BMI<30 kg/m^2) and obese (BMI≥30 kg/m^2).

Blood pressure (BP) was measured thrice using an Omron® HEM-907 (Matsusaka, Japan) automated oscillometric sphygmomanometer after at least a 10-min rest in a seated position, and the average of the last two measurements was computed. Hypertension was defined by a systolic BP ≥ 140 mm Hg and/or a diastolic BP ≥ 90 mm Hg and/or presence of antihypertensive drug treatment.

2.6. Inclusion and exclusion criteria

All participants of the first follow-up of the CoLaus|PsyCoLaus study (April 2009 to September 2012) were eligible for the study. Participants were excluded from any analysis if they took immune-affecting drugs such as corticoids, immunosuppressants, immunostimulatory or anticancer drugs, or missed any data regarding covariates. Participants were excluded from the analysis regarding

serologies, inflammatory markers or blood elements if they had missing data for each of the variables of interest.

2.7. Data analysis

Statistical analysis was conducted using Stata version 16.1 (Stata Corp, College Station, TX, USA). Descriptive values were presented as number of participants (percentage) for categorical variables and as mean ± standard deviation or median [interquartile range] for quantitative variables. Bivariate comparisons between groups were conducted using chi-square for categorical variables and Student's t-test or Kruskal−Wallis test for quantitative 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 age (continuous), gender (man, woman), educational level (high, medium, low), BMI categories (normal, overweight, obese), smoking categories (never, former, current), alcohol consumption (yes, no), diabetes (yes, no), hypertension (yes, no). Statistical significance was considered for a two-side test with p-value <0.05.

2.8. 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.

3. Results

3.1. Association between vitamin supplement consumption and positivity for different human pathogens

Of the initial 5064 participants, 3769 (74.5 %) were retained for analysis regarding seropositivity for human pathogens. The reasons for exclusion are summarized in Fig. 1 and the comparison between included and excluded participants is provided in Supplementary Table 1. Included participants were older, of lesser educational level, more frequently alcohol drinkers, or with hypertension.

The characteristics of the participants according to presence or absence of vitamin supplements are summarized in Table 1. Participants taking vitamin supplements were older, more often women, less often married, had a higher level of education, smaller alcohol consumption, and presented with lower levels of obesity and hypertension.

Table 2 reports the number (percentage) of participants with positive serologies for each of the tested viruses, bacteria, or parasite. On bivariate analysis, significant differences were found for five markers, for which participants taking vitamins presented with higher positivity levels in three of them and lower positivity levels in two. These differences were no longer statistically significant after multivariable analysis, which only found one statistically significant difference: participants taking vitamin supplements had a higher likelihood of being positive for HHV-7 (Table 2).

3.2. Association between vitamin supplement consumption and inflammatory markers or blood elements

Of the initial 5064 participants, 4489 (88.6 %) had data for inflammatory markers (Fig. 2). The characteristics of participants with and without inflammatory markers are summarized in
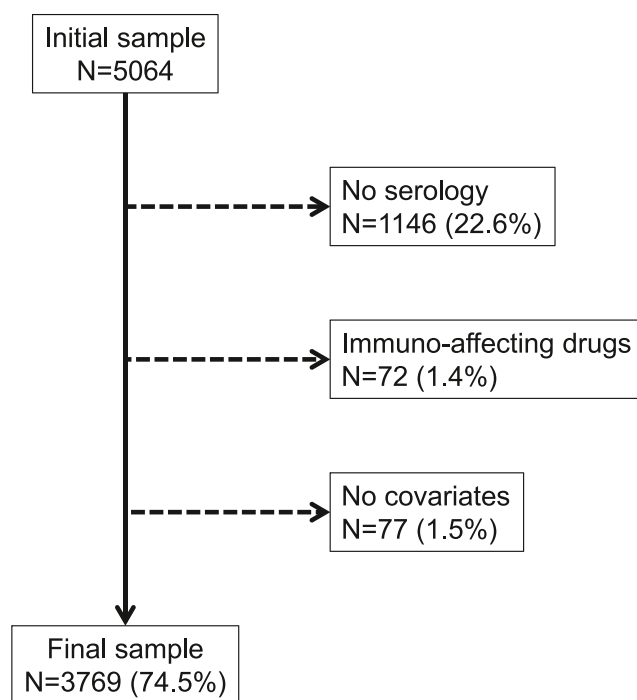
Fig. 1. Flow-chart for serological analyses
Initial sample was collected from the first follow-up of the CoLaus|PsyCoLaus study (April 2009 to September 2012).

Table 1
Characteristics of the participants, by vitamin supplement consumption, CoLaus|PsyColaus study, Lausanne, Switzerland. Participants selected for serological analysis.

	No supplements	Supplements	p-value
N	**3278**	**491**	
Age (years)	58.0 ± 10.6	60.6 ± 9.8	<0.001
Female (%)	1667 (50.9)	353 (71.9)	<0.001
Married (%)	1911 (58.3)	232 (47.3)	<0.001
Educational level (%)			<0.001
High	659 (20.1)	107 (21.8)	
Middle	805 (24.6)	158 (32.2)	
Low	1814 (55.3)	226 (46.0)	
Smoking status (%)			0.557
Never	1325 (40.4)	210 (42.8)	
Former	1245 (38.0)	183 (37.3)	
Current	708 (21.6)	98 (20.0)	
Alcohol consumption (%)	2544 (77.6)	357 (72.7)	0.016
Body mass index (kg/m^2)	26.4 ± 4.6	24.7 ± 4.3	<0.001
BMI categories (%)			<0.001
Normal	1374 (41.9)	279 (56.8)	
Overweight	1302 (39.7)	163 (33.2)	
Obese	602 (18.4)	49 (10.0)	
Hypertension (%)	1424 (43.4)	175 (35.6)	0.001
Diabetes (%)	366 (11.2)	46 (9.4)	0.234

BMI, body mass index, BP, blood pressure. Results are expressed as number of participants (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.

Supplementary Table 2. Participants without inflammatory markers were less frequently married, consumed less alcohol, and had a higher average BMI. The characteristics of participants with inflammatory markers according to their vitamin use are summarized in Supplementary Table 3. Participants taking vitamin supplements were older, more often women, less often married, had a higher level of education, and presented with lower levels of obesity and hypertension. The association between vitamin

Table 2
Bivariate and multivariable association between vitamin supplement intake and serological positivity for different human pathogens, CoLaus|PsyColaus study, Lausanne, Switzerland.

	Bivariate		P-value	Multivariable	P-value
	No	Yes		Odds ratio (95 % Ci)	
Sample size	**3278**	**491**			
Viruses					
Herpes Virus (HSV1), 1gG	2430 (74.1)	339 (69.0)	0.017	0.81 (0.65–1.00)	0.053
Herpes Virus (HSV2), mgG	563 (17.2)	95 (19.4)	0.237	0.96 (0.74–1.23)	0.731
Herpes Virus (VZV), gE/gI	2897 (88.4)	425 (86.6)	0.245	0.94 (0.70–1.25)	0.662
Herpes Virus (EBV), Zebra	2893 (88.3)	433 (88.2)	0.965	0.88 (0.65–1.19)	0.409
Herpes Virus (EBV), EA-D	2539 (77.5)	384 (78.2)	0.710	0.88 (0.70–1.12)	0.303
Herpes Virus (EBV), VCA p18	3033 (92.5)	454 (92.5)	0.961	0.95 (0.65–1.38)	0.783
Herpes Virus (EBV), EBNA (peptide)	2959 (90.3)	439 (89.4)	0.551	0.95 (0.69–1.31)	0.768
Herpes Virus (HHV), U14	1720 (52.5)	295 (60.1)	0.002	1.18 (0.96–1.44)	0.107
Herpes Virus (KSHV), LANA3	107 (3.3)	19 (3.9)	0.486	1.36 (0.81–2.27)	0.244
Herpes Virus (KSHV), K8.1	42 (1.3)	7 (1.4)	0.792	1.28 (0.56–2.95)	0.556
Herpes Virus (HCVM), pp150	1635 (49.9)	251 (51.1)	0.608	1.04 (0.85–1.26)	0.723
Herpes Virus (HCVM), pp 52	1771 (54.0)	254 (51.7)	0.341	0.89 (0.73–1.08)	0.233
Herpes Virus (HCVM), pp 28	1784 (54.4)	263 (53.6)	0.721	0.96 (0.78–1.17)	0.662
Herpes Virus (HHV6), IE1B	876 (26.7)	135 (27.5)	0.719	1.04 (0.83–1.29)	0.739
Herpes Virus (HHV7), IE1A	601 (18.3)	105 (21.4)	0.106	1.28 (1.01–1.63)	0.044
Herpes Virus (HHV8), p101 K	607 (18.5)	108 (22.0)	0.067	1.18 (0.93–1.50)	0.170
Herpes Virus (HHV9), p100	301 (9.2)	36 (7.3)	0.180	0.79 (0.55–1.14)	0.211
Parvovirus, VP1 unique	2276 (69.4)	358 (72.9)	0.117	1.14 (0.92–1.42)	0.229
Polyomavirus, BK VP1	2787 (85.0)	408 (83.1)	0.268	0.86 (0.66–1.12)	0.276
Polyomavirus, JC VP1	1703 (52.0)	254 (51.7)	0.927	1.03 (0.85–1.25)	0.752
Polyomavirus, WU VP1	3149 (96.1)	471 (95.9)	0.884	0.99 (0.60–1.62)	0.964
Polyomavirus, HPyV6 VP1	2812 (85.8)	413 (84.1)	0.326	0.89 (0.68–1.16)	0.378
Rubella virus, E1	2332 (71.1)	353 (71.9)	0.731	1.08 (0.87–1.34)	0.489
Bacteria					
Chlamydia trachomatis, pGP3	1119 (34.1)	203 (41.3)	0.002	1.16 (0.95–1.43)	0.145
Clostridium tetani, Tet X	2536 (77.4)	372 (75.8)	0.431	1.10 (0.87–1.40)	0.440
Corynebacterium diphtheriae, DTA	1693 (51.7)	218 (44.4)	0.003	0.88 (0.71–1.08)	0.216
Fusobacterium nucleatum, FadA (Fn0264)	170 (5.2)	21 (4.3)	0.392	0.81 (0.50–1.30)	0.377
Fusobacterium nucleatum, Fn1449	271 (8.3)	35 (7.1)	0.389	0.83 (0.57–1.21)	0.343
Fusobacterium nucleatum, Fn1859	121 (3.7)	13 (2.7)	0.244	0.70 (0.38–1.26)	0.230
Helicobacter pylori, HP 10 GroEL	911 (27.8)	119 (24.2)	0.099	0.95 (0.75–1.20)	0.662
Helicobacter pylori, HP 73 UreaseA	482 (14.7)	78 (15.9)	0.492	1.20 (0.92–1.58)	0.176
Helicobacter pylori, HP 547 CagA	572 (17.5)	75 (15.3)	0.233	0.96 (0.73–1.26)	0.772
Helicobacter pylori, HP 875 Catalase	462 (14.1)	58 (11.8)	0.172	0.95 (0.70–1.28)	0.734
Helicobacter pylori, HP 887 VacA	577 (17.6)	76 (15.5)	0.246	0.97 (0.74–1.26)	0.799
Helicobacter pylori, HP 1564 OMP	929 (28.3)	114 (23.2)	0.018	0.86 (0.68–1.08)	0.194
Streptococcus gallolyticus, Gallo_2178	137 (4.2)	14 (2.9)	0.162	0.63 (0.35–1.11)	0.107
Parasites					
Toxoplasma gondii, p22	1033 (31.5)	155 (31.6)	0.980	1.00 (0.81–1.23)	1.000
Toxoplasma gondii, sag-1	1038 (31.7)	150 (30.6)	0.620	0.94 (0.76–1.16)	0.558

Results are expressed as number of participants and (column percentage) for bivariate analysis and as odds-ratio and (95 % confidence interval) for multivariable analysis. Bivariate comparisons performed using chi-square and multivariable analyses performed using logistic regression adjusting for age (continuous), gender (man, woman), educational level (high, medium, low), BMI categories (normal, overweight, obese), smoking categories (never, former, current), alcohol consumption (yes, no), diabetes (yes, no), hypertension (yes, no).

supplement consumption and inflammatory markers is summarized in Table 3. No association was found between vitamin supplement use and inflammatory markers both on bivariate and multivariable analysis.

Of the initial 5064 participants, 3349 (66.1 %) had data for blood elements (Fig. 3). The characteristics of participants with and without blood elements are summarized in Supplementary Table 4. Participants without blood elements were older, of lower educational level, less often consumed alcohol, and had a higher prevalence of hypertension. The characteristics of participants with blood elements according to their vitamin use are summarized in Supplementary Table 5. Participants taking vitamin supplements were older, more often women, less often married, had a higher level of education, and presented with lower levels of obesity and hypertension. The association between vitamin supplement consumption and blood elements is summarized in Table 3. Vitamin supplement users had lower levels of haemoglobin and lymphocytes, but those differences were no longer significant after multivariable adjustment (Table 3).

4. Discussion

In this study, we found no association between vitamin supplement use and markers of immune status.

4.1. Association between vitamin supplement consumption and positivity for different human pathogens

No association was found between vitamin supplement consumption and positivity for the different pathogens. Our findings replicate those of other studies, which failed to find any association between antibody levels or antibody response and vitamin D [9,11–13]. Conversely, other studies found a positive association between antibody levels or antibody response and vitamin A [24,25], vitamin B_{12} [26], vitamin C [15] or zinc [15]. Still, most positive findings stem from single studies, some of which included participants with vitamin deficiency [24,26]. Overall, our results suggest that vitamin supplement consumption is not associated with antibody positivity, and it would be of interest to confirm
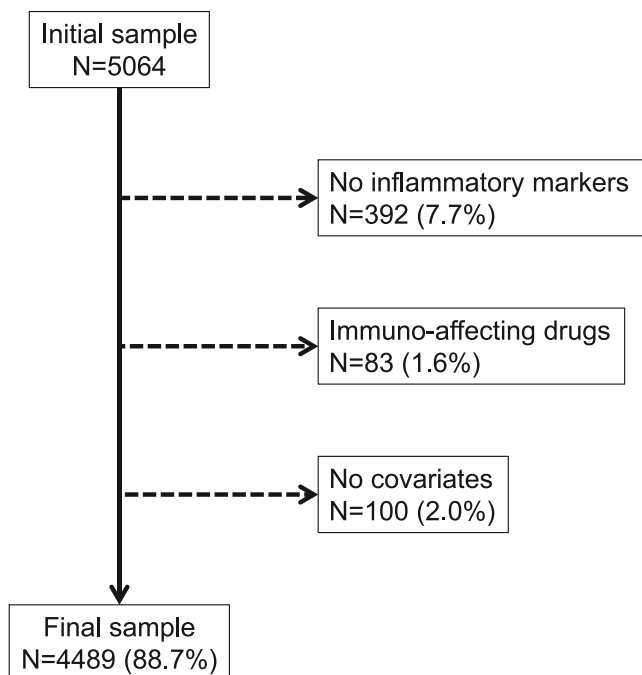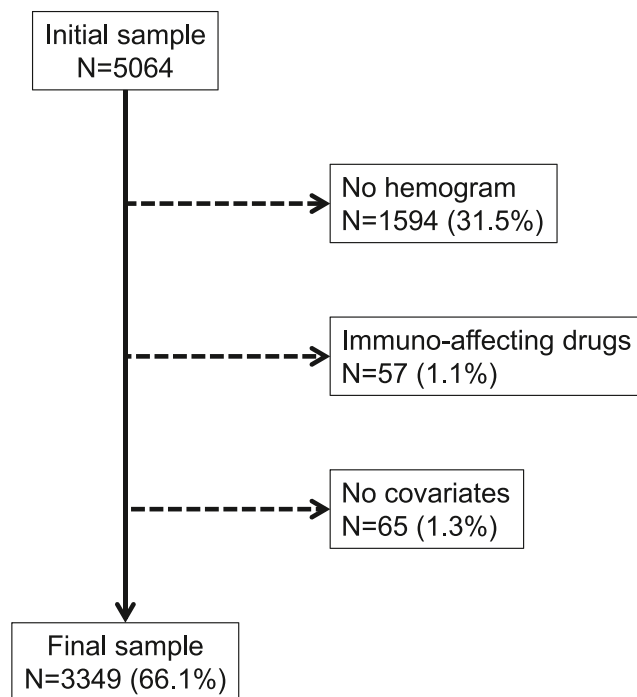
Fig. 2. Flow-chart for inflammatory marker analyses.

Fig. 3. Flow-chart for blood element analyses.

these findings in an adequately monitored randomized controlled trial.

4.2. Association between vitamin supplement consumption and inflammatory markers or blood elements

No association was found between consumption of vitamin supplements and inflammatory markers. Our findings do not replicate those from other studies, namely a negative association between vitamin D supplementation and inflammatory markers IL-6, TNF-α, and CPR (Laird, BD, [11,27]. On the other hand, the consumption of vitamin B_6 supplements had no effect on inflammatory marker IL-6 in kidney transplant recipients [18]. Similarly, consumption of vitamin D and C supplements did not change plasma levels of IL-1β in elderly women [27,28].

No association was found between consumption of vitamin supplements and blood elements. A previous study reported a positive effect of vitamin C supplementation on lymphocytes' function, but no information regarding lymphocyte number was provided [29].

4.3. Strengths and limitations

Our large study encompasses a broad array of serological and immunological markers and was conducted in a population-based sample. However, it also has some limitations. As mentioned above, wide differences in the composition of Swiss VMS [22] and inaccurate reporting prevented us from assessing the amounts of vitamins and minerals consumed by participants. Future studies

Table 3
Bivariate and multivariable association between vitamin supplement intake and inflammatory markers or blood elements, CoLaus|PsyColaus study, Lausanne, Switzerland.

	Bivariate		P-value	Multivariable		P-value
	No	Yes		No	Yes	
Inflammatory markers, N	**3919**	**570**				
Interleukin 1-β quartiles			0.922			
First	1045 (26.7)	147 (25.8)			1 (ref.)	
Second	926 (23.7)	131 (23.0)			1.03 (0.80−1.34)	0.796
Third	973 (24.9)	144 (25.3)			1.08 (0.84−1.39)	0.565
Fourth	970 (24.8)	147 (25.8)			1.14 (0.88−1.46)	0.319
Interleukin 6 (pg/mL)[a]	2.8 [1.1−8.8]	2.6 [1.1−7.5]	0.499	3.49 ± 1.03	3.39 ± 1.07	0.714
TNF-α (pg/mL)[a]	4.8 [2.6−8.4]	4.7 [2.9−8.4]	1.000	4.73 ± 1.02	4.72 ± 1.04	0.969
CRP (mg/L)[a]	1.3 [0.7−2.8]	1.2 [0.6−2.5]	0.063	1.40 ± 1.02	1.38 ± 1.04	0.804
Blood elements, N	**2920**	**429**				
Haemoglobin (g/L)	145 [137−153]	140 [134−149]	<0.001	144.6 ± 0.2	144.9 ± 0.5	0.610
Lymphocytes (G/L)	1.93 [1.59−2.35]	1.86 [1.54−2.29]	0.022	2.00 ± 0.01	2.00 ± 0.03	0.923
Lymphocytes (%)	32 [27−38]	32 [27−38]	0.613	32.7 ± 0.1	32.5 ± 0.4	0.724
Platelets (G/L)	239 [206−275]	242 [211−280]	0.168	244 ± 1	242 ± 3	0.426

[a] tests performed on log-transformed data; results were back-transformed for presentation. Results are expressed number of participants and (column percentage) or as median [interquartile range] for bivariate analyses and as multivariable-adjusted mean ± standard error for multivariable analysis. Bivariate comparisons performed using Kruskal−Wallis test and multivariable analyses performed using logistic regression for Interleukin 1-β quartiles and ANOVA for the other variables. Multivariable analyses adjusting for age (continuous), gender (man, woman), educational level (high, medium, low), BMI categories (normal, overweight, obese), smoking categories (never, former, current), alcohol consumption (yes, no), diabetes (yes, no), hypertension (yes, no).

should try to collect more detailed information on vitamin supplements so that the exact intake can be estimated. Moreover, the associations observed were cross-sectional; hence, no causal relationship can be inferred; it would be important that controlled trials assessing the effect of vitamin supplements on immune status be conducted. The immune status of our sample might not be generalizable to other countries with different vaccination protocols or with a high level of infections. Still, the results might be applicable to countries with a similar health system.

5. Conclusion

In a cross-sectional, population-based study, we found no association between vitamin supplement use and markers of immune status.

Statement of authorship

Bazil Grivat: visualisation, writing − original draft. **Pedro Marques-Vidal**: conceptualization, data curation, formal analysis, supervision writing - review & editing. **Vanessa Kraege**: supervision, writing - review & editing.

Data availability statement

The data of CoLaus|PsyCoLaus studies 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/.

Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2024.01.013.

References

[1] Reece J, Urry L, Cain M, Wassermann S, Minorsky P, Jackson R, et al. Campbell Biology. 3rd ed. Montréal, Canada: Pearson Canada; 2020. p. 1552. 2020 February 25.

[2] Parkin J, Cohen B. An overview of the immune system. Lancet 2001;357(9270):1777−89.

[3] Libby P. Inflammation and cardiovascular disease mechanisms. Am J Clin Nutr 2006;83(2):456S−60S.

[4] Adinolfi LE, Rinaldi L, Nevola R. Chronic hepatitis C, atherosclerosis and cardiovascular disease: what impact of direct-acting antiviral treatments? World J Gastroenterol 2018;24(41):4617−21.

[5] Hodel F, Xu ZM, Thorball CW, de La Harpe R, Letang-Mathieu P, Brenner N, et al. Associations of genetic and infectious risk factors with coronary heart disease. Elife 2023;12.

[6] Wang B, Yu M, Zhang R, Chen S, Xi Y, Duan G. A meta-analysis of the association between Helicobacter pylori infection and risk of atherosclerotic cardiovascular disease. Helicobacter 2020;25(6):e12761.

[7] Campbell LA, Rosenfeld ME. Infection and atherosclerosis development. Arch Med Res 2015;46(5):339−50.

[8] Lee MD, Lin CH, Lei WT, Chang HY, Lee HC, Yeung CY, et al. Does vitamin D deficiency affect the immunogenic responses to influenza vaccination? A systematic review and meta-analysis. Nutrients 2018;10(4).

[9] Sundaram ME, Talbot HK, Zhu Y, Griffin MR, Spencer S, Shay DK, et al. Vitamin D is not associated with serologic response to influenza vaccine in adults over 50 years old. Vaccine 2013;31(16):2057−61.

[10] Godan Hauptman A, Lukic-Grlic A, Vranes J, Milosevic M, Gagro A. The effect of standard-dose wintertime vitamin D supplementation on influenza infection in immunized nursing home elderly residents. Croat Med J 2021;62(5):495−503.

[11] Goncalves-Mendes N, Talvas J, Duale C, Guttmann A, Corbin V, Marceau G, et al. Impact of vitamin D supplementation on influenza vaccine response and immune functions in deficient elderly persons: a randomized placebo-controlled trial. Front Immunol 2019;10:65.

[12] Pavel-Tanasa M, Constantinescu D, Cianga CM, Anisie E, Mereuta AI, Tuchilus CG, et al. Adipokines, and not vitamin D, associate with antibody immune responses following dual BNT162b2 vaccination within individuals younger than 60 years. Front Immunol 2022;13:1000006.

[13] Jolliffe DA, Vivaldi G, Chambers ES, Cai W, Li W, Faustini SE, et al. Vitamin D supplementation does not influence SARS-CoV-2 vaccine efficacy or immunogenicity: sub-studies nested within the CORONAVIT randomised controlled trial. Nutrients 2022;14(18).

[14] Viard JP, Assuied A, Levy Y, Souberbielle JC, Thiebaut R, Carrat F, et al. No positive association between vitamin D level and immune responses to hepatitis B and Streptococcus pneumoniae vaccination in HIV-infected adults. PLoS One 2016;11(12):e0168640.

[15] Quek AML, Ooi DSQ, Teng O, Chan CY, Ng GJL, Ng MY, et al. Zinc and vitamin C intake increases spike and neutralising antibody production following SARS-CoV-2 infection. Clin Transl Med 2022;12(2):e731.

[16] Moore A, Khanna D. The role of vitamin C in human immunity and its treatment potential against COVID-19: a review article. Cureus 2023;15(1):e33740.

[17] Zen Rahfiludin M, Ginandjar P. The effect of zinc and vitamin C supplementation on hemoglobin and hematocrit levels and immune response in patients with Plasmodium vivax malaria. Southeast Asian J Trop Med Publ Health 2013;44(5):733−9.

[18] Jankowska M, Marszall M, Debska-Slizien A, Carrero JJ, Lindholm B, Czarnowski W, et al. Vitamin B6 and the immunity in kidney transplant recipients. J Ren Nutr 2013;23(1):57−64.

[19] Cheng CH, Chang SJ, Lee BJ, Lin KL, Huang YC. Vitamin B6 supplementation increases immune responses in critically ill patients. Eur J Clin Nutr 2006;60(10):1207−13.

[20] Gombart AF, Pierre A, Maggini S. A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Nutrients 2020;12(1).

[21] Firmann M, Mayor V, Vidal PM, Bochud M, Pecoud A, Hayoz D, et al. The CoLaus study: a population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. BMC Cardiovasc Disord 2008;8:6.

[22] Droz N, Marques-Vidal P. Multivitamins/multiminerals in Switzerland: not as good as it seems. Nutr J 2014;13:24.

[23] Marques-Vidal P, Bochud M, Bastardot F, Luscher T, Ferrero F, Gaspoz JM, et al. Levels and determinants of inflammatory biomarkers in a Swiss population-based sample (CoLaus study). PLoS One 2011;6(6):e21002.

[24] Ahmad SM, Alam MJ, Khanam A, Rashid M, Islam S, Kabir Y, et al. Vitamin A supplementation during pregnancy enhances pandemic H1N1 vaccine response in mothers, but enhancement of transplacental antibody transfer may depend on when mothers are vaccinated during pregnancy. J Nutr 2018;148(12):1968—75.

[25] Palmer AC, Schulze KJ, Khatry SK, De Luca LM, West Jr KP. Maternal vitamin A supplementation increases natural antibody concentrations of preadolescent offspring in rural Nepal. Nutrition 2015;31(6):813—9.

[26] Abu Hilu R, Dudeen O, Barghouthi SA. Correlation between serum levels of vitamin B12 and anti-Helicobacter pylori IgA antibodies in vitamin B12 deficient Palestinian patients. Turk J Med Sci 2015;45(3):627—33.

[27] Bueloni-Dias FN, Orsatti CL, Cangussu LM, Poloni PF, Spadoto-Dias D, Nahas-Neto J, et al. Isolated vitamin D supplementation improves the immune-inflammatory biomarkers in younger postmenopausal women: a randomized, double-blind, placebo-controlled trial. Menopause 2018;25(8): 897—903.

[28] Zychowska M, Grzybkowska A, Zasada M, Piotrowska A, Dworakowska D, Czerwinska-Ledwig O, et al. Effect of six weeks 1000 mg/day vitamin C supplementation and healthy training in elderly women on genes expression associated with the immune response - a randomized controlled trial. J Int Soc Sports Nutr 2021;18(1):19.

[29] De la Fuente M, Sanchez C, Vallejo C, Diaz-Del Cerro E, Arnalich F, Hernanz A. Vitamin C and vitamin C plus E improve the immune function in the elderly. Exp Gerontol 2020;142:111118.