Original Communication

Vitamin Intake from Food Supplements in a German Cohort – Is there a Risk of Excessive Intake?

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Abstract: Food supplements, if not properly used, may lead to potentially harmful nutrient intake. The purpose of this survey was to examine vitamin intake from food supplements. Taking into account the intake from food, as obtained from the National Nutrition Survey, it was determined whether the tolerable upper intake levels (ULs) were exceeded via supplements alone, or in combination with food. Data from 1070 supplement users (18–93 years) was available. The dietary and supplemental vitamin intakes of three groups were analyzed: average intake (50^{th} percentile food + 50^{th} percentile supplements), middle-high intake (50^{th} + 95^{th}) and high intake (95^{th} + 95^{th}). Vitamin C (53 %), vitamin E (45 %) and B vitamins (37–45 %) were consumed most frequently. Few subjects (n = 7) reached or exceeded the ULs through supplements alone. The UL for vitamin A and folate was reached by a few men in the middle-high group, and by a few men and women in the high intake group. Otherwise, even in the high intake group, the recommended vitamin D intake of 20 μg/day (in case of insufficient endogenous synthesis) could not be achieved. The use of food supplements was not associated with excessive vitamin intake in this survey, except in a small number of cases. Vitamin A intake above the UL was the result of high dietary intake which also included the intake of β-carotene, rather than the result of overconsumption of food supplements. Diets mainly included folate from natural sources, which has no associated risk.

Key words: food supplements, vitamins, survey, Tolerable Upper Intake Level, excessive intake

Introduction

Vitamins are essential to human nutrition and play important roles in maintaining health and preventing disease. As they do for many other substances, critical conditions occur at both ends of vitamins intake range [1]. Inadequate intake of vitamins is a risk factor for damage to health. A deficient vitamin status is commonly a consequence of low dietary intake and/or consumption of micronutrient-poor food [2]. On the other hand, the intake of excessively high amounts of vitamins may also cause adverse effects [3]. In general, the average diet has very little risk of excessive and toxicologically relevant intake levels. A frequently asked question is whether excessive intake of vitamins could be reached when daily food and supplements are combined as sources of nutrients. Previous studies have shown that the use of food supplements was appropriate to compensate for inadequate dietary intakes of several vitamins [4, 5] and to prevent clinical symptoms of deficiencies [6]. The effects of supplemental vitamin D in fractures and fall prevention [7] and folate supplementation in the prevention of neural tube defects [8, 9] are well documented. On the other hand, there is evidence that a permanent vitamin intake far above the UL can have negative or toxic effects [10]. There is a high risk in exceeding the UL for vitamins such as vitamin A, vitamin D and folate, where dosages ranging between recommended intake and UL are very narrow. In Germany little quantitative data on intake from supplements is available [11–13].

The aim of this study was therefore to assess the mean vitamin intake via supplements and to determine whether supplemental and dietary intakes might accumulate to excessive levels. Special focus was placed on the characteristics and consumer habits of those supplement users who exceeded the UL for single vitamins through supplement intake alone, or in combination with food intake.

Subjects and Methods

Data collection

A survey was carried out as a representative survey by the Association for Consumer, Marketing and Sales Research (GfK, Nürnberg, Germany). Personal interviews (face-to-face) as well as the equivalent online interviews took place in two waves: summer 2012 and winter 2013. In the face-to-face interviews, the interviewees were representatively selected on the basis of official statistics based on state, city size, gender, age, household size, and occupation of the head of the household. The online respondents were selected through a representative consumer panel of GfK and were selected based on their supplement use.

Personal and general demographic questions were asked, as well as specific questions relating to the use of food supplements. Product-specific information (product name, pack size, manufacturer, European Article Number (EAN) or Pharmazentralnummer (PZN)), and consuming behavior for each product mentioned were retrieved and analyzed. Individual nutrient compositions were obtained by investigating product-specific information. Details related to the study performance and methods can be seen here [14].

Analysis

The average daily intake for each individual nutrient was calculated using the nutrient composition as unit/day multiplied by the respective consumption habits (frequency of intake: daily (factor *1), 3–4 times/week (factor *3.5/7), 3–4 times/month (factor *3.5/30.4) or very irregular (factor *12/365); seasonal supply: all year (factor *1), only in summer (factor *6/12), only in winter (factor *6/12), only on special occasions, such as sickness (factor *3/12)). A sample calculation for a preparation containing the daily dosage of 100 mg vitamin C, which has been used several times a week (3–4 times/week) and only in winter is: 100 mg * 3.5/7 * 6/12 = 25 mg vitamin C average daily intake. Duration of intake was queried as: <3 months, ≥3 to <6 months, ≥6 to <12 months, ≥1 to <5 years, ≥5 to <10 years, and ≥10 years.

In our analysis, we considered food supplements, food for special medical purposes in the form of capsules or tablets and dietetic food as supplements. Drugs containing micronutrients were excluded from this analysis.

To compare vitamin intakes with German recommendations, we used the reference values for nutritional intake [15]. The data for the nutrient intake from food was taken from the 2008 published National Nutrition Survey II (NVS II) [11]. In order to be able to compare our survey with the latter, the 50th and 95th percentiles of nutrient intake from food were used. Nutrient intake data was not available for vitamin K, pantothenic acid and biotin. The total intake of vitamins was calculated for three groups based on dietary intake and the consumption of food supplements: average intake (by adding intakes from the 50th percentile from food and the 50th percentile from supplements), middle-high intake (50th percentile food + 95th percentile supplements) or high intake (95th percentile food + 95th percentile supplements). The last can be seen as a "worst case scenario".

In order to assess the general risk of excessive vitamin intake from food supplements, the proportion of subjects exceeding UL was calculated for each vitamin. The UL as defined by the EFSA was used in case of vitamin A, D, E, niacin, and folate [16], for vitamin C the UL from the Food Nutrition Board (FNB) of the Institute of Medicine (IOM) was considered [17, 18].

Additionally, the difference between the UL and the mean vitamin intake from food at the 95th percen-

Table I: Characteristics of the supplement users (n = 1070).

Characteristics	Men			Women		
	n	%	Mean ± SD	n	%	Mean ± SD
Number of subjects	437	40.8		633	59.2	
Age [years][1]						
18-24	6	1.4	20.7 ± 1.8	20	3.2	21.8 ± 1.4
25-34	26	5.9	29.0 ± 3.2	73	11.5	30.0 ± 2.9
35-50	96	22.0	44.8 ± 4.2	196	31.0	43.8 ± 4.5
51-64	154	35.2	57.7 ± 4.0	200	31.6	57.4 ± 3.9
≥ 65	155	35.5	72.1 ± 4.8	144	22.7	72.4 ± 5.5
All			57.8 ± 14.0			52.3 ± 15.1[2]
Supplement users taking specific vitamins						
Vitamin A [μg/d]	84	19.2	361.8 ± 262.4	94	14.8	339.4 ± 261.0
Vitamin D [μg/d]	140	32.0	5.3 ± 11.4	203	32.1	3.9 ± 4.0
Vitamin E [mg/d]	211	48.3	16.8 ± 22.5	274	43.3	13.4 ± 19.1
Vitamin K [μg/d]	72	16.5	35.6 ± 33.4	90	14.2	37.0 ± 30.2
Vitamin C [mg/d]	224	51.3	116.6 ± 207.8	339	53.6	81.6 ± 114.5[2]
Vitamin B_1 [mg/d]	186	42.6	2.2 ± 4.5	248	39.2	2.3 ± 7.7
Vitamin B_2 [mg/d]	171	39.1	2.8 ± 8.0	225	35.5	4.0 ± 21.3[2]
Pantothenic acid [mg/d]	159	36.4	8.0 ± 10.1	220	34.8	7.2 ± 15.8[2]
Niacin [mg/d]	162	37.1	16.1 ± 14.2	213	33.6	14.5 ± 16.4
Vitamin B_6 [mg/d]	197	45.1	3.0 ± 7.5	278	43.9	2.3 ± 3.0
Folate [μg/d]	199	45.5	236.5 ± 211.1	274	43.3	216.9 ± 189.4
Vitamin B_{12} [μg/d]	190	43.5	20.0 ± 102.6	289	45.7	12.2 ± 71.2
Biotin [μg/d]	146	33.4	84.2 ± 115.2	217	34.3	74.2 ± 84.1
β-Carotene [mg/d]	63	14.4	3.3 ± 3.5	76	12.0	2.1 ± 2.1[2]
Reasons for supplement use[3]						
For the general well-being		70.5			72.0	
Because of an acute illness		36.4			38.9	
Because of getting older		51.7			51.3	
To improve physical and mental health		67.0			64.9	
To do something good for the health		76.4			80.4	
Because of an unbalanced diet		43.2			38.0	
Physician's recommendation		34.3			33.0	
To improve quality of life		65.7			67.6[4]	
To remain healthy in the long term		72.0			74.7[4]	

[1] The distribution of the age groups between men and women is statistically different ($P < 0.001$, chi-square test)
[2] Significant difference between men and women ($P < 0.001$, Mann-Whitney U test)
[3] Data in percentages, multiple responses possible
[4] Significant difference between men and women ($P < 0.05$, chi-square test)

tile ($\Delta = UL - 95^{th}$ percentile intake food) was calculated. This calculation model has already been used and adopted by [19–22].

Data acquisition was performed using input masks in Excel and SPSS software (Version 21.0, SPSS Inc., Chicago IL, USA) for statistical analyses. Descriptive results were determined as case number, mean and standard deviation, 5^{th} percentile, median (50^{th} percentile), 95^{th} percentiles, and maximum. To test for statistically significant differences between two groups, the chi-square test was used. There are non-parametric distributions of the intakes for all vitamins.

Table II: Vitamin intake from food supplements only, among all supplement users (n = 1070).

	Current national reference value		Supplement users taking specific vitamins	Mean intake from supplements ± SD	5th percentile	Median	95th percentile	Maximum
	m	w	n (%)					
Vitamin A [µg/d]	1000	800	178 (16.6)	350.0 ± 261.2	2.75	387.5	800.0	1035.0
Vitamin D [µg/d]	20[1]		343 (32.1)	4.5 ± 7.9	0.04	3.8	10.0	130.0
Vitamin E [mg/d]	14[2]	12	485 (45.3)	14.9 ± 20.7	0.17	10.0	46.0	173.8
Vitamin K [µg/d]	70[3]	60[3]	162 (15.1)	36.4 ± 31.5	0.33	30.0	85.0	150.0
Vitamin C [mg/d]	100		563 (52.6)	95.6 ± 159.1	0.91	60.0	288.0	2551.0
Vitamin B_1 [mg/d]	1.24	1.0	434 (40.6)	2.3 ± 6.5	0.01	1.1	7.5	101.4
Vitamin B_2 [mg/d]	1.45	1.2	396 (37.0)	3.5 ± 16.9	0.01	1.4	10.8	300.0
Pantothenic acid [mg/d]	6		379 (35.4)	7.5 ± 13.7	0.05	6.0	24.0	200.1
Niacin [mg/d]	166	13	375 (35.0)	15.2 ± 15.5	0.15	15.0	48.0	128.0
Vitamin B_6 [mg/d]	1.57	1.2	475 (44.4)	2.6 ± 5.3	0.02	1.4	8.0	100.0
Folate [µg/d]	300		473 (44.2)	225.1 ± 198.9	1.65	200.0	600.0	1000.0
Vitamin B_{12} [µg/d]	3.0		479 (44.8)	15.3 ± 85.1	0.02	2.0	10.0	1000.0
Biotin [µg/d]	30–60		363 (33.9)	78.2 ± 97.8	0.83	50.0	200.0	1000.0
β-Carotene [mg/d]	2–4		139 (13.0)	2.7 ± 2.9	0.01	2.0	7.5	18.0

[1] In the absence of endogenous synthesis
[2] 15–25 years: 15 mg/d; 25–51 years: 14 mg/d; 51–65 years: 13 mg/d; >65 years: 12 mg/d
[3] 15–51 years: 70 µg/d (m) 60 µg/d (w); 51–> 65 years: 80 µg/d (m) 65 µg/d (w)
[4] 15–25 years: 1.3 mg/d; 25–51 years: 1.2 mg/d; 51–65 years: 1.1 mg/d; >65 years: 1.0 mg/d
[5] 15–25 years: 1.5 mg/d; 25–51 years: 1.4 mg/d; 51–65 years: 1.3 mg/d; >65 years: 1.2 mg/d
[6] 15–25 years: 17 mg/d; 25–51 years: 16 mg/d; 51–65 years: 15 mg/d; >65 years: 13 mg/d
[7] 15–19 years: 1.6 mg/d; 19–65 years: 1.5 mg/d; >65 years: 1.4 mg/d
* Percentage of those supplement users taking the specific vitamin

The Mann-Whitney U test was therefore used as a statistical method for comparison of intake between specific groups. Statistical significance was generally accepted at $P \leq 0.05$.

This research was in compliance with the Declaration of Helsinki. All participants were informed about the proposed research while ensuring anonymity of their data. The GfK emphasizes compliance with ethical practice and professional standards as well as data protection regulations. The questionnaire was performed on the basis of market research industry guidelines, both national (ADM) and international (Esomar, CASRO).

Results

Characteristics of the sample

A total of n = 4963 face-to-face interviews were carried out, of which n = 804 (16.2 %) supplement users were identified. Additional online surveys took place in order to achieve the desired sample size of n = 1250 subjects. As a result, data from another n = 623 supplement users were available. Overall, n = 1427 supplement users surveyed named n = 2352 products, of which n = 738 (31.4 %) were excluded in the further analysis as they were not defined as food supplements or similar dietetic foods, or they could not be adequately characterized. With the exclusion of products not specified as food supplements, the anonymous dataset of n = 1070 supplement users (59 % women, 41 % men) aged 18–93 years (55 ± 14.9 years) was complete and finally analyzed.

Use of food supplements

The characteristics of this collective are presented in Table I. 71.8 % of the products mentioned contain one or more vitamins (14.5 % exclusively vitamins, 57.3 % vitamins and/or minerals and/or other substances).

Table III: Vitamin intake from food supplements plus food.

	UL	Intake from supplements		Intake from food[1]		Intake from food + supplements		
		50th	95th	50th	95th	50th + 50th	50th + 95th	95th + 95th
Men (n = 437)								
Vitamin A [µg/d]	3000[2,3]	400	800	1800	**4400**	2200	2600	**5200**
Vitamin D [µg/d]	50[2]	5.0	10.0	2.90	9.60	7.9	12.9	19.6
Vitamin E [mg/d]	300[2]	12.0	58.8	13.7	32.5	25.7	72.5	91.3
Vitamin K [µg/d]	–	30.0	100	–	–	–	–	–
Vitamin C [mg/d]	2000[4]	75	430	130	332	205	560	762
Vitamin B_1 [mg/d]	–	1.1	9.1	1.6	3.5	2.7	10.7	12.6
Vitamin B_2 [mg/d]	–	1.4	7.5	1.9	4.3	3.3	9.4	11.8
Pantothenic acid [mg/d]	–	6.0	25.0	-	-	-	-	-
Niacin [mg/d]	900[2,5]/10[2,6]	15.0	48.0	36.3	69.7	51.3	84.3	118
Vitamin B_6 [mg/d]	25[2]	1.8	8.8	2.3	4.8	4.1	11.1	13.6
Folate [µg/d]	1000[2,7]	200	750	283	672	483	**1033**	**1422**
Vitamin B_{12} [µg/d]	–	2.50	14.9	5.80	12.4	8.3	20.7	27.3
Biotin [µg/d]	–	50.0	200	–	–	–	–	–
β-Carotene [mg/d]	–	2.4	12.1	4.3	11.7	6.7	16.4	23.8
Women (n = 633)								
Vitamin A [µg/d]	3000[2,3]	317	800	1500	**3700**	1817	2300	**4500**
Vitamin D [µg/d]	50[2]	3.75	10.1	2.20	7.00	5.95	12.3	17.1
Vitamin E [mg/d]	300[2]	9.00	36.1	12.0	25.1	21.0	48.1	61.2
Vitamin K [µg/d]	–	30.0	82.3	–	–	–	–	–
Vitamin C [mg/d]	2000[4]	60.0	238	134	317	194	372	555
Vitamin B_1 [mg/d]	–	1.0	7.5	1.2	2.5	2.2	8.7	10.0
Vitamin B_2 [mg/d]	–	1.2	15.0	1.5	3.3	2.7	16.5	18.3
Pantothenic acid [mg/d]	–	4.5	18.0	–	–	–	–	–
Niacin [mg/d]	900[2,5]/10[2,6]	10.0	48.0	26.7	47.2	36.7	74.7	95.2
Vitamin B_6 [mg/d]	25[2]	1.4	6.0	1.8	3.7	3.2	7.8	9.7
Folate [µg/d]	1000[2,7]	200	600	252	550	452	852	**1150**
Vitamin B_{12} [µg/d]	–	1.6	10.0	4.0	8.2	5.6	14.0	18.2
Biotin [µg/d]	–	50.0	200	–	–	–	–	–
β-Carotene [mg/d]	–	1.2	6.7	4.4	12.6	5.6	11.1	19.3

[1] Data from the German National Nutrition Survey II [11]
[2] EFSA, SCF Tolerable Upper Intake Levels for vitamins and minerals [16]
[3] UL for preformed vitamin A (retinol and retinyl esters) µg RE/day
[4] Food and Nutrition Board, Institute of Medicine [17, 18]
[5] UL for nicotinamide
[6] UL for free nicotinic acid
[7] only applies to synthetic folic acid
Values of vitamin intake exceeding the UL are in **bold**

In men, vitamin C (51.3 % of all supplement users), vitamin E (48.3 %) and folate (45.5 %) were the most frequently consumed vitamins as food supplements. In addition, 40–45 % of men used B vitamins. The most frequent vitamin intake as supplements in women were vitamin C (53.6 %), vitamin B_{12} (45.7 %), vitamin B_6 (43.9 %), vitamin E and folate (each 43.3 %). Significant differences in mean intakes from supplements

Table IV: Vitamin intake from food supplements plus food in relation to the reference value of intake.

	Intake from food + supplements		
	$50^{th} + 50^{th}$	$50^{th} + 95^{th}$	$95^{th} + 95^{th}$
Men (n = 437)	% of the reference value		
Vitamin A [µg/d]	220	260	520
Vitamin D [µg/d]	39.5	64.5	98.0
Vitamin E [mg/d]	184	518	652
Vitamin K [µg/d]	–	–	–
Vitamin C [mg/d]	205	560	762
Vitamin B1 [mg/d]	225	892	1050
Vitamin B2 [mg/d]	236	671	843
Pantothenic acid [mg/d]	–	–	–
Niacin [mg/d]	321	527	738
Vitamin B6 [mg/d]	273	740	907
Folate [µg/d]	161	344	474
Vitamin B12 [µg/d]	277	690	910
Biotin [µg/d]	–	–	–
β-Carotene [mg/d]	168–335	410–820	595–1190
Women (n = 633)			
Vitamin A [µg/d]	227	288	563
Vitamin D [µg/d]	29.8	61.5	85.5
Vitamin E [mg/d]	175	401	510
Vitamin K [µg/d]	–	–	–
Vitamin C [mg/d]	194	372	555
Vitamin B1 [mg/d]	220	870	1000
Vitamin B2 [mg/d]	225	1375	1525
Pantothenic acid [mg/d]	–	–	–
Niacin [mg/d]	282	575	732
Vitamin B6 [mg/d]	267	650	808
Folate [µg/d]	151	284	383
Vitamin B12 [µg/d]	187	467	607
Biotin [µg/d]	–	–	–
β-Carotene [mg/d]	140–280	278–555	483–965

between male or female users were found for vitamin C, pantothenic acid, vitamin B_2, and β-carotene. Table I also illustrates the reasons for supplement use. In Table II the mean, 5^{th}, 50^{th}, 95^{th} percentiles and maximum vitamin intakes for all supplement users are shown.

Addition of supplemental vitamin intake to foods

Table III presents the vitamin intake from supplements only, from food only and from food plus supplements for male and female supplement users. A theoretical model was carried out to simulate a "worst case scenario" by adding together the 50^{th} + 50^{th} (average intake), 50^{th} + 95^{th} (middle-high intake) and 95^{th} + 95^{th} (high intake) percentiles of vitamin intake from food and supplements.

Only a few subjects (n = 7) surpassed the UL by supplemental intake alone. Those were n = 1 (0.3 %) for vitamin D (130 µg/d), n = 1 (0.2 %) for vitamin C (2551 mg/d), n = 2 (0.4 %) for vitamin B_6 (25.2 mg/d and 100 mg/d), and n = 3 (0.6 %) for folate (each 1000 µg/d). This was either due to the intake of one preparation containing a single vitamin (e. g. vitamin D, B_6 and folate) or due to the simultaneous intake of several different preparations each containing the specific vitamin. For example, one subject took three internet-sourced preparations each containing vitamin C (daily doses ranging from 400 mg up to 1551 mg). Altogether, five of these seven subjects sourced their high-dosage preparations through the internet.

The UL set for vitamin A (3000 µg RE/d) was exceeded through food intake alone at the 95^{th} percentile in men and women. The UL for folate (1000 µg/d) was surpassed in the middle-high intake group (only men) and in the high intake group by men and women (Figure 1). The 95^{th} percentile of supplemental folate intake (men: 750 µg/d, women: 600 µg/d) was exceeded by n = 10 men and n = 21 women, corresponding to 6.6 % of those subjects who took folic acid.

The recommended vitamin D intake of 20 µg per day (in the absence of endogenous synthesis) was not reached, even in the high intake group. A maximum vitamin D intake of 98 % (men) and 85.5 % (women) of the reference value was reached.

Based on the assumption of a median food and supplemental intake ($50^{th} + 50^{th}$), the total vitamin intake was on average about 200 % of the specific reference value, but the total vitamin intakes varied widely, from 30 % (vitamin D) to 1500 % (vitamin B_2) of the reference value. The total vitamin intake as percentages of the reference values are shown in Table IV.

Calculation model (Δ = UL – 95^{th} percentile intake food)

All supplement users taking vitamin A (n = 178, 100 %) exceeded the safety maximum amount (Δ) of this vitamin as the 95^{th} percentile from food (m: 4400 µg RE/d, w: 3700 µg RE/d) was already higher than the UL. In each case, one male supplement user exceeded the safety amount of vitamin D (Δ = 40.4 µg), vitamin C (Δ = 1668 mg) and vitamin B_6 (Δ = 20.2 mg). Two women exceeded the maximum amount of vita-

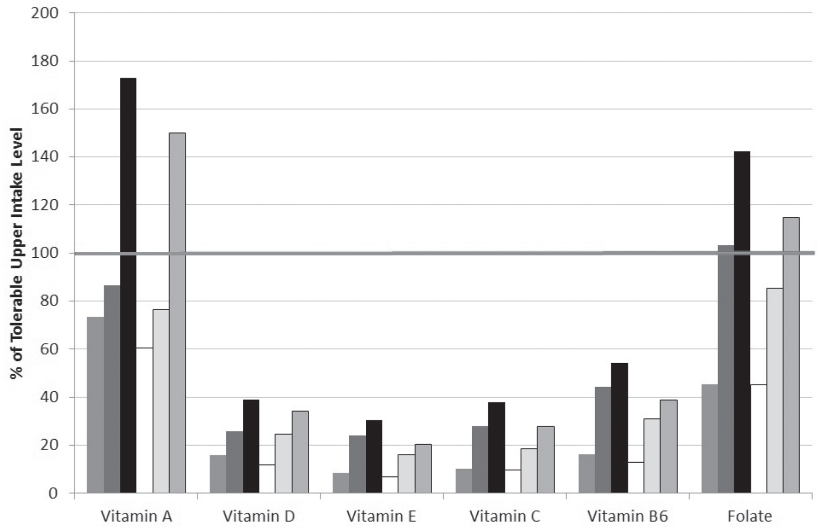

Figure 1: Vitamin intake from food supplements plus food and percentages of the Tolerable Upper Intake Level. From left to right, men: bars 1 to 3, women: bars 4 to 6 Bars 1 and 4: average intake group (50^{th} percentile food + 50^{th} percentile supplements); bars 2 and 5: middle-high intake group (50^{th} percentile food + 95^{th} percentile supplements); bars 3 and 6: high intake group (95^{th} percentile food + 95^{th} percentile supplements)

min B_6 ($\Delta = 21.3$ mg). Approximately 25.1 % (n = 50) of all men and 12.0 % (n = 33) of all women who used food supplements reached or exceeded the maximum amount of folate (m: $\Delta = 328$ µg, w: $\Delta = 450$ µg).

Discussion

As part of a survey about the consumption of food supplements in a German population [14], this publication focuses on supplemental vitamin intake. The question was whether the intake of food supplements combined with food results in exceeding the UL for vitamins.

Overall, vitamin C, E and B vitamins were the most frequently consumed vitamins with food supplements. Sole supplement use resulted in intakes above the UL in only a few cases. The addition to an already high vitamin intake from a standard diet created a potential increase in total vitamin intake.

In only one previous study [23], has the individual nutrient intake from supplements been calculated in an elderly (≥60 years) German population. Vitamins C, E and B_6 were the vitamins supplemented most often by men, and vitamin E and D by women. Apart from this, other studies have reported that the most commonly used supplements were multivitamins, followed by vitamin C and vitamin E preparations [4, 12, 13, 24–26]. Considering that B vitamins are usually the most common vitamins in multivitamin/mineral supplements [27], the data found in this study is consistent with these results. As shown in Tables I and II, the intake prevalence of B-vitamins in men and women was between 40 and 45 %, and these classic multivitamin/mineral preparations still play the most significant role in consumer behavior [27]. The characterization of the supplements by label or positioning revealed that in this survey – with view on vitamin and mineral supplementation – magnesium, calcium and vitamin C products, as well as multivitamin/mineral preparations with a comprehensive range of micronutrients, were consumed most often [14]. In fact, this is partly reflected in the common motivations for supplement purchase. General health-related motives such as “doing something good for the health”, “long term health”, or “general well-being” were mentioned most frequently. The CRN (Council for Responsible Nutrition) consumer surveys similarly reported that multivitamins are the most commonly used food supplements and that the primary reason given for supplement use was overall health and wellness [24]. Multivitamin/mineral preparations seemed to be associated with a general health-promoting character by the users. It should, however, be noted that no precise definitions of multivitamin/mineral preparations exist so far. For instance the number of components in “multi”-supplements (at least three, five or ten vitamins and/or minerals) varies greatly [27–30].

The sole use of food supplements increased the intake levels above the UL (vitamin D, C, B_6, and folate) in seven cases only. Even in the middle-high ($50^{th}+95^{th}$) or high intake groups ($95^{th}+95^{th}$, “worst case scenario”), the consumption of supplements did not result in excessive intake – except for vitamin A and folate. These results are in line with the findings of Bailey et al. [4] and Murphy et al. [31]. The calculation model (Δ = UL – 95^{th} percentile intake food) also confirmed these results. It was not unexpected to observe excessive intake for vitamin A, since the

95th percentile from food intake (men: 4400 µg RE/d, women: 3700 µg RE/d) already exceeded the UL. The UL for vitamin A is comparatively low, and only by a factor of 3 to 3.75 higher than the national reference value. Excessive intake of fat-soluble vitamin A can be associated with adverse effects such as skin disorders, nausea, vomiting, bone pain, and teratogenicity [16], however, the nutritional data based on the German National Nutrition Survey II [11] considered the intake of β-carotene from food sources for the calculation of the total vitamin A intake but the UL of 3000 µg Retinol Equivalent (RE) per day applies only to intakes of preformed vitamin A and explicitly excludes the intake of β-carotene [16], thus, the NVS II results do not reflect the intake of preformed Vitamin A itself. Nevertheless, careful thought should be given to safe levels of supplementary vitamin A in food supplements as well as fortified foods. There should also be discussion of whether the use of vitamin A in food supplements and fortified foods should generally be replaced by β-carotene to minimize the risks of excessive intake of preformed vitamin A.

Folate is a critical nutrient in Germany [11] and has the potential to be a public health problem [32, 33]. Based on the data available [11], 86 % of women and 79 % of men did not achieve the validated recommended intake level of folate (400 µg per day) at that time. It must be noted, however, that the German recommendation was reduced from 400 to 300 µg folate equivalent per day in 2013 [15]. In the case of folate particularly, the use of food supplements can decrease the prevalence of inadequate vitamin status and associated adverse effects [8, 9, 34, 35]. In this survey, supplement use above the 95th percentile increased the likelihood of folate intakes above the UL of 1 mg/d when added to the diet, but this was relevant only for 31 subjects (6.6 %), and it should however be borne in mind that the upper safe level only applies to synthetic folic acid which is commonly used for supplementation and food fortification [16, 36]. High intake levels of synthetic folic acid at 5 mg/d and above – mainly used for therapeutic purposes – can cause, for example, masking of haematological symptoms, epileptogenic and neurotoxic symptoms, adverse effects on zinc absorption and status, as well as carcinogenicity [16]. The EFSA, as well as the Food and Nutrition Board (FNB) of the Institute of Medicine (IOM), did not establish an UL for folate from food because high intakes of folate from natural sources have not been reported to cause adverse effects so far [16, 36]. In this survey, three subjects did have folate intakes at the UL from supplement use only which largely resulted from the use of high-potency food supplements. These were, however, marginal cases. Bearing in mind that the NVS II included fortified foods in the calculation of the folate equivalent by a factor of 1.7 [11], there is a possibility that further single subjects reached or surpassed the UL for synthetic folate with the intake of food supplements in addition to fortified food, however, due to the fact that we had no detailed information about the percentage of fortified foods in general nutrition, a final estimation of the risk of surpassing the UL for synthetic folate due to a cumulative intake from fortified foods and food supplements was not possible. Data is lacking on the specific contributions made by fortified foods [37]. This should be taken into consideration in further studies. Enriched foods provide a substantial share of the supply of some nutrients [38].

The intake of vitamin D has to be emphasized at this point. Even in the "worst case scenario" (high intake group), only one food supplement user was able to reach the reference value of 20 µg per day which applies in the absence of endogenous synthesis. This highlights the fact that adequate vitamin D intake from food only is unlikely. Although supplemental vitamin D intake decreased the prevalence of inadequate intake in this survey, there is still a nutritional gap. Similarly to our study, Cashman et al. [39] found that in both winter and summer supplement users had higher mean serum 25(OH) D concentrations and lower prevalence rates of suboptimal status than did non-users.

It must be stressed that ULs do not exist for all nutrients. ULs have been set either by the EFSA [16] or the IOM [17, 18] only for a limited number of vitamins (vitamin A, D, E, C, B_6, nicotinic acid, nicotinamide, and folate). No valid risk characterization can be made for other vitamins because of the lack of evidence of adverse effects.

There was huge variation in the total intake levels of many vitamins, as illustrated in Table IV. In the high intake group (95th + 95th), as a "worst case scenario", the total vitamin intake level was partly more than 10-fold greater than the specific reference values. It must, however, be critically noted that the nutritional data from the NVS II is secondary data and has not been specifically collected from the supplement users, so that our calculation model certainly has weaknesses.

Conclusions

In this survey, it appeared that vitamin intake from food supplements generally bears no risk of overdose. It could not be established that the parallel use of several food supplements leads to dangerously high intake of vitamins. When looking at the total vitamin intake from food and food supplements, vitamin A intake appeared critical, but this was predominantly caused by an already high intake from food sources. The exact intake of preformed vitamin A is not known, however, so that the risk of excessive intake of preformed vitamin A cannot currently be evaluated. According to a statement made by the EFSA and IOM, the intake of folate from natural sources bears no risk. The number of cases with supplemental folate intake at the UL in this study was almost negligible.

Ideally, food supplements should be able to fill nutritional gaps and at the same time reduce the risk of excessive intake. Setting maximum levels for vitamins and minerals in food supplements at European level could help to further minimize the risk of excessive intake - although few cases exceeding the UL were found in this study. More information about total nutrient intake from all sources (food, fortified foods and food supplements) is needed for precise estimations.

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JW and AH designed and coordinated the survey and drafted the manuscript. MH was involved in product research, statistical analysis and revising the manuscript. NB participated in the statistical analysis. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

List of abbreviations

ADM = Arbeitskreis Deutscher Markt- und Sozialforschungsinstitute e.V.

CASRO = Code of Standards and Ethics for Survey Research

DACH = German, Austrian and Swiss reference values for nutritional intake

EFSA = European Food Safety Authority

Esomar = worldwide society for social and market research

FNB = Food Nutrition Board

GfK = Association for Consumer, Marketing and Sales Research

IOM = Institute of Medicine

NVS II = National Nutrition Survey II (Nationale Verzehrsstudie II)

RE = Retinol Equivalent

SCF = Scientific Committee on Food

UL = Tolerable Upper Intake Level

References

1. Mulholland, C.A., Benford, D.J. (2007) What is known about the safety of multivitamin-multimineral supplements for the generally healthy population? Theoretical basis for harm. Am J Clin Nutr 85, 318S.
2. Ames, B.N. (2006) Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage. Proc Natl Acad Sci USA 103, 17589.
3. Renwick, A.G., Walker, R. (2008) Risk assessment of micronutrients. Toxicology Letters 180, 123.
4. Bailey, R.L., Fulgoni, V.L., Keast, D.R., Dwyer, J.T. (2012) Examination of vitamin intakes among US adults by dietary supplement use. J Acad Nutr Diet 112, 657.
5. Touvier, M., Boutron-Ruault, M.C., Volatier, J.L., Martin, A. (2005) Efficacy and Safety of Regular Vitamin and Mineral Supplement Use in France: Results from the ECCA Study. Int J Vitam Nutr Res 75(3), 201.
6. Ward, E. (2014) Addressing nutritional gaps with multivitamin and mineral supplements. Nutr J 13, 72.
7. Bischoff-Ferrari, H.A., Dawson-Hughes, B., Staehelin, H.B., Orav, J.E., Stuck, A.E., Theiler, R., Wong, J.B., Egli, A., Kiel, D.P., Henschkowski, J. (2009) Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomized controlled trials. BMJ, 339, b3692.
8. Czeizel, A.E. (2011) Periconceptional folic acid-containing multivitamin supplementation for the prevention of neural tube defects and cardiovascular malformations. Ann Nutr Metab 59, 38.

9. Goh, Y.I., Bollano, E., Einarson, T.R., Koren, G. (2006) Prenatal multivitamin supplementation and rates of congenital anomalies: a meta-analysis. J Obstet Gynaecol Canm 28, 680.

10. Renwick, A.G. (2006) Toxicology of Micronutrients: Adverse effects and uncertainty. J Nutr 136, 493S.

11. Max Rubner-Institute (2008) National Nutrition Survey II. Final report part 2. http://www.was-esse-ich.de/uploads/media/NVSII_Abschlussbericht_Teil_2.pdf (in German).

12. Beitz, R., Mensink, G.B.M., Fischer, B., Thamm, M. (2002) Vitamins—dietary intake and intake from dietary supplements in Germany. Eur J Clin Nutr 56, 539.

13. Mensink, G.B.M., Ströbel, A. (1999) Intake of dietary supplements and nutritional behaviour. Gesundheitswesen 132, S137 (in German).

14. Heinemann, M., Willers, J., Bitterlich, N., Hahn, A. (2014) Use of food supplements with vitamins and minerals – results of a nationwide consumer survey. J. Verbr. Lebensm. doi: 10.1007/s00003–014–0912-x (in German).

15. German Nutrition Society, Austrian Nutrition Society, Swiss Society for Nutrition Research, Swiss Nutrition Association (2013) Reference values for nutrient intake. Neustadt an der Weinstraße: Neuer Umschau Buchverlag (in German).

16. EFSA, Scientific Committee on Food (2006) Tolerable upper intake levels for vitamins and minerals. (http://www.efsa.europa.eu/de/ndatopics/docs/ndatolerableuil.pdf).

17. Institute of Medicine. Food and Nutrition Board (2001) Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington D.C., National Academy Press.

18. Institute of Medicine. Food and Nutrition Board (1997) Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. Washington D.C., National Academy Press.

19. Flynn, A., Moreiras, O., Stehle, P., Fletcher, R.J., Müller, D.J.G., Rolland, V. (2003) Vitamins and minerals: A model for safe addition to foods. Eur J Nutr 42, 118.

20. Domke, A., Großklaus, R., Niemann, B., Przyrembel, H., Richter, K., Schmidt, E., Weißenborn, A., Wörner, B., Ziegenhagen, R. (2005) Use of Minerals in Foods – Toxicological and nutritional-physiological aspects. http://www.bfr.bund.de/cm/350/use_of_minerals_in_foods.pdf.

21. Dufour, A., Wetzler, S., Touvier, M., Lioret, S., Gioda, J., Lafay, L., Dubuisson, C., Calamassi-Tran, G., Kalonji, E., Margaritis, I., Volatier, J.L. (2010) Comparison of different maximum safe levels in fortified foods and supplements using probabilistic risk assessment approach. Br J Nutr 104, 1848.

22. Flynn, A., Hirvonen, T., Mensink, G.B.M., Ocké, M.C., Serra-Majem, L., Stos, K., Szponar, L., Tetens, I., Turrini, A., Fletcher, R., Wildemann, T. (2009) Intake of selected nutrients from foods, from fortification and from supplements in various European countries. Food & Nutrition Research 53, 1.

23. Schwarzpaul, S., Strassburg, A., Lührmann, P.M., Neuhäuser-Berthold, M. (2006) Intake of Vitamin and Mineral Supplements in an Elderly German Population. Ann Nutr Metab 50, 155.

24. Dickinson, A., Blatman, J., El-Dash, N., Franco, J.C. (2014) Consumer usage and reasons for using dietary supplements: report of a series of surveys. J Am Coll Nutr 33, 176.

25. Sebastian, R.S., Cleveland, L.E., Goldman, J.D., Moshfegh, A.J. (2007) Older adults who use vitamin/mineral supplements differ from nonusers in nutrient intake adequacy and dietary attitudes. J Am Diet Assoc 107, 1322.

26. Radimer, K., Bindewald, B., Hughes, J., Ervin, B., Swanson, C., Picciano, M.F. (2004) Dietary supplement use by US adults: Data from the National Health and Nutrition Examination Survey, 1999–2000. Am J Epidemiol 160, 339.

27. Droz, N., Marques-Vidal, P. (2014) Multivitamins/multiminerals in Switzerland: not as good as it seems. Nutrition Journal 13, 24.

28. Shakur, Y.A., Tarasuk, V., Corey, P., O'Connor, D.L. (2012) A comparison of micronutrient inadequacy and risk of high micronutrient intakes among vitamin and mineral supplement users and nonusers in Canada. J Nutr 142, 534.

29. Bailey, R.L., Gahche, J.J., Lentino, C.V., Dwyer, J.T., Engel, J.S., Thomas, P.R., Beth, J.M., Sempos, C.T., Picciano, M.F. (2011) Dietary Supplement Use in the United States, 2003–2006. J Nutr 141, 261.

30. Yetley, E.A. (2007) Multivitamin and multimineral dietary supplements: definitions, characterization, bioavailability, and drug interactions. Am J Clin Nutr 85, 269S.

31. Murphy, S.P., White, K.K., Park, S.Y., Sharma, S. (2007) Multivitamin-multimineral supplements' effect on total nutrient intake. Am J Clin Nutr 85, 280S.

32. McLean, E., de Benoist, B., Allen, L. (2008) Review of the magnitude of folate and vitamin B12 deficiencies worldwide. Food & Nutrition Bulletin 29, 38.

33. Eichholzer, M., Tönz, O., Zimmermann, R. (2006) Folic acid: a public-health challenge. The Lancet 367, 1352.

34. Berti, C., Fekete, K., Dullemeijer, C., Trovato, M., Souverein, O.W., Cavelaars, A., Dhonukshe-Rutten, R., Massari, M., Decsi, T., Van't Veer, P., Cetin, I. (2012) Folate intake and markers of folate status in women of reproductive age, pregnant and lactating women: a meta-analysis. J Nutr Metab, 470656.

35. Brämswig, S., Prinz-Langenohl, R., Lamers, Y., Tobolski, O., Wintergerst, E., Berthold, H.K., Pietrzik, K. (2009) Supplementation with a multivitamin containing 800 microg of folic acid shortens the time to reach the preventive red blood cell folate concentration in healthy women. Int J Vitam Nutr Res 79, 61.

36. Institute of Medicine. Food and Nutritional Board (1998) Dietary Reference Intakes: Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington D.C., National Academy Press.

37. Berner, L.A., Keast, D.R., Bailey, R.L., Dwyer, J.T. (2014) Fortified foods are major contributors to nutrient intakes in diets of US children and adolescents. J Acad Nutr Diet, 114(7), 1009.

38. Freisling, H., Elmadfa, I., Schmid, I.T. (2008) A high proportion of nutrient-enriched food in the vitamin supply of Austrian adults. Ernährungs Umschau, 55(3), 158 (in German).

39. Cashman, K.D., Muldowney, S., McNulty, B., Nugent, A., FitzGerald, A.P., Kiely, M., Walton, J., Gibney, M.J., Flynn, A. (2013) Vitamin D status of Irish adults: findings form the National Adult Nutrition Survey. Br J Nutr 109, 1428.

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