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ORIGINAL CONTRIBUTION

Quantitative assessment of dietary supplement intake in 77,000 French adults: impact on nutritional intake inadequacy and excessive intake

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Abstract

Background Dietary supplements (DS) are largely consumed in Western countries without demonstrating their nutritional benefits and safety in the general population. The aims, in a large population-based study of French adults, were: (1) to compare the prevalence of nutrient intake inadequacy and the proportion of individuals exceeding tolerable upper intake levels (UL) between DS users and non-users, and (2) to quantify the extent of potentially "at-risk" DS use practices (e.g., DS/drugs contraindicated association or use of beta-carotene DS in smokers).

Methods 76,925 participants, 47.6% men and 52.4% women, mean age 46.9 ± 16.3 years were enrolled to the NutriNet-Santé cohort and they completed a quantitative DS questionnaire and three 24 h dietary records. A composition database including > 8000 DS was developed. Variance reduction was applied to estimate usual intakes and analyses were weighted according to the French census data.

Results Among DS users of the specific nutrient, DS contributed to 41% of total intake for vitamin D in men, 55% in women; and to 20% of total intake for pyridoxine in men, 21% in women. Compared to dietary intakes only, their prevalence of inadequacy was reduced by 11% for vitamin C, 9% for magnesium, 6% for pyridoxine in men, and 19% for calcium, 12% for iron, and 11% for magnesium in women ($p < 0.0001$). The proportion of subjects exceeding UL reached 6% for iron and 5% for magnesium in men, and 9% for iron in women. 6% of DS users had potentially "at-risk" practices.

Conclusion While DS use contributed to decrease the prevalence of insufficient intake for several nutrients, it also conveyed excessive intake of iron and magnesium. Besides, a substantial proportion of potentially "at-risk" DS use practices was reported.

Keywords Dietary supplements · Nutrient intake inadequacy · Tolerable upper intake levels · Drug interactions

Abbreviations

DS	Dietary supplements
EAR	Estimated average requirement
OR	Odds ratio
CI	Confidence interval
SFA	Saturated fatty acids
MUFA	Monounsaturated fatty acids
PUFA	Polyunsaturated fatty acids

Introduction

Dietary supplements (DS) are defined as nutrients (e.g., vitamins, minerals), or other bioactive compounds (e.g., herbs and other natural products, phytoestrogens) marketed in dose form such as tablets, pills, or ampoules of

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liquids (European Directive2002/46/CE). Without yet reaching consumption levels observed in the US [1–3] where > 50% of adults regularly use DS [3], their popularity increased in Europe over the last decades [4–8]. In France, several thousands of different DS are distributed over the counter. The national INCA3 survey (ANSES 2014–2016) [9] showed an increase of dietary supplement use: it was observed that 1 out of 3 adults took at least 1 DS during the year preceding the study, compared with 1 out of 5 in the INCA2 survey (ANSES 2014–2016) [10]. In the NutriNet-Santé cohort, this proportion reached 46% in women and 24% in men in 2013 [6].

Previously, we showed that, in France [6, 11] as in other Western countries [8, 12], DS users generally had higher nutrient intake from diet than non-users. Thus, it is important to assess whether nutritional DS, as currently used by the general population, truly contribute to reduce insufficient intake, as suggested in some studies [12–15]—or whether they are mostly consumed by people who already reach daily recommendations with their diet.

Conversely, excessive nutrient intake may convey adverse health effects. Thus, it is necessary to evaluate the proportion of individuals exceeding tolerable upper intake levels when all sources (foods and DS) are taken into account.

Indeed, some US studies have observed non-negligible proportions of subjects exceeding upper levels when DS use was taken into account [4, 12, 14, 15]. However, this point remains poorly documented in Europe [4]. In France, only one survey, based on a representative sample of the French population investigated the prevalence of inadequacy and excessive intake associated with DS use. This study included a small number of DS users ($n = 458$) and has not been internationally published [16].

Moreover, several practices of DS use are considered as potentially "at risk" by health authorities. For instance, this is the case for high doses of beta-carotene supplements when taken by smokers—which increase lung and gastric cancer risk [17]. Besides, many interactions between DS and drugs have been documented [18–26]; leading to moderate-to-severe adverse health effects (e.g., niacin and cholesterol-lowering drugs; St John's Wort and antiretroviral treatments). We previously showed in the NutriNet-Santé study, that such practices affected 18% of DS users in cancer patients [27]. However, the extent of such "at-risk" DS use practices has never been quantified in France for the general population.

Based on a large population sample of about 77,000 French adults with quantitative data on DS intakes, our study aimed: (1) to compare the prevalence of inadequate nutrient intake and the proportion of individuals exceeding tolerable upper intake levels between DS users and non-users, and (2) to quantify the extent of potentially "at-risk" DS use practices (e.g., DS/drugs discouraged associations).

Materials and methods

Study population

The NutriNet-Santé study is a French ongoing web-based cohort launched in 2009 with the objective to study the association between nutrition and health as well as the determinant of dietary behaviors and nutritional status. This cohort has been previously described in detail [28]. Participants aged over 18 years with access to the Internet are recruited by vast multimedia campaigns. All questionnaires are completed online using a dedicated website (http://www.etude-nutrinet-sante.fr). The NutriNet-Santé study is conducted according to the Declaration of Helsinki guidelines. It was approved by the Institutional Review Board of the French Institute for Health and Medical Research (IRB Inserm n°0000388FWA00005831) and the "Commission Nationale de l'Informatique et des Libertés" (CNIL n° 908450/n° 909216). Electronic informed consent is obtained from each participant (EudraCT no. 2013-000929-31).

Data collection

At inclusion and each year thereafter, participants completed a set of five questionnaires related to socio-demographic and lifestyle characteristics [29] (e.g., occupation, educational level, smoking status, number of children at home), anthropometrics [30, 31] (e.g., height, weight), dietary intakes (see below), physical activity (validated IPAQ questionnaire) [32], and health (e.g., personal and family history of diseases, drug use). Drugs declared at baseline and 1 year after inclusion were considered in the present analysis and were classified using the French drug registry VIDAL (Société Vidal, France) [33]. NutriNet-Santé is registered at clinicaltrials.gov as NCT03335644.

Dietary supplement use

Two months after inclusion, participants were invited to complete a questionnaire regarding DS use [6]. In the questionnaire, participants were asked whether they took any supplement during the past 12 months (at least once). They had to specify the name and the brand of the DS (open-ended questionnaire), the form used, the number of days of consumption, and the number of units generally used when they consumed the supplement. A DS composition database including about 8000 DS consumed by the participants of the NutriNet-Santé study was created and implemented based on information found on official brands' websites or direct contact with manufacturers. This database was used to calculate the average daily intake from DS during the last 12 months for each subject. In the present study, true DS and medicinal supplements (supplements considered as pharmaceutical products in France, and mainly composed of vitamins and minerals) were both considered as DS. However, use of very highly dosed medicinal supplements only consumed in specific pathologies and under medical prescription were excluded from this study when they conducted extreme supplemental intake (> 99th percentile). Vitamins, minerals, prebiotics, and other types of DS (herbal, phytoestrogens, etc.) were considered in this study.

Participants were categorized into "DS users" or "DS non-users". For analyses, DS use was considered as (1) overall DS users (including all participants consuming at least one DS, whatever the type) and (2) DS users of the specific nutrient corresponding to DS users who consumed supplements containing at least the specific nutrient (consumed as a single nutrient or among other nutrients in the same product).

Dietary data

At inclusion and twice a year thereafter, participants were invited to complete three non-consecutive validated 24 h dietary records, randomly assigned over a 2-week period (2 weekdays and 1 weekend day) [34–36]. Participants reported all foods and beverages consumed at each eating occasion and their preparation methods (e.g., fried or grilled chicken). They estimated consumed amounts using validated photographs of portion sizes [37], household measures or by indicating the exact quantity (grams) or volume (milliliters). Amounts consumed from composite dishes were estimated using French recipes validated by food and nutrition professionals. Nutrient intakes were estimated using the published NutriNet-Santé composition table including > 3300 foods and beverage items [38].

Energy underreporting was identified using Black's method [39, 40] based on the original method developed by Goldberg et al. [41], relying on the hypothesis that energy expenditure and intake, when weight is stable, are equal. In this study, only subjects with abnormally low intakes were excluded since these data were considered as declaration error. Indeed, participants who were categorized as under-reporters according to the Black criteria were not excluded if they reported a recent weight variation or a current practice of a weight-loss restrictive diet or if they proactively declared that they ate less than usual on the day of the dietary record. Indeed, in this case, very low energy intakes were not considered as mistakes but as plausible low energy intakes.

Statistical analyses

88,403 participants included in the NutriNet-Santé study between May 2009 and June 2016 completed three valid 24-h dietary records and sociodemographic data. Among them, 77,735 individuals (88%) provided information on their DS use. Subjects whose supplemental intake exceeded the 99th percentile using a medicinal supplement were excluded ($n = 810$ subjects). Thus, our final population included 76,925 participants.

The data were weighted according to the French population socio-demographic distribution using the %CALMAR SAS macro. Weighting was calculated separately for each sex using an iterative proportional fitting procedure and the 2009 national Census data [42] on age, educational level, area of residence, and presence of children in the household.

To correct intra-individual variability, we performed variance reduction by calculating usual daily dietary nutrient intakes with the method proposed by the U.S. National Cancer Institute (i.e., SAS macros %MIXTRAN followed by %INDIVINT) [43–45]. Usual intake from supplements was calculated as the mean intake over the 12 months addressed by the DS questionnaire. For each subject and each nutrient, usual intakes from (1) diet, (2) supplements, and (3) diet + supplements (total) were calculated.

For each nutrient, dietary and total intakes were compared by Student's *t* tests between DS non-users and (1) overall DS users and (2) DS users of a specific nutrient. Contribution (%) of DS to total nutrient intake was calculated in both overall and specific DS users.

The proportion of subjects with reported intake below the estimated average requirement (EAR) for the French population [46] was estimated for each nutrient by gender. It was established that, at the population level, this proportion represents an unbiased estimate of the proportion of subjects whose intake is below their respective requirements, also called "prevalence of inadequate nutrient intakes" [46]. Conversely, the proportion of subjects exceeding the tolerable upper intake levels was assessed [16]. The values of EAR were those used in the 2015 ANSES (French Agency for Food, Environmental and Occupational Health & Safety) opinion [16] which corresponded to the French EAR established in 2001 for most of nutrients [47], or later values for vitamin C (estimated by the European Food Safety Authority [48]), for vitamin E (estimated by the Nordic Nutrition Recommendations [49]), and for vitamin D (estimated by the Institute of Medicine [50]). The tolerable upper intakes taken into account were those defined in the European framework between 2000 and 2003 [51–55] when existing, or French limits established in 2001 [47]. Values of EAR and of tolerable upper limits are detailed in the Table 3 footnotes and in the Table 4 footnotes, respectively. These proportions were calculated taking into account diet only and diet + supplements, and were compared by Chi square tests between DS users (overall and specific) and non-users.

The number of subjects with potentially harmful practices of DS use was assessed. Such practices included: (1) the use of beta-carotene DS in smokers [17, 56]; (2) the simultaneous use of DS and drugs for which harmful interactions of moderate-to-major severity have been well-documented in the literature [18–26] (2.a) and those for which deleterious interactions have been suspected but are still debated [57–59] (2.b); and (3) we also considered DS highlighted by the "Nutrivigilance" device of the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) and that are currently under evaluation (e.g., St John's Wort, yam, spirulina, lutein or zeaxanthin).

A p value < 0.05 was considered statistically significant. However, due to the large sample size, a very small difference can be statistically significant. Thus, we only commented on relative differences higher than 5%. All tests were two-sided. Analyses were carried out with SAS software (version 9.4; SAS Institute, Inc.).

Results

In all, 43.1% (n = 33,179) of the subjects reported the use of at least one DS during the 12 months preceding the DS questionnaire. Individual characteristics of the study population (before and after weighting) are shown in Table 1.

Contribution of dietary supplements to total nutrient intake (Table 2)

Compared to non-users, overall DS users had higher dietary intakes of fiber (Δ = 16.5% in men and 11.2% in women), folate (Δ = 8.7% in men and 7.6% in women), beta-carotene (Δ = 13.0% in men and 9.6% in women), vitamin C (Δ = 8.0% in men and 8.5% in women), iron (Δ = 8.8% in men and 7.1% in women), and magnesium (Δ = 11.7% in men and 9.3% in women). When DS were additionally taken into account in the calculation of total nutrient intakes, this broadened the gap between DS users and non-users, especially for fiber (Δ = 24.5% in men and 21.3% in women), thiamin (Δ = 23.1% in men and 18.2% in women), riboflavin (Δ = 10.5% in men and 11.8% in women), niacin (Δ = 10.6% in men and 8.8% in women), pantothenic acid (Δ = 10.3% in men and 11.8% in women), pyridoxine (Δ = 26.3% in men and 29.4% in women), folate (Δ = 20.6% in men and 19.5% in women), vitamin B12 (Δ = 43.6% in men and 10.2% in women), beta-carotene (Δ = 17.3% in men and 13.2% in women), vitamin C (Δ = 30.0% in men and 23.6% in women), vitamin D (Δ = 55.6% in men and 184.0% in women %), vitamin E (Δ = 20.3% in men and 20.4% in women), iron (Δ = 12.9% in men and 16.7% in women), and

Table 1 Baseline characteristics of the study population before and after weighting, NutriNet-Santé cohort, France, 2016 (n = 76,925)

	Unweighted		Weighted	
	N	%	*N*	%
Sex				
Male	18,353	23.9	36,648	47.6
Female	58,572	76.1	40,276	52.4
Age (years)				
< 35	24,288	31.6	20,953	27.2
35–44	13,417	17.4	13,172	17.1
45–55	17,167	22.3	15,484	20.1
> 55	22,053	28.7	21,715	35.5
Geographical region				
Paris/Paris suburb	15,732	20.5	14,194	18.5
North	12,527	16.3	14,518	18.9
North-west	12,957	16.8	12,489	16.2
Central	18,642	24.2	18,012	23.4
South-west	7773	10.1	7935	10.3
South-east	9294	12.1	9777	12.7
Marital status				
Married or living with a partner	54,909	71.4	55,473	72.1
Divorced—separated/widowed	7770	10.1	8569	11.1
Single	14,246	18.5	12,884	16.8
Number of children at home				
0	51,550	67.0	48,770	63.4
1 or 2	21,464	27.9	24,226	31.5
≥ 3	3911	5.1	3928	5.1
Education				
< 12 years of schooling	28,367	36.9	57,777	75.1
≥ 12 years of schooling	48,558	63.1	19,148	24.9
Socio-professional categories				
Executive and intellectual professions	17,323	22.5	7001	9.1
Intermediate professions	12,939	16.8	11,151	14.5
Manual workers	14,781	19.2	23,986	31.2
Self-employed/farmers	1464	1.9	3421	4.5
Unemployed	9084	11.8	6806	8.9
Retired	15,181	19.7	21,097	27.4
Students	6155	8.0	3463	4.5
Smoking status				
Never smoker	38,522	50.1	34,417	44.7
Former smoker	26,203	34.0	29,521	38.4
Current smoker	12,200	15.9	12,988	16.9
BMI (kg/m^2)				
Normal weight (< 25)	53,018	68.9	45,207	58.8
Overweight (]25–30[)	16,846	21.9	22,086	28.7
Obese (≥ 30)	7061	9.2	9632	12.5

BMI body mass index

Table 2 Comparison of usual nutrient intakes from diet only and from diet + supplements between dietary supplement users ($n = 33{,}179$) and non-users ($n = 43{,}746$) and contribution of supplements to the total of nutrient intakes, NutriNet-Santé cohort, France, 2016

	Intakes from diet only						Total Intakes (from diet + supplements)									
	DS non-user $n = 43{,}746$		Overall DS users $n = 33{,}179$		Δ[a]	p value[b]	Overall DS users $n = 33{,}179$		Δ[c]	p value[d]	% from DS	DS users of the specific nutrient			
	Mean	SD	Mean	SD			Mean	SD				n	Mean	SD	% from DS
Men															
Energy (kcal)	2204.6	549.2	2201.8	456.1	−0.1	0.7	2211.9	479.6	0.3	0.2889	0.3	1275	2262.1	531.9	1.2
Total carbohydrates (g)	226.1	74.8	232.4	65.3	2.8	<0.0001	233.2	66.4	3.1	<0.0001	0.3	1096	242.1	69.7	1.1
Simple carbohydrates (g)	100.3	42.8	105.1	37.9	4.8	<0.0001	105.2	38.0	4.9	<0.0001	0.1	694	111.1	40.3	0.5
Fiber (g)	20	9	23.3	9.4	16.5	<0.0001	24.9	24.2	24.5	<0.0001	1.7	690	34.5	58.2	10.8
Proteins (g)	90.9	25.5	89.5	21.9	−1.5	<0.0001	90.8	24.3	−0.1	0.7391	1	970	96.5	32.2	4.7
Total lipids (g)	92.5	26.8	91.7	22.1	−0.9	0.02	91.9	22.3	−0.6	0.0627	0.2	1033	93.7	23	0.8
MUFA (g)	34.7	10.4	34.7	9	0	0.9	34.7	9.0	0	0.9768	0	81	34.6	10	0.9
PUFA (g)	12.8	4.5	13.4	4.2	4.7	<0.0001	13.4	6.6	4.7	<0.0001	0.1	120	15.5	32.3	3.3
Thiamin (mg)	1.3	0.5	1.3	0.4	0	<0.0001	1.6	1.9	23.1	<0.0001	6.9	1759	2.0	3.1	17.9
Riboflavin (mg)	1.9	0.6	1.9	0.6	0	<0.0001	2.1	1.9	10.5	<0.0001	5.3	1782	2.5	3.1	13.4
Niacin (mg)	20.8	6.8	21.5	5.8	3.4	<0.0001	23	25.4	10.6	<0.0001	4	1649	26.5	42.3	10.9
Pantothenic acid (mg)	5.8	1.7	5.9	1.4	1.7	<0.0001	6.4	3.6	10.3	<0.0001	4.7	1526	7.5	5.8	13.7
Pyridoxine (mg)	1.9	0.6	2	0.6	5.3	<0.0001	2.4	2.3	26.3	<0.0001	7.6	2086	2.9	3.3	17.1
Folate (µg)	338.1	117.3	367.4	115.4	8.7	<0.0001	407.6	237.7	20.6	<0.0001	5.7	1614	490.4	353.6	16.3
Vitamin B12 (µg)	5.5	2	5.4	2	−1.8	0.002	7.9	35.4	43.6	<0.0001	3.9	1363	14.2	65.8	13.6
Retinol (µg)	495.4	226.4	478.7	193.7	−3.4	<0.0001	505.2	241.6	2	0.0009	3.4	860	653.9	335.2	20.4
Beta-carotene (µg)	3176.1	1744.4	3590.2	1863	13	<0.0001	3726	2236.6	17.3	<0.0001	2.2	456	5375.7	4100.3	19.4
Vitamin C (mg)	116.9	72.1	127.4	66.6	9	<0.0001	152	239.9	30	<0.0001	7.9	2206	187.0	342.1	18.0
Vitamin D (µg)	2.7	0.8	2.7	0.9	0	0.0007	4.2	8.8	55.6	<0.0001	9.4	1184	9.3	16.1	40.8
Vitamin E (mg)	12.3	4.1	13.1	4	6.5	<0.0001	14.8	12.5	20.3	<0.0001	5.4	1605	18.3	20.1	16.4
Na (mg)	3120.1	931.9	3077.9	801.4	−1.4	0.0003	3082	805.2	−1.2	0.0010	0.1	770	3101.1	851.8	0.6
Ca (mg)	982.9	351.6	1009.5	300.8	2.7	<0.0001	1026.8	330.4	4.5	<0.0001	1.1	815	1130.0	439	6
Fe (mg)	14.7	4.9	16	4.9	8.8	<0.0001	16.6	6.4	12.9	<0.0001	2.6	1399	18.4	8.5	9
Mg (mg)	356.3	132.5	397.9	139.5	11.7	<0.0001	412.8	164.0	15.9	<0.0001	2.6	1937	451.1	184.3	6.4
P (mg)	1396.4	414.1	1431.4	356.3	2.5	<0.0001	1449.7	421.9	3.8	<0.0001	0.8	620	1602.8	692.3	5.5
K (mg)	3206.3	975.6	3383.8	930.9	5.5	<0.0001	3394	985.5	5.9	<0.0001	0.2	576	3502.9	1200.2	1.4
Zn (mg)	12.1	3.3	12.3	2.9	1.7	0.0003	13	4.7	7.4	<0.0001	3.9	1668	14.8	6.3	11.3
Women															
Energy (kcal)	1845.4	268	1868.9	221.4	1.3	<0.0001	1870.8	221.8	1.4	<0.0001	0.1	6923	1891.6	224.3	0.4
Total carbohydrates (g)	187.6	35.9	191.1	30.8	1.9	<0.0001	191.4	30.9	2	<0.0001	0.1	5483	195.9	31.2	0.7
Simple carbohydrates (g)	88.3	21.3	91.4	17.9	3.5	<0.0001	91.5	17.9	3.6	<0.0001	0	2815	95.6	16.4	0.4
Fiber (g)	17.8	4.3	19.8	4.2	11.2	<0.0001	21.6	17.2	21.3	<0.0001	1.4	3055	37.9	49.3	12.8

Table 2 (continued)

	Intakes from diet only						Total Intakes (from diet + supplements)									
	DS non-user $n = 43{,}746$		Overall DS users $n = 33{,}179$		Δ[a]	*p* value[b]	Overall DS users $n = 33{,}179$		Δ[c]	*p* value[d]	% from DS	DS users of the specific nutrient			
	Mean	SD	Mean	SD			Mean	SD				*n*	Mean	SD	% from DS
Proteins (g)	78.1	11.6	78.3	10.2	0.3	0.0166	80.3	17.0	2.8	< 0.0001	1.1	4989	89.8	32.8	6.4
Total lipids (g)	80.6	13.9	81.3	11.7	0.9	< 0.0001	81.4	11.7	1	< 0.0001	0.1	5525	82.6	12.2	0.6
MUFA (g)	30.3	5.4	30.8	4.7	1.7	< 0.0001	30.8	4.7	1.7	< 0.0001	0	407	30.3	5.0	0.6
PUFA (g)	11.3	2.2	11.8	2.1	4.4	< 0.0001	11.8	2.1	4.4	< 0.0001	0.1	663	13.2	3.1	1.9
Thiamin (mg)	1.1	0.2	1.2	0.2	9.1	< 0.0001	1.3	0.9	18.2	< 0.0001	5.8	9526	1.7	1.4	18.5
Riboflavin (mg)	1.7	0.3	1.7	0.3	0	< 0.0001	1.9	0.6	11.8	< 0.0001	4.5	9647	2.2	0.9	14.2
Niacin (mg)	18.2	3.2	18.6	2.9	2.2	< 0.0001	19.8	9.8	8.8	< 0.0001	3.9	9184	22.7	16.5	12.7
Pantothenic acid (mg)	5.1	0.8	5.2	0.7	2	< 0.0001	5.7	1.8	11.8	< 0.0001	5	8866	6.8	2.8	17.1
Pyridoxine (mg)	1.7	0.3	1.7	0.3	0	< 0.0001	2.2	1.5	29.4	< 0.0001	9.5	13,044	2.8	2.2	22.3
Folate (μg)[e]	310	63	333.6	58.1	7.6	< 0.0001	370.5	338.5	19.5	< 0.0001	6.2	10,006	450.7	560.0	18.7
Vitamin B12 (μg)	4.9	1.1	4.9	1	0	0.0016	5.4	4.7	10.2	< 0.0001	2.3	7224	6.9	9.1	10.1
Retinol (μg)	447.3	115.9	448.5	100.4	0.3	0.2597	471.5	128.1	5.4	< 0.0001	3.4	4532	599.3	198.7	20.8
Beta-carotene (μg)	3129.8	1002.7	3429.7	929	9.6	< 0.0001	3542.2	1662.9	13.2	< 0.0001	1.1	2252	5168.0	4827.3	19.4
Vitamin C (mg)	109.5	38	118.8	34.6	8.5	< 0.0001	135.3	88.2	23.6	< 0.0001	7	11,345	163.9	129.6	18.9
Vitamin D (μg)	2.5	0.5	2.6	0.4	4	< 0.0001	7.1	30.2	184	< 0.0001	18.9	8884	15.7	53.3	55.4
Vitamin E (mg)	11.3	2.2	11.9	2	5.3	< 0.0001	13.6	7.8	20.4	< 0.0001	6	9287	17.2	12.9	18.2
Na (mg)	2637.2	459.8	2654.9	400.1	0.7	< 0.0001	2655.9	400.2	0.7	< 0.0001	0	3138	2678.4	390	0.3
Ca (mg)	888.7	174.4	911.6	152.8	2.6	< 0.0001	965.1	218.1	8.6	< 0.0001	3.4	5372	1178.9	340.7	16.2
Fe (mg)	12.6	2.4	13.5	2.2	7.1	< 0.0001	14.7	4.6	16.7	< 0.0001	4.2	8393	18.2	7.2	15.5
Mg (mg)	307.1	65.4	335.6	64.1	9.3	< 0.0001	348.9	89.1	13.6	< 0.0001	2.8	11,781	373.4	112.1	7.4
P (mg)	1222.9	184.8	1254.5	169.3	2.6	< 0.0001	1258.3	172.7	2.9	< 0.0001	0.2	2457	1328.5	193.1	3
K (mg)	2846.4	487.4	2986.1	435.3	4.9	< 0.0001	2988.7	436.3	5	< 0.0001	0.1	2489	3032.8	438.8	0.9
Zn (mg)	10.6	1.6	10.8	1.4	1.9	< 0.0001	11.5	2.2	8.5	< 0.0001	4.2	9246	13.0	2.9	12.9

DS dietary supplements, *MUFA* monounsaturated fatty acids, *PUFA* polyunsaturated fatty acids

[a]Relative difference of intake from diet only, between DS users and non-users

[b]*p* value for the comparison between nutrient intakes from diet only between DS users and non-users by Student's *t* test

[c]Relative difference of total nutrient intakes (i.e., from diet only in DS non-users and from diet + supplements in DS users) between DS users and non-users

[d]*p* value for the comparison of total intakes between DS users and non-users by Student's *t* test

[e]Folate intakes were estimated as Dietary Folate Equivalent (DFE): 1 μg of dietary folate = 1 μg DFE and 1 μg of folic acid supplement = 1.7 μg DFE [64]

magnesium ($\Delta = 15.9\%$ in men and 13.6% in women) (all $p < 0.0001$).

DS substantially contributed to nutrient intakes by providing > 15% of the total intake in users of DS specifically containing thiamin (17.9% of total thiamin intake in men and 18.5% in women), pyridoxine (17.1% in men and 22.3% in women), folate (16.3% in men and 18.7% in women), retinol (20.4% in men and 20.8% in women), beta-carotene (19.4% in men and women), vitamin C (18.0% in men and 18.9% in women), vitamin D (40.80% in men and 55.4% in women), vitamin E (16.4% in men and 18.2% in women) calcium (16.2% in women), and iron (15.5% in women).

Prevalence of inadequate nutrient intakes (Table 3)

When we considered intakes from diet only, DS users already had lower prevalence of inadequacy than non-users for folate, vitamin C, magnesium, and iron (in women) (all $p < 0.0001$).

In male DS users of the specific nutrient, the prevalence of inadequacy was reduced when considering diet + supplement intakes compared to diet only, especially for pyridoxine (9% with diet only vs 3% with diet + supplement), vitamin C (21% vs 9%), and magnesium (30% vs 21%) (all $p < 0.0001$). Similar results were observed in women for vitamin C (13% vs 5%) and magnesium (35% vs 24%), but also for calcium (36% vs 17%) and iron (23% vs 11%) (all $p < 0.0001$).

Proportion of participants exceeding tolerable upper intake levels (Table 4)

Proportions of excessive nutrient intakes from diet only were close to 0%. In contrast, in specific nutrient DS users of the specific nutrient, the proportion of subjects exceeding the upper levels reached 6% for iron in men and 9% in women, and 5% for magnesium in men.

In sensitivity analysis, when comparison of prevalence of inadequate nutrient intakes and of percentage exceeding upper limits, were adjusted for physical activity, all results remained unchanged (data not shown).

Potentially "at-risk" supplementation (Table 5)

Among the 33,179 DS users, 6% reported at least one DS use practice that has been contraindicated due to potential adverse effects reported in the literature: 1372 (4%) participants with smoking history consumed beta-carotene DS [17] and 678 (2%) participants simultaneously used DS and drugs for which interactions of moderate-to-major severity have been well-documented [18–26]. Besides, 529 (1.6%) declared DS/drugs associations for which potentially harmful effects have been suggested in the literature but are still debated [57–59]. Moreover, 4547 (14%) users consumed DS for which the French agency for food safety (ANSES) has identified some potential adverse effects that are currently under evaluation.

Discussion

This quantitative study provided estimates of the contribution of DS to total nutrient intakes for a large population-based sample of about 77,000 French adults. DS use was associated with (1) higher nutrient intakes from diet only and (2) reduced prevalence of inadequacy in DS users of each specific nutrient, especially for vitamin C, calcium, iron, and magnesium. Conversely, substantial proportions of subjects exceeded tolerable upper intake levels for iron (in men and women) and magnesium (in men). Besides, 7% of DS users declared potentially "at-risk" practices, such as DS-drugs contraindicated associations or beta-carotene DS use in smokers, and 14% used DS that have been pointed out by the surveillance system of the French food safety agency (such as red yeast rice or St John's Wort DS).

DS users already had higher nutrient intakes from diet only, as shown previously in this cohort for cancer patients and in other countries [4, 6, 12, 15]. Notably, this resulted in lower prevalence of inadequacy for folate, vitamin C, magnesium, and iron, even before taking into account supplemental intake. However, DS use contributed to further improve nutrient adequacy (i.e., significantly reduce prevalence of inadequacy) in DS users of the specific nutrient, compared to food intake only. This was especially true for pyridoxine, vitamin C, and magnesium in males and vitamin C, magnesium, calcium and iron in women. Consistently, Bailey et al. also found a dramatically lowered prevalence of inadequate total intakes (from diet + supplements) among DS users for most studied vitamins [12]. Aparicio-Ugarriza et al., in a Spanish study on 324 adults, also showed a high proportion of inadequate nutrient intakes with 8.3% of participants presenting inadequate intake of 11 micronutrients [60].

Chronic excessive magnesium intake is associated with reversible adverse effects of mild gravity such as nausea, acceleration transit intestinal and abdominal cramping [61]. Excessive iron intake could have some reversible adverse effects, such as gastric upset, constipation, nausea, abdominal pain, but also more serious consequences, such as iron accumulation in parenchymal cells causing damage to organ (liver, pancreas, heart) and increased oxidative stress [62]. In our study, the proportion of excessive intakes reached 6% for iron in men and 9% in women, and 5% for magnesium in men. These findings are in line with an US study [15] in which about 15% of men and 5% of women consuming DS exceeded upper limits for iron. Another survey in the USA [14] also observed that DS use increased the prevalence

Table 3 Comparison of the prevalence of inadequate nutrient intakes between dietary supplement users ($n=33{,}179$) and non-users ($n=49{,}746$), calculated for diet only and for diet + supplements, NutriNet-Santé cohort, France, 2016

	Prevalence of inadequacy in men											
	DS non-users $n=13{,}549$	Overall DS users $n=4804$						Specific DS users				
	Diet only	Diet only	Δ[a]	*p* value[b]	Diet + DS	Δ[c]	*p* value[d]	*n*	Diet only	Diet + DS	Δ[e]	*p* value[f]
Thiamin	14.2	10.4	−3.8	< 0.0001	8.5	−5.7	< 0.0001	1759	8	3.2	−4.8	< 0.0001
Riboflavin	3.2	2.4	−0.8	0.0003	1.9	−1.3	< 0.0001	1782	1.6	0.4	−1.2	< 0.0001
Niacin	0.1	0.1	0	0.1	0.1	0	0.07	1649	0	0	0	< 0.0001
Pantothenic acid	2.6	1.7	−0.9	< 0.0001	1.6	−1	< 0.0001	1526	0.5	0.3	−0.2	0.01
Pyridoxine	14.3	11.4	−2.9	< 0.0001	8.7	−5.6	< 0.0001	2086	9.1	3	−6.1	< 0.0001
Folate[g]	8.4	3.3	−5.1	< 0.0001	2.7	−5.7	< 0.0001	1614	3.4	1.7	−1.7	< 0.0001
Vitamin B12	0.6	2.2	1.6	< 0.0001	1.2	0.6	< 0.0001	1363	4.7	1.4	−3.3	< 0.0001
Vitamin A[h]	4.2	1.4	−2.8	< 0.0001	1.2	−3	< 0.0001	860	0.9	0.4	−0.5	0.001
Vitamin C	27.6	19.8	−7.8	< 0.0001	15.1	−12.5	< 0.0001	2206	20.1	9.4	−10.7	< 0.0001
Vitamin E	2.9	1.9	−1	< 0.0001	1.6	−1.3	< 0.0001	1605	0.9	0.2	−0.7	< 0.0001
Calcium	16.9	15.9	−1	0.03	15.3	−1.6	< 0.0001	815	13.3	10.2	−3.1	< 0.0001
Iron	0.2	0.1	−0.1	0.007	0	−0.2	< 0.0001	1399	0.2	0	−0.2	0.07
Magnesium	53.2	36.7	−16.5	< 0.0001	33.3	−19.9	< 0.0001	1937	29.7	21.2	−8.5	< 0.0001
Phosphorus	0	0	0	0.9	0	0	0.08	620	0	0	0	< 0.0001
Zinc	6.3	6.3	0	0.9	5.6	−0.7	0.02	1668	2.9	0.9	−2	< 0.0001
	Prevalence of inadequacy in women											
	DS non-users $n=30{,}197$	Overall DS users $n=28{,}375$						Specific DS users				
	Diet only	Diet only	Δ[a]	*p* value[b]	Diet + DS	Δ[c]	*p* value[d]	*n*	Diet only	Diet + DS	Δ[e]	*p* value[f]
Thiamin	5.6	3.4	−2.2	< 0.0001	2.6	−3	< 0.0001	9526	2.8	0.6	−2.2	< 0.0001
Riboflavin	7.6	4.6	−3	< 0.0001	3.6	−4	< 0.0001	9647	4.6	1.6	−3	< 0.0001
Niacin	0.1	0.1	0	0.02	0	−0.1	0.9	9184	0.2	0	−0.2	< 0.0001
Pantothenic acid	8.4	5.8	−2.6	< 0.0001	4.7	−3.7	< 0.0001	8866	5.4	1.6	−3.8	< 0.0001
Pyridoxine	8.1	4.9	−3.2	< 0.0001	3.5	−4.6	< 0.0001	13,044	4.4	1.2	−3.2	< 0.0001
Folate[g]	7.1	3	−4.1	< 0.0001	2.3	−4.8	< 0.0001	10,006	3.1	0.8	−2.3	< 0.0001
Vitamin B12	1	1	0	0.6	0.6	−0.4	< 0.0001	7224	1.9	0.5	−1.4	< 0.0001
Vitamin A[h]	1.1	0.3	−0.8	< 0.0001	0.2	−0.9	< 0.0001	4532	0.2	0.0	−0.2	0.01
Vitamin C	20.3	12.8	−7.5	< 0.0001	10	−10.3	< 0.0001	11,345	12.5	4.8	−7.7	< 0.0001
Vitamin E	0.6	0.3	−0.3	0.003	0.3	−0.3	< 0.0001	9287	0.3	0.1	−0.2	0.0001

Table 3 (continued)

	Prevalence of inadequacy in women											
	DS non-users $n = 30{,}197$	Overall DS users $n = 28{,}375$						Specific DS users				
	Diet only	Diet only	Δ[a]	p value[b]	Diet + DS	Δ[c]	p value[d]	n	Diet only	Diet + DS	Δ[e]	p value[f]
Calcium	31.0	32.9	1.9	< 0.0001	28.9	− 2.1	< 0.0001	5372	36.2	17	− 19.2	< 0.0001
Iron	34.7	20.6	− 14.1	< 0.0001	17.3	− 17.4	< 0.0001	8393	22.6	10.5	− 12.1	< 0.0001
Magnesium	51.6	35.9	− 15.7	< 0.0001	31.7	− 19.9	< 0.0001	11,781	34.5	23.6	− 10.9	< 0.0001
Phosphorus	0	0	0	0.3	0	0	0.3	2457	0	0	0	< 0.0001
Zinc	6.1	5.4	− 0.7	0.002	4.3	− 1.8	< 0.0001	9246	4.9	1.5	− 3.4	< 0.0001

EAR for adult men: thiamin: ≤ 75 years: 1 mg, > 75 years: 0.9 mg; riboflavin: 1.2 mg; niacin: ≤ 75 years: 10.8 mg, > 75 years: 9.6 mg; pantothenic acid: 3.9 mg; pyridoxine: ≤ 75 years: 1.5 mg, > 75 years: 1.8 mg; folate:234 µg; vitamin B12: ≤ 75 years: 2 µg, > 75 years: 2.5 µg; vitamin A: ≤ 75 years: 616 µg, > 75 years: 501 µg; vitamin C: 85 mg; Vitamin E: 7.7 mg; calcium: ≤ 65 years: 693 mg, > 65 years: 924 mg; iron: ≤ 75 years: 6.9 mg, > 75 years: 7.7 mg; magnesium: ≤ 75 years: 349 mg, > 75 years: 332 µg; phosphorus: ≤ 75 years: 578 mg, > 75 years: 616 mg; zinc: ≤ 65 years: 9.2 mg,]65–75]y: 8.5 mg, > 75 years: 9.2 mg

EAR for adult women: thiamin: ≤ 75 years: 0.8 mg, > 75 years: 0.9 mg; riboflavin: 1.2 mg; niacin: ≤ 75 years: 8.5 mg, > 75 years: 9.6 mg; pantothenic acid: 3.9 mg; pyridoxine: ≤ 75 years: 1.2 mg, > 75 years: 1.8 mg; folate: ≤ 75 years: 213 µg, > 75 years: 234 µg; vitamin B12: ≤ 75 years: 2 µg, > 75 years: 2.5 µg; vitamin A: ≤ 75 years: 462 µg, > 75 years: 501 µg; vitamin C: 73 mg; vitamin E: 6.2 mg; calcium: ≤ 55 years: 693 mg, > 55 years: 924 mg; iron: ≤ 55 years: 12.3 mg,]55–75]y: 6.9 mg, > 75 years: 7.7 mg; magnesium: ≤ 75 years: 299.0 mg, > 75 years: 322 µg; phosphorus: ≤ 55 years: 578 mg, > 55 years: 616 mg; zinc: ≤ 55 years: 7.7 mg,]55–75]y: 8.5 mg, > 75 years: 9.2 mg

DS dietary supplements

[a]Absolute difference in the prevalence of inadequate nutrient intakes from diet only, between DS users and non-users

[b]*p* value for the comparison of the prevalence of inadequate nutrient intakes from diet only between DS users and non-users by Chi square test

[c]Absolute difference in the prevalence of inadequate nutrient intakes from total nutrient intake (i.e., from diet only in DS non-users and from diet + supplements in DS users) between DS users and non-users

[d]*p* value for the comparison of the prevalence of inadequate nutrient intakes from total nutrient intake (i.e., from diet only in DS non-users and from diet + supplements in DS users) between DS users and non-users by Chi square test

[e]Absolute difference in the prevalence of inadequate nutrient intakes among specific DS users between nutrient intake from diet + supplements and from diet only

[f]*p* value for the comparison of the prevalence of inadequate nutrient intakes among specific DS users between nutrient intake from diet + supplements and from diet only by McNemars's test

[g]Folate intakes were estimated in Dietary Folate Equivalent (DFE): 1 µg of dietary folate = 1 µg DFE and 1 µg of folic acid supplement = 1.7 µg DFE [64]

[h]Vitamin A intakes were estimated in retinol equivalent (RE) 1 µg of retinol = 1 µg ER and 1 µg of β-carotène = 1/12 µg ER [64]

Table 4 Comparison of the proportion of subjects exceeding tolerable upper levels between dietary supplement users ($n = 33{,}179$) and non-users ($n = 49{,}746$), calculated for diet only and for diet + supplements, NutriNet-Santé cohort, France, 2016

	% of men exceeding upper limits												% of women exceeding upper limits											
	Non-users $n = 13{,}549$	Overall DS users $n = 4804$						Specific DS users					Non-users $n = 30{,}197$	Overall DS users $n = 28{,}375$						Specific DS users				
	Diet only	Diet only	Δ[a]	p value[b]	Diet + DS	Δ[c]	p value[d]	n	Diet only	Diet + DS	Δ[e]	p value[f]	Diet only	Diet only	Δ[a]	p value[b]	Diet + DS	Δ[c]	p value[d]	n	Diet only	Diet + DS	Δ[e]	p value[f]
Niacin	0.0	0.0	0.0	NA	0.0	0.0	NA	1.649	0.0	0.1	0.1	NA	0.0	0.0	0.0	NA	0.0	0.0	NA	9.184	0.0	0.0	0.0	NA
Pyridoxine	0.0	0.0	0.0	NA	0.1	0.1	< 0.0001	2.086	0.0	0.3	0.3	NA	0.0	0.0	0.0	NA	0.0	0.0	NA	13.044	0.0	0.1	0.1	NA
Folate[g]	0.0	0.0	0.0	NA	0.8	0.8	< 0.0001	1.614	0.0	2.1	2.1	< 0.0001	0.0	0.0	0.0	NA	0.6	0.6	< 0.0001	10.006	0.0	1.9	1.9	<0.0001
Retinol	0.0	0.0	0.0	NA	0.0	0.0	NA	860	0.0	0.1	0.1	NA	0.0	0.0	0.0	NA	0.0	0.0	NA	4.532	0.0	0.1	0.1	NA
Vitamin C	0.0	0.0	0.0	NA	0.3	0.3	< 0.0001	2.206	0.0	0.6	0.6	NA	0.0	0.0	0.0	NA	0.1	0.1	< 0.0001	11.345	0.0	0.2	0.2	NA
Vitamin E	0.0	0.0	0.0	NA	0.0	0.0	NA	1.605	0.0	0	0	NA	0.0	0.0	0.0	NA	0.0	0.0	NA	9.287	0.0	0.0	0.0	NA
Calcium	0.0	0.0	0.0	NA	0.0	0.0	NA	815	0.0	0.1	0.1	NA	0.0	0.0	0.0	NA	0.1	0.1	0.0002	5.372	0.0	0.3	0.3	NA
Iron	0.2	0.3	0.1	0.3	1.9	1.6	< 0.0001	1.399	0.3	5.9	5.6	< 0.0001	0.0	0.0	0.0	NA	2.5	2.5	< 0.0001	8.393	0.0	9.3	9.3	< 0.0001
Magnesium	0.6	0.9	0.3	0.003	2.5	1.6	< 0.0001	1.937	1.0	4.9	3.9	< 0.0001	0.1	0.2	0.1	< 0.0001	0.6	0.4	< 0.0001	11.781	0.3	1.2	0.9	< 0.0001
Zinc	0.0	0.0	0.0	NA	0.9	0.9	< 0.0001	1.668	0.0	2.7	2.7	< 0.0001	0.0	0.0	0.0	NA	0.6	0.6	< 0.0001	9.246	0.0	1.7	1.7	NA

DS dietary supplements, *NA* not applicable (similar effectives)

Upper limits: niacin: 900 mg, pyridoxine: 25 mg, folate: 1000 µg, retinol: 3000 µg, vitamin C: 1000 mg, vitamin E: 300 mg, calcium: 2500 mg, Fe: 28 mg, magnesium: 700 mg, zinc: 25 mg

[a] Absolute difference in the prevalence of exceeding UL from diet only between DS users and non-users

[b] *p* value for the comparison of the prevalence of exceeding UL from diet only between DS users and non-users by Chi square test

[c] Absolute difference in the prevalence of exceeding UL from total nutrient intake (i.e. from diet only in DS non-users and from diet + supplements in DS users) between DS users and non-users

[d] *p* value for the comparison of the prevalence of exceeding UL from total nutrient intake (i.e. from diet only in DS non-users and from diet + supplements in DS users) between DS users and non-users by Chi square test

[e] Absolute difference in the prevalence of exceeding UL among specific DS users between nutrient intake from diet + supplements and from diet only

[f] *p* value for the comparison of exceeding UL among specific DS users between nutrient intake from diet + supplements and from diet only by McNemars's test

[g] Folate intakes were estimated in dietary folate equivalent (DFE) : 1 µg of dietary folate = 1 µg DFE and 1 µg of folic acid supplement = 1.7 µg DFE [64]

Table 5 Potentially at-risk dietary supplement (DS) use

	Number of declarations
1. Use of beta-carotene DS in smokers (number of subjects = 1.372 (4.1%))	
Beta-carotene/current smokers	268
Beta-carotene/former smokers	1.104
2. Simultaneous use of DS and medications that may lead to moderate-to-severe harmful interactions (number of subjects = 995 (3.0%))	
2.a. Well-documented interactions (number of subjects = 678 (2.0%))[a]	
Cholesterol-lowering medications	
Niacin	790
Anticoagulant/antiplatelet agents	
Ginseng	28
Glucosamine	17
Ginkgo	20
Turmeric	16
Green tea	9
Coenzyme Q10	6
Vitamin K	5
Garlic	1
Antiretroviral	
St John's Wort	10
Protein kinase	
Potassium/ramipril	7
Diuretic	
Potassium/spironolactone	5
Antidepressant	
Tryptophan/zolpidem tartrate	14
Tryptophan/venlafaxine	5
Melatonin/zolpidem tartrate	1
Tryptophan/duloxetine	1
Contraceptives and hormone menopausal treatments	
DHEA	6
Gattilier	3
Alfalfa	2
2.b. Suspected interactions (number of subjects = 529 (1.6%))[b]	
Cholesterol-lowering medications	
Red yeast rice	33
Anticoagulant/antiplatelet agents	
Vitamin E	607
Royal jelly	8
Milk thistle	5
Aloe vera	4
Soy	4
Flaxseed	4
Echinacea	4
Evening primrose	3
Cohosh	1
Safflower	1
3. Use of DS pointed out by the Nutrivigilance device of the French food safety agency[c] (number of subjects = 4.547 (13.7%))	
Lutein	1.618
Spirulina	1.243
Red yeast rice	247
Citrus/p-synephrine	180
Yam	112
St John's Wort	95
Caffeine	770
β-Alanine	2
Garcinia cambogia	12
Branch chain amino acids	20
Glutamine	185
Theobromine	4
L-Tyrosine	171
L-Arginine	350
L-Carnitine	91
2-Phenylethyamine	1
Total (1) + (2a): number of declarations = 2.318. Corresponding to n = 2.002 subjects (6.0%)	
Total (1) + (2a) + (2b) + (3): number of declarations = 7.376 Corresponding to n = 5.926 subjects (17.9%)	

NutriNet-Santé cohort study. France 2016

DS dietary supplements

[a]Corresponding references: [18–26]

[b]Corresponding references: [57–59]

[c]The Nutrivigilance device of the French Agency for Food. Environmental and Occupational Health & Safety (ANSES) has identified some potential adverse effects for these DS. These are currently under evaluation

of excessive iron intakes above the tolerable upper intake level by 9% in men (from 5% without DS to 14% with DS) and 7% in women (4 to 11%). The nationally representative INCA2 French survey [16] included only 458 DS users, but also observed a proportion of 9% of women exceeding upper levels for iron and 6.5% in men. No excessive intake was observed for magnesium in this study (0% in men and women) [16]. Some US studies [12, 14, 15] observed excessive nutrient intakes associated with DS use for other nutrients such as zinc [14, 15] and vitamin A [12, 15]. Long-term excessive intake of zinc can cause copper deficiency and subsequent neutropenia [62]. However, in our study, only 2.7% of men and 1.7% of women among specific DS users excessed the ULs for this nutrient. Excessive vitamin A intake can cause headache, vomiting, diplopia, alopecia, dry mucous membranes, bone and joint pain, bone fractures and birth defects [62]. No excess of vitamin A intake was observed in our study.

Several vitamin/mineral or herbal DS may modify the pharmacokinetic of drugs, and either foster or attenuate drug efficiency. These interactions may lead to moderate-to-severe adverse effects and have been well-documented [18–26]. For instance, St John's Wort should be avoided in patients treated with antiretroviral drugs since the former decreases the efficacy of the treatment [22]. In the present study, 10 subjects consumed St John's Wort DS with antiretroviral treatment. Beta-carotene DS should also be avoided due to increased lung and gastric cancer risk [17, 63, 64] in current smokers but also maybe in former smokers [56]. This effect, demonstrated for high doses of beta-carotene supplements is still under evaluation with lower doses. In our study, 4% of DS users consumed beta-carotene and had smoking history. In a previous study conducted in the NutriNet-Santé cohort, we showed that a substantial proportion (35%) of cancer patients who used DS did not discuss it with a physician [27]. A US review estimated that about 77% of the patients did not disclose their use of complementary or alternative medicine (CAM) to their medical practitioners, mainly because they feared a negative reaction from their physicians, they believed that the practitioners did not need to know about their CAM use, or the practitioner did not ask them about it [65]. This remains of concern, considering potential interactions between some DS and drugs.

Methodological strengths of this study pertained to its large sample size, with a high number of DS users, the quantitative assessment of nutrient intakes from DS, based on a unique composition table including > 8000 products, the detailed estimation of usual dietary intake with repeated 24 h records and variance reduction, and the information on concomitant drug use.

Nevertheless, some limitations should be acknowledged. Even if the population study was weighted to improve representativeness of the French population as regards sociodemographic and economic characteristics, caution is needed regarding the extrapolation of these results to the entire French population. Indeed, this study included volunteers involved in a long-term cohort on nutrition and health, with overall more health-conscious behaviors, an overrepresentation of women and individuals with higher educational level (before weighting the data) [66]. Similarly, percentages of overweight (28.7%) and of obese (12.5%) in our study were slightly lower than those of the French population (32% and 17%, respectively) [67].Thus, the proportion of DS users and their contribution to dietary intakes were higher than in the general population (43.1% of DS users in our study vs 29.0% in the French INCA2 study [79] using a nationally representative sample). Besides, data collection is based on self-administered questionnaires and memory bias may have occurred since participants were asked about their DS use during the past 12 months. Lastly, precise information is still lacking in food and supplement composition tables regarding the bioavailability of nutrients according to their matrix.

In conclusion, this large-scale population based study underlines the important contribution of DS to nutrient intakes of users. While DS use contributed to decrease the prevalence of insufficient intakes for several nutrients, it also conveyed excessive intakes for iron and magnesium. Besides, a substantial proportion of potentially "at-risk" practices (such as DS-drugs contraindicated associations or beta-carotene DS use in smokers) have been reported. Physicians should be encouraged to more routinely discuss DS use with their patients and to warn them about potential adverse effects. Given the widespread DS use in Western countries, further research studying the impact of DS consumption on long-term health is needed. In the meanwhile, individual and collective efforts should be put on maximising the proportion of the population achieving nutritional adequacy without DS but rather with a balanced diet and lifestyle.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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