Use of dietary supplements in the European Prospective Investigation into Cancer and Nutrition calibration study

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Background: Dietary supplement use is increasing, but there are few comparable data on supplement intakes and how they affect the nutrition and health of European consumers. The aim of this study was to describe the use of dietary

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supplements in subsamples of the 10 countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC).
Methods: Specific questions on dietary supplement use were asked as a part of single 24-h recalls performed on 36 034 men and women aged 35–74 years from 1995 to 2000.
Results: Between countries, the mean percentage of dietary supplement use varied almost 10-fold among women and even more among men. There was a clear north–south gradient in use, with a higher consumption in northern countries. The lowest crude mean percentage of use was found in Greece (2.0% among men, 6.7% among women), and the highest was in Denmark (51.0% among men, 65.8% among women). Use was higher in women than in men. Vitamins, minerals or combinations of them were the predominant types of supplements reported, but there were striking differences between countries.
Conclusions: This study indicates that there are wide variations in supplement use in Europe, which may affect individual and population nutrient intakes. The results underline the need to monitor consumption of dietary supplements in Europe, as well as to evaluate the risks and benefits.

Introduction

The use of dietary supplements is increasing in many European countries (Messerer *et al.*, 2001; Knudsen *et al.*, 2002; Ocké *et al.*, 2005; Touvier *et al.*, 2006; Reinert *et al.*, 2007), but there is a lack of information with regard to the prevalence and types of dietary supplements used that can be compared across Europe. Consequently, it is difficult to compare between-country supplement use and how it affects nutritional status and health (Brownie and Myers, 2004).

Nutrient intakes are usually calculated on the basis of food intake data and concentration values derived from food composition databases. The nutrient contribution from dietary supplements is not always included in overall nutritional estimates, despite their contribution to dietary intakes. The reason could be that questions regarding supplements were not asked, answers were not given with sufficient detail and/or because the nutritional contents of supplements are not covered by standard food composition databases (Radimer, 2003; Park *et al.*, 2006).

This omission has two important consequences for nutritional research. First, exclusion of the contribution of dietary supplements to nutrient intake estimates leads to an underestimation of overall nutritional consumption, which may bias the comparison of dietary intakes between populations (or individuals) with large variations in supplement use, and distort their association with diseases. Second, when dietary intake (typically obtained by questionnaires, interviews or diaries) is compared with biomarkers of nutritional intake or status, the true relationship may be underestimated if the dietary intake calculations do not include nutrient intake from dietary supplements, and the validity of the dietary intake method might seem poorer than it actually is (Block *et al.*, 1994; Bates *et al.*, 1998; Messerer *et al.*, 2004).

Comparison of dietary supplement use between different studies is challenging because of different and changing definitions of supplements, different methods of data collection, different reference periods and different frequencies of use required for a subject to be defined as a user (Dwyer *et al.*, 2003; Radimer, 2003; Brownie and Myers, 2004; Yetley, 2007). Apart from a study including Spain, Italy, Germany and the United Kingdom, where supplement use was defined as any use during the year preceding the survey (Serra Majem *et al.*, 1996), to our knowledge, the only European comparison using standardized data collection of dietary supplement use is the SENECA study (Brzozowska *et al.*, 2002). The first SENECA study surveyed elderly people in 12 countries (Cruz *et al.*, 1991). Participants were asked whether they took dietary supplements (yes/no), without any reference period. A large variation in use was found, both between and within countries, with much more frequent use in Northern Europe.

Some claim that dietary supplement use is a way of taking charge of one's own health (Conner *et al.*, 2001; Greger, 2001). Although the percentage of supplement users is higher among cancer survivors, for example, than in the general population (Rock *et al.*, 2004; Skeie *et al.*, 2006), much is unknown or poorly documented regarding the associations between supplement use and health (Huang *et al.*, 2006; Bjelakovic *et al.*, 2007).

The purpose of this paper is to describe the type and mean frequency of dietary supplement use reported through a single highly standardized computerized 24-h dietary recall (24-HDR) obtained from the calibration subsample of the European Prospective Investigation into Cancer and Nutrition (EPIC) study. In addition, we present the most frequently used supplement ingredients and supplement use according to certain dietary and health variables.

Methods

Population

The EPIC study started in 1992 and includes more than half a million participants in 23 centres in 10 European countries: Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden and the United Kingdom (Riboli *et al.*, 2002). In some centres, the source population consisted of blood donors and their spouses (some of the Italian and Spanish centres), other centres recruited members of a health insurance for teachers and school workers (France) or women attending mammography screening (parts of the Dutch and Italian cohorts), but in most centres the participants were from the general population. The majority of the Oxford (UK) cohort was recruited from among so-called 'health-conscious' persons from all over the United Kingdom, and comprises a high proportion of vegans, vegetarians and fish eaters. The cohorts in France, Norway, Naples (Italy) and Utrecht (the Netherlands) included only women. At baseline (1992–1998), the participants provided information regarding diet, lifestyle and health, in most centres by answering questionnaires. All participants consented to participation, and the EPIC study was approved by the ethical review boards of the International Agency for Research on Cancer and the other participating institutions.

The EPIC calibration study was carried out between 1995 and 2000, and has been described in detail elsewhere (Slimani *et al.*, 2002). Briefly, a stratified sample ($n = 36\,994$) of the total cohort was selected for a 24-HDR interview, which was performed using a highly standardized interview program, EPIC-SOFT, either face to face or by telephone (only in Norway) (Slimani *et al.*, 2000; Brustad *et al.*, 2003). After exclusion of subjects <35 and >74 years of age, the final sample included 36 034 subjects (23 009 women, 13 025 men).

Dietary supplement information

At the end of the 24-HDR, the participants were asked: *Did you take any vitamins…?* If the answer was yes, the interviewer could choose the vitamin or other supplement from a country-specific pre-defined list, or add new product names. Questions were asked with regard to the physical state of the supplement (11 modalities: liquid (spoon), powdered (sachet), powdered (spoon), tablet, pill, capsule, injection, lemonade tablet, drops, ampoule and unknown), and the number of units taken per consumption occasion. The participants were asked about the frequency of use on the recalled day. There was no restriction on the number of supplements that could be reported. If several drops, tablets or capsules of the same supplement were consumed at the same time, it was counted as only one record in current analyses (e.g., if a participant reported taking 80 drops of *Echinacea* on one occasion, it was counted as one record).

For this paper, a dietary supplement user is defined as anyone who reported taking at least one dietary supplement during the recalled period.

In the current analyses, a dietary supplement has been defined according to the *Directive 2002/46/EC of the European Parliament and of the Council, of 10 June 2002*:

"'Food supplements' means foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in measured small unit quantities" (European Parliament and Council, 2002).

For this study, we developed a common qualitative classification, together with guidelines on how to classify the supplements across countries (Table 1). The categories were vitamins, minerals, multivitamins and multiminerals (MVM), oil-based supplements, herbs/plants, other

Table 1 Classification of supplements

Class	*Short definition*	*Example*
Vitamins	Supplements containing only vitamins	Vitamin C, vitamin B-complex
Minerals	Supplements containing only minerals	Selenium, multimineral tablets
MVM	Supplements containing combinations of both vitamins and minerals, and no other active ingredients	MVM, vitamin D and calcium supplements
Oil-based supplements	Oils, including oils with added vitamins, minerals and/or herbs/plants	Cod liver oil, evening primrose oil
Herbs/plants	Only herbs/plants or their constituents	Ginseng, fibre
Other single-substance supplements[a]	Single-substance supplement, the substance is clearly defined chemically as one substance	Single amino acids, ubiquinon
Other complex substance supplements[a]	Complex (multi)-substances that are recognized as one entity, e.g., proteins built from several amino acids, but still recognized as protein. Also these are all non-distinguishable compounds	Protein, yeast, royal jelly, algae
Other combination supplements[a]	Combinations of single compounds not mentioned above, consisting of various single compounds. These are 'artificial' complexes, combinations of substances that do not occur naturally.	Mainly combinations of vitamins, minerals and herbs/plants, e.g. multivitamin with ginseng
Non-specified supplements[b]	Supplements that could not be specified from the information recorded during the recalls	

Abbreviation: MVM, multivitamins and multiminerals.
[a]These categories were combined into one category named 'other supplements' for some of the analyses, because of their low frequency of use.
[b]Users of these were only included in the results in Tables 2 and 4.

single-substance supplements, other complex substances and other combination supplements. The last three categories were combined into one category named 'other supplements' for some of the analyses because of their low frequency of use. In addition, there was a category for non-specified supplements, but users of these were only included in analyses including all users (i.e., Tables 2 and 4). Although some EPIC countries have databases with information on contents of dietary supplements, there is no overall dietary supplement database available for Europe. No attempt was therefore made to quantify the contents of the supplements.

Table 2a Percentage of supplement users the previous day, crude and age-adjusted, weighted for season and period of the week in the EPIC calibration study—men

Country	*Men*															
	All	*Overall percentage of users*			*35–44 years % users*			*45–54 years % users*			*55–64 years % users*			*65–74 years % users*		
	N	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*
Greece	1311	2.0	0.5	1.1	1.7	1.2	3.2	2.9	2.0	2.2	1.3	1.3	2.0	2.1	2.1	1.7
Spain	1777	5.9	6.6	0.9	4.1	4.4	2.9	5.7	5.3	1.5	6.5	6.2	1.4	6.0	6.6	2.8
Italy	1442	6.8	7.8	1.0	4.3	3.3	3.5	4.6	4.5	1.8	7.8	8.2	1.4	12.8	15.1	3.8
Germany	2267	20.7	22.0	0.8	10.9	12.2	2.2	18.3	18.1	1.4	24.4	24.6	1.1	20.0	21.7	3.9
The Netherlands	1024	16.0	19.7	1.2	11.6	12.3	2.3	15.1	15.1	1.9	20.3	20.3	2.1	—	—	—
UK general population	402	36.3	34.6	1.9	13.2	13.3	6.3	27.6	27.0	3.4	43.1	42.3	3.5	44.8	43.2	3.5
UK health-conscious	114	51.8	44.8	3.6	—	—	—	55.6	49.5	5.8	57.5	49.3	5.5	—	—	—
Denmark	1923	51.0	48.8	0.9				43.0	41.1	1.4	55.7	53.6	1.2	64.1	60.0	4.8
Sweden	2765	30.5	28.3	0.7	20.4	20.3	3.5	19.9	20.0	1.6	31.6	32.0	1.1	36.3	35.8	1.3

Abbreviations: EPIC, European Prospective Investigation into Cancer and Nutrition; —, estimate not given if there were fewer than 20 participants per stratum; s.e., standard error for the adjusted percentage.
If no figures are indicated, this means that strata were not sampled.

Table 2b Percentage of supplement users the previous day, crude and age-adjusted, weighted for season and period of the week in the EPIC calibration study—women

Country	*Women*															
	All	*Overall percentage of users*			*35–44 years % users*			*45–54 years % users*			*55–64 years % users*			*65–74 years % users*		
	N	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*	*Crude %*	*Adjusted %*	*s.e.*
Greece	1373	6.7	6.7	1.2	5.3	4.8	3.2	6.7	7.5	2.1	7.6	8.4	2.1	6.3	6.6	2.4
Spain	1443	12.1	13.4	1.2	9.9	9.4	2.7	13.0	13.0	1.9	13.3	13.6	1.9	5.7	6.2	4.4
Italy	2511	12.6	12.4	0.9	10.5	9.7	2.7	11.9	10.6	1.5	13.0	13.0	1.3	16.3	15.7	3.2
France	4735	32.4	31.1	0.6				29.0	27.9	1.0	33.5	33.0	1.0	37.8	38.9	1.5
Germany	2148	27.0	26.9	1.0	19.0	16.8	1.7	26.5	24.9	1.8	32.1	30.5	1.5	24.1	13.9	7.6
The Netherlands	2956	32.1	32.5	0.8	21.1	21.3	2.4	28.6	28.8	1.3	34.2	34.6	1.3	43.6	43.6	2.0
UK general population	570	47.5	46.9	1.8	45.3	46.8	5.5	45.1	44.5	3.0	49.1	50.5	3.3	50.4	47.4	3.9
UK health-conscious	197	51.8	50.3	3.1	32.1	32.1	9.9	60.3	58.4	5.1	52.2	49.8	4.9	48.2	40.9	8.7
Denmark	1994	65.8	64.3	1.0				62.3	61.1	1.6	67.5	67.0	1.3	75.0	74.8	5.0
Sweden	3285	42.4	40.8	0.8	28.8	30.3	2.7	36.8	37.3	1.5	44.4	44.6	1.2	49.2	48.6	1.5
Norway	1797	60.6	61.7	1.1	50.0	47.4	2.4	62.0	60.7	1.3	66.4	61.8	2.6			

Abbreviations: EPIC, European Prospective Investigation into Cancer and Nutrition; —, estimate not given if there were fewer than 20 participants per stratum; s.e., standard error for the adjusted percentage.
If no figures are indicated, this means that strata were not sampled.

Initially, the collected data included some misclassified items such as medications without nutrients (1334 records), foods (13 records), homeopathic medicines (74 records) and other items (11 records). These 659 different products (7% of the original records) were excluded from current analyses. In addition, 261 records of PABA (para-aminobenzoic acid)—used to verify complete urine collection for a validation study and wrongly reported as a supplement—were excluded. Medications containing nutrients (1090 records of 285 medications) were included in the database. These included prescribed and over-the-counter vitamins/minerals aimed at preventing or restoring deficiencies (e.g., calcium and iron), as well as medications such as paracetamol with vitamin C and others containing nutrients. For this paper, the medications with nutrients and the supplements were combined in the analyses. Medication containing vitamins and no other nutrients (e.g., paracetamol with vitamin C) was grouped with vitamins, medication containing minerals was grouped with minerals, and so on. In the final data set, medication with nutrients amounted to 5.8% of the records (range: 0–36.2% across EPIC countries).

In addition to classifying the collected supplements, selected food groups recorded in the 24-HDRs were searched in order to check whether any supplements were misreported as foods. The search was limited to the following groups: cereals (bran), fats and oils (fish oil), soy products (soy supplements), dieting products (protein supplements) and miscellaneous foods (lecithin, royal jelly). This revealed some differences of opinion between countries regarding what are foods and what are supplements. In total, 1.6% of records in the final data set originated from food data (range: 0–21.7% across EPIC countries).

Diet and health information

During the 24-HDRs, the subjects reported whether the recalled day had been a special day with regard to their diet and whether they followed a special diet (Slimani *et al.*, 2002). The special day variable had the following modalities: religious holiday, celebration meals, travel/on trip, illness/tiredness, holidays and others. Reasons for following a special diet included allergy, stomach problems, intestinal problems, hypertension, hyperlipidemia/cholesterolemia, obesity, diabetes, vegetarian diet and others. One alternative for special day, and two different special diets could be listed.

In the baseline questionnaires, the participants provided information on myocardial infarction (yes, no, do not know), diabetes (yes, no, do not know) and self-reported health (excellent, good, moderate, poor). This information was provided between 3 years and a few days before the 24-HDR, depending on country (Slimani *et al.*, 2002). Follow-up data on cancer, based on cancer registries or a combination of health insurance, cancer and pathology registries and active follow-up, were used to determine whether the subject had a prevalent cancer diagnosis at the time of 24-HDR.

Statistical analyses

All statistical analyses were carried out with SAS (version 9.1; SAS Institute Inc., Cary, NC, USA). Owing to the low proportion of users in some countries, results were stratified by country instead of centre, but the health-conscious cohort in the United Kingdom was kept separate. Results are also stratified by gender and presented according to a geographical south–north gradient. Adjusted mean percentages and standard errors (s.e.) at country level were calculated using generalized linear models (GENMOD procedure). The models were weighted for sampling differences in seasons (four levels) and weekdays (Monday–Thursday) versus long weekend (Friday–Sunday) at the centre level. The overall estimates (Tables 2 and 4) were adjusted for age as a continuous variable, whereas the age-specific estimates (Table 2) were stratified by 10-year age classes. As there were few users and/or participants in some strata (particularly for men), age-adjusted overall estimates were outside the range of age-stratified estimates in some of the countries. This was because of the low precision in some of the estimates, and not because of real statistical differences.

As the 24-HDRs were weighted for season and day of the week, supplements not intended to be used daily (e.g., injections), or used only during parts of the year (e.g., vitamin D, cod liver oil), should be well represented at the group level. Figure 1 and Table 3 are based on crude data, as weighting among users would remove the effect of seasonal and weekday variation in supplement use.

Overall gender differences were tested in analyses of variance, and age differences by centre and gender were tested in a regression model with age in 10-year age groups as the predictor variable. We carried out stratified analyses to determine differences in the percentages of supplement users according to special diet (yes/no), special day (yes/no), self-reported health status (excellent/good/moderate–poor) and prevalence of cancer.

Results

There were striking differences in dietary supplement use between countries (Tables 2a and b). The crude mean percentage of supplement users was almost 10 times higher among Danish women (65.8%) than among Greek women (6.7%); among men, the corresponding difference was over 25-fold (51.0 versus 2.0%). Adjustment for season, weekday and age did not affect the estimates much, compared with the unadjusted models, but some effects were observed in strata with skewed age distributions or few participants. For both genders, there was a clear north–south gradient, with Scandinavian countries showing the highest percentage of use and Mediterranean countries the lowest. In all countries, there were more female than male users, although this was less pronounced among the health conscious. The overall gender difference was significant with a P-value <0.0001.

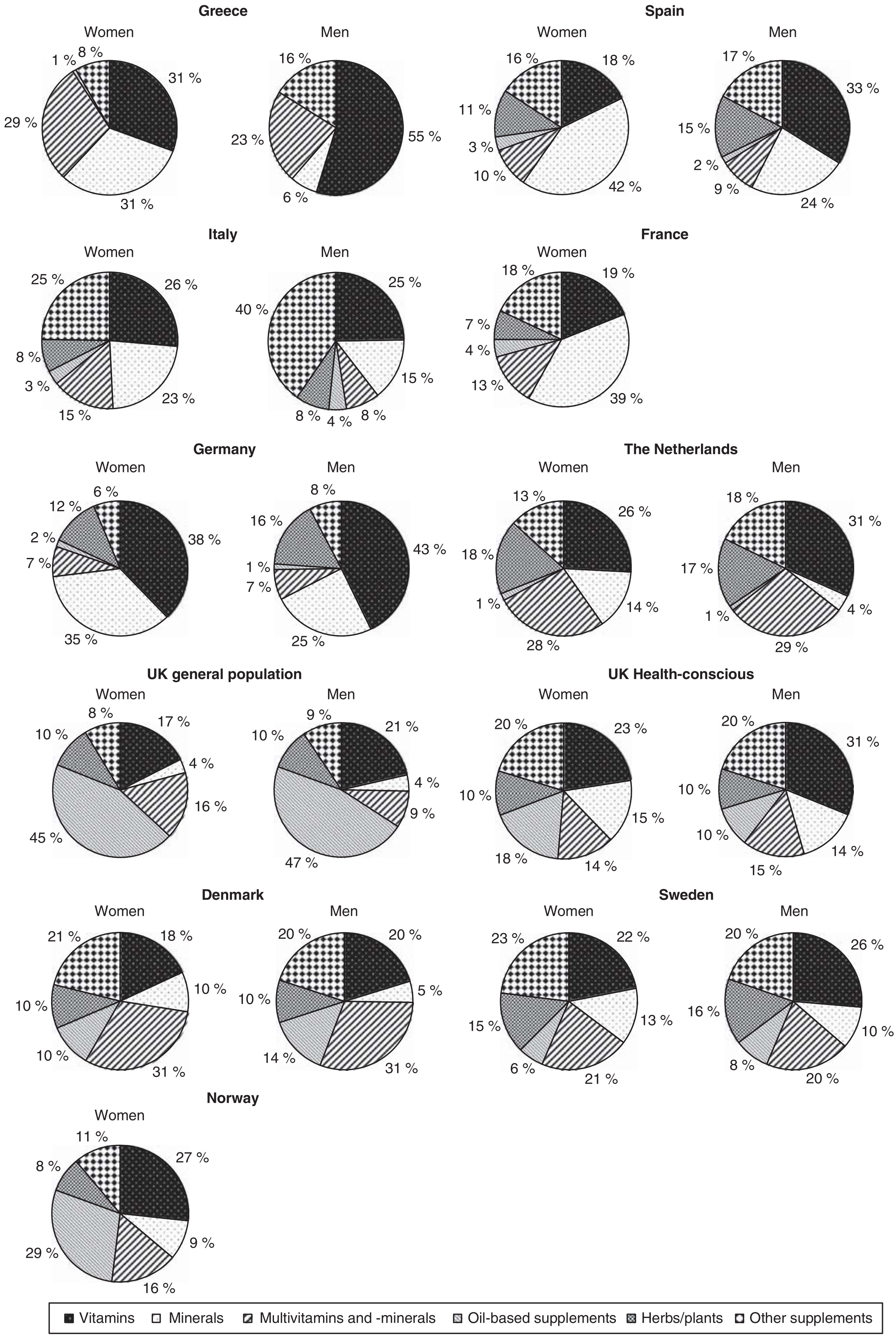

Figure 1 Types of dietary supplements used (%) in the EPIC calibration study, by country and gender.

Table 3 Most frequently used supplement ingredients by country by men and women in the EPIC calibration study[a]

Country	Men		Women	
	Most popular supplement ingredients (N = users)	Used as a % of supplement records (n times)[b,c]	Most popular supplement ingredients (N = users)	Used as a % of supplement records (n times)[b,c]
Greece	Vitamin B6 (N = 11)	38.7 (12)	Calcium (N = 49)	46.3 (50)
	Vitamin E (N = 11)	35.6 (11)	Vitamin D (N = 33)	32.4 (35)
	Thiamine (N = 9)	29.0 (9)	Vitamin C (N = 31)	29.6 (32)
Spain	Vitamin C (N = 35)	28.3 (36)	Calcium (N = 56)	26.8 (56)
	Magnesium (N = 16)	13.4 (17)	Iron (N = 39)	19.1 (40)
	Calcium (N = 17)	13.4 (17)	Vitamin C (N = 27)	12.9 (27)
	Bran (N = 17)	13.4 (17)		
Italy	Lecithin (N = 30)	24.6 (30)	Vitamin C (N = 63)	16.7 (65)
	Vitamin C (N = 18)	14.8 (18)	Calcium (N = 49)	13.4 (52)
	Vitamin E (N = 9)	7.4 (9)	Vitamin n.s (N = 47)	12.9 (50)
	Vitamin n.s (N = 9)	7.4 (9)		
France			Magnesium (N = 429)	20.3 (462)
			Vitamin C (N = 377)	18.0 (411)
			Calcium (N = 389)	17.7 (404)
Germany	Magnesium (N = 127)	18.3 (127)	Magnesium (N = 174)	20.4 (179)
	Vitamin E (N = 113)	17.3 (120)	Calcium (N = 152)	18.0 (158)
	Vitamin C (N = 104)	15.7 (109)	Vitamin E (N = 144)	17.6 (154)
The Netherlands	Vitamin C (N = 75)	34.7 (82)	Calcium (N = 417)	32.4 (465)
	Calcium (N = 46)	20.7 (49)	Vitamin C (N = 327)	24.8 (356)
	Vitamin B6 (N = 44)[d]	18.6 (44)	Vitamin D (N = 266)	20.5 (295)
UK general population	Vitamin E (N = 100)	50.7 (114)	Vitamin E (N = 187)	48.0 (232)
	Vitamin D (N = 102)	50.2 (113)	Vitamin D (N = 173)	41.8 (202)
	Retinol (N = 103)[d]	50.2 (113)	Retinol (N = 160)[d]	37.7 (182)
UK health-conscious	Vitamin C (N = 35)	31.0 (45)	Vitamin C (N = 50)	24.3 (68)
	Vitamin E (N = 31)	24.1 (35)	Vitamin E (N = 47)	20.4 (57)
	Vitamin D (N = 26)[d]	19.3 (28)	Vitamin D (N = 40)[d]	15.7 (44)
Denmark	Vitamin E (N = 804)	52.5 (966)	Vitamin C (N = 989)	43.0 (1251)
	Vitamin C (N = 763)	51.1 (941)	Vitamin E (N = 1004)	41.9 (1221)
	Vitamin D (N = 739)[d]	43.3 (796)	Vitamin D (N = 1007)	40.6 (1182)
Sweden	Vitamin C (N = 455)	39.0 (506)	Vitamin C (N = 806)	38.3 (908)
	Vitamin E (N = 393)	33.4 (433)	Vitamin E (N = 696)	32.3 (767)
	Vitamin D (N = 313)[d]	25.0 (324)	Vitamin D (N = 586)[d]	25.4 (603)
Norway			Vitamin E (N = 803)	46.0 (1101)
			Vitamin D (N = 708)	36.4 (872)
			Vitamin C (N = 552)[d]	27.7 (663)

Abbreviation: EPIC, European Prospective Investigation into Cancer and Nutrition.
[a]The three most frequently used ingredients are listed per country for men and for women. If some ingredients were used an equal number of times, four are mentioned.
[b]As most supplements contain more than one ingredient, and the participants might have ingested the same ingredient from different supplements, the percentages do not add up to 100.
[c]A supplement record is defined as any use of a supplement. A participant might have multiple records if multiple supplements were consumed. If several drops, tablets or capsules of the same supplement were consumed at the same time, it is only counted as one record.
[d]When all vitamin A components (retinol, beta-carotene, other carotenoids and non-specified vitamin A) were summed together, vitamin A was also one of the most frequently used ingredients.

Table 4a Use of dietary supplements in the EPIC calibration study according to special diet, special day, self-reported health and prevalent cancer status, age-adjusted and weighted by season and period of the week—men

Country	*Men*																	
	No special diet		*Special diet*		*No special day*		*Special day*		*Excellent self-reported health*		*Good self-reported health*		*Moderate/poor self-reported health*		*Free from cancer*		*Prevalent cancer*	
	% Users	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*
Greece																		
Spain	6.1	1.0	9.9	2.6	6.6	1.0	6.9	2.4							6.4	0.9	14.3	7.6
Italy	7.6	1.0	8.5	3.7	7.7	1.1	8.9	3.2							7.6	1.0	13.0	6.6
Germany	21.1	0.9	26.1	1.9	22.6	0.9	19.0	1.9	19.6	1.7	21.1	1.1	21.8	2.1	21.7	0.8	28.9	4.6
The Netherlands	19.4	1.3	20.5	5.0	20.1	1.3	17.6	3.1	14.7	4.4	18.1	1.5	25.9	3.4	19.5	1.2	26.3	8.5
UK general population	33.1	2.0	45.2	5.7	36.4	2.0	23.1	5.4	53.7	6.1	31.3	3.1	36.1	6.5	33.8	2.0	45.0	7.8
UK health-conscious	30.9	7.5	50.2	4.3	45.8	3.7	—	—							45.8	3.7	—	—
Denmark	48.3	0.9	53.9	3.5	51.2	1.0	39.4	2.0										
Sweden[a]	26.2	0.8	35.9	1.6	28.7	0.8	26.6	1.7	23.0	2.2	22.2	1.6	27.5	2.4	28.0	0.8	35.4	3.8

Abbreviations: EPIC, European Prospective Investigation into Cancer and Nutrition; s.e., standard error.
[a]Results for self-reported health in Sweden are based on the Umeå centre only.
If no figures are indicated, this means that strata were not sampled.
—, estimate not given if there were fewer than 20 participants per stratum.

Table 4b Use of dietary supplements in the EPIC calibration study according to special diet, special day, self-reported health and prevalent cancer status, age-adjusted and weighted by season and period of the week—women

Country	*Women*																	
	No special diet		*Special diet*		*No special day*		*Special day*		*Excellent self-reported health*		*Good self-reported health*		*Moderate/poor self-reported health*		*Free from cancer*		*Prevalent cancer*	
	% Users	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*	*% Users*	*s.e.*
Greece	6.3	1.3	8.4	2.5	6.5	1.3	7.7	2.9							6.6	1.2	8.9	7.1
Spain	12.6	1.3	16.9	2.9	13.6	1.2	12.5	3.1							13.4	1.2	10.8	6.8
Italy	11.6	0.9	15.8	2.3	12.4	1.0	12.2	2.2							12.3	0.9	11.7	4.5
France	29.2	0.7	38.1	1.4	30.8	0.7	32.7	1.7							30.3	0.7	38.9	2.2
Germany	26.1	1.0	30.0	2.4	26.8	1.0	27.2	2.4	26.0	2.0	23.5	1.3	30.1	2.5	26.3	1.0	34.3	3.9
The Netherlands[a]	31.0	0.9	38.3	1.9	32.5	0.9	32.0	1.8	29.7	4.4	24.6	1.7	38.6	3.4	31.7	0.8	43.0	3.3
UK general population	44.1	2.1	56.3	4.0	47.5	2.0	44.4	4.2	39.2	5.3	45.2	3.3	26.1	6.0	48.0	1.9	37.3	6.1
UK health-conscious	64.5	6.2	46.4	3.7	50.9	3.3	45.0	10.6							47.5	3.3	77.2	10.6
Denmark	63.4	1.0	70.7	3.2	66.2	1.1	57.7	2.1										
Sweden[b]	39.3	0.9	45.1	1.5	42.6	0.9	35.3	1.6	33.0	2.4	36.9	1.7	38.9	2.3	40.4	0.8	44.1	2.3
Norway	59.8	1.1	70.2	2.8	62.0	1.2	60.9	2.1	57.1	1.9	60.8	1.5	68.7	4.5	60.8	1.1	79.5	5.6

Abbreviations: EPIC, European Prospective Investigation into Cancer and Nutrition; s.e., standard error.
[a]Results for self-reported health in the Netherlands are based on the Bilthoven centre only.
[b]Results for self-reported health in Sweden are based on the Umeå centre only.
If no figures are indicated, this means that strata were not sampled.

In most countries, the percentage of use was highest in one of the two oldest age groups (Tables 2a and b). There was an overall positive trend for use by age in men ($P = 0.01$), but not in women. The relation with age differed between countries. As only 26 Greek men reported dietary supplement use, the estimates for age groups are unstable, and data on Greek men were omitted from further analyses using adjusted data (Table 4a).

Most users took only one supplement, but 23.8% reported taking two and an additional 18.3% reported taking three or more different supplements. The participant with the highest consumption reported taking 17 different products. Of the 17 participants taking 10 or more supplements on the recalled day, 7 came from Oxford, 4 each from Denmark and Norway, and 1 each from Germany and Sweden.

Types of supplements used

As shown in Figure 1, vitamins were the category of supplements most frequently used by Greek men, Spanish men, Italian women, Germans, Dutch men, the UK health-conscious group and Swedish men. Minerals were the category of supplements most frequently used by women in Greece, Spain and France. MVMs were the category of supplements most frequently used by Dutch women and Danes. The supplements most frequently used by the UK general population and Norwegian women were oil based (e.g., cod liver oil). The category 'other supplements' concerned most frequently Italian men (mainly lecithin) and Swedish women (mainly multivitamins with ginseng and supplements of ubiquinone). The sum of vitamins, minerals and MVMs made up more than 50% (52–91%) of the supplements used in all countries, except the UK general population and Italian men. Except in the Scandinavian countries and both UK cohorts, oil-based supplements represented <5% of the supplements used. In most countries, herbs/plant-based supplements represented 8–17% of the products used, but no use was recorded in Greece.

When the three most frequently consumed supplement ingredients were examined, the picture differed slightly (Table 3): vitamins, particularly C, E and D, were the most frequently used ingredients in most countries. Among women, however, minerals, particularly calcium, were also often in the top three list of ingredients used. When all vitamin A components were added together (beta-carotene, other carotenoids, retinol and unspecified vitamin A), vitamin A was seen to be one of the most popular ingredients in the Netherlands (men), in the UK general population, among the UK health-conscious, in Denmark (men), Sweden and Norway (women). These results underestimate the use of ingredients of supplements when several units of the supplement are consumed on the same occasion (particularly drops), as each ingredient was counted only once per consumption occasion.

Comparing the number of users and the number of times the most frequently consumed supplement ingredients was used revealed differences of more than 20% (Table 3). For example, when vitamin C contributions from vitamins, MVMs, oils and other combination supplements were added up, there were 26% more records of vitamin C consumption among Danish women ($n = 1251$) than there were sole users of vitamin C ($n = 989$), which means that some participants supplemented their diet with the same nutrient from two or more different supplements.

Supplement use according to health and dietary variables

Table 4 shows how supplement use varied with dietary and health variables. In all countries, the mean percentage of supplement use was higher in those reporting a special diet on the recalled day than for other participants, except in UK health-conscious women. In Britain and the Scandinavian countries, there tended to be less use of dietary supplements on special days, but elsewhere no clear conclusion could be drawn. Data on self-reported health were collected in only a few countries. Although the mean frequency of use was higher in those reporting moderate/poor health, except in the UK general population, no clear pattern emerged.

In all cohorts, there were more supplement users among men with prevalent cancer than among men free of cancer at the time of the 24-HDR. In 7 of 10 cohorts, the mean percentage of use was higher among women with prevalent cancer than in cancer-free women. Neither diabetes nor heart attack (self-reported at baseline) affected the mean percentage of dietary supplement use for either gender (results not shown).

Discussion

In this large European comparative study, dietary supplement use varied markedly in frequency and type across countries. The mean percentage of dietary supplement use was higher in Northern than in Southern Europe, and was higher among women than among men, except in the UK health-conscious cohort, in which a similar consumption was observed for men and women. The mean frequency of use was higher in the older age groups, but a linear trend was observed only among men, although there was some heterogeneity between countries.

The geographical pattern was in line with results from the SENECA study, which focused on the elderly (Cruz *et al.*, 1991), but the mean levels in our study were somewhat higher. Given the methodological differences (e.g., type of question asked, age of study sample, representativeness) and the increasing use of supplements seen in many countries, this could be expected.

The types of supplements used differed between countries, although vitamins, minerals and/or MVMs dominated in most countries. Oil-based supplements were popular in Norway, Denmark and the United Kingdom. The differences in supplement types result most likely from cultural patterns. For example, in Norway, cod liver oil has traditionally been consumed as a part of diet, particularly in the northern coastal areas (Brustad *et al.*, 2004), and health authorities have recommended a daily consumption of cod liver oil supplements as an effective means of preventing vitamin D deficiency. A similar tradition existed in the United Kingdom and Denmark. Not surprisingly, minerals were more often used by women than by men. This can largely be ascribed to the use of iron and calcium supplements against anaemia and osteoporosis, respectively, which are more prevalent among women. Not all surveys report on the use of oil-based supplements or herbal remedies, for example, the SENECA study only reported on vitamins and minerals, and noted that vitamins were taken much more frequently than were mineral supplements (Cruz *et al.*, 1991; Brzozowska *et al.*, 2002). There is no commonly recognized way of classifying dietary supplements; hence, detailed comparisons of types of supplement used are difficult. Nevertheless, the overall results are comparable with results from studies in EPIC countries (Elmståhl *et al.*, 1994; Johansson *et al.*, 1997; Klipstein-Grobusch *et al.*, 1998; Food Standards Agency, 2002; Knudsen *et al.*, 2002; Ocké *et al.*, 2005; Reinert *et al.*, 2007).

In total, vitamins C, E and D were the most frequently consumed ingredients, reflecting the popularity of vitamins, MVMs and oils. When vitamin A components were added together, vitamin A was almost as frequently used as vitamin D. Vitamin E is often added to supplements as an antioxidant to preserve the supplement itself, for example, in oils, which contributed to its frequent consumption. A number of participants consumed the same ingredient from two or more supplements. Particularly for fat-soluble vitamins, which accumulate in the body, this raises questions regarding the risks of overdosing and potential negative effects of supplements (Palmer *et al.*, 2003; Timbo *et al.*, 2006; Mulholland and Benford, 2007).

We could not quantify the nutrient contents of the dietary supplements in this study. No dietary supplement database was available, and labelled values have limitations (Dwyer *et al.*, 2007), particularly if collected years after the original data collection. However, it is likely that the food-based intakes of minerals (Welch *et al.*, 2009), water-soluble vitamins (Olsen *et al.*, 2009), fat-soluble vitamins (Jenab *et al.*, 2009) and polyunsaturated fatty acids (Linseisen *et al.*, 2009) from the EPIC calibration study underestimate the actual total nutrient intakes, given that the contribution from supplements is not included. This concern is particularly strong for the Northern European countries in which the mean percentage of supplement use is high.

Some health variables seemed to be associated with dietary supplement use. Those who reported eating a special diet on the recalled day (often because of health-related conditions) generally had a higher mean frequency of supplement use than those who did not report a special diet. Some of these health conditions could require special diets to compensate for nutrient malabsorption or exclusion of certain foods, and also supplementation. It may be that those reporting supplement use and special diets are those who really manage to follow their doctor's advice and change their diet after experiencing health problems. More supplement use among people on special diets can also show a desire for control over one's own health, or self-medication (Conner *et al.*, 2001).

The mean percentage of supplement use was highest among those reporting moderate/poor health, except in the UK general population. In most countries, the differences between the various categories of health were not very large; hence, no strong conclusions should be drawn from this analysis. In addition, as the 24-HDRs took place up to 3 years after the baseline study, it is likely that information on self-reported health was no longer correct for some of the participants. Earlier studies showed mixed results (Wallström *et al.*, 1996; de Jong *et al.*, 2003; Brustad *et al.*, 2004).

Those who had prevalent cancer at the time of the 24-HDR (6.1%) reported a higher mean percentage of dietary supplement use than those who were free of cancer in most cohorts. Higher supplement use among cancer survivors is consistent with literature (Rock *et al.*, 2004; Molassiotis *et al.*, 2005; Skeie *et al.*, 2006; Velicer and Ulrich, 2008), despite the lack of evidence that it is an effective means of secondary (or primary) prevention of cancer (Bjelakovic *et al.*, 2004; Huang *et al.*, 2006; WCRF/AICR, 2007).

The definition of dietary supplements in this paper is broad, and was chosen because of the widespread use of non-vitamin-mineral supplements in some of the EPIC countries, and its official status regarding the current dietary supplement market in Europe (European Parliament and Council, 2002). During the 24-HDR, no particular definition was presented to the participants; hence, the interpretation of what constitutes a dietary supplement, and therefore whether and how it was reported, may have differed between countries, which could have introduced reporting bias. The question used to determine supplement consumption during the 24-HDR only specified vitamins; hence, it is possible that non-vitamin supplements have been under-reported. As the pre-defined, country-specific lists of supplements included more than just vitamins, this is not considered to be a major issue. In addition, training of the interviewers and the *post hoc* reclassification, which corrected items that were misreported, either as foods or supplements, should have minimized possible under-reporting. However, if in some countries certain items were systematically not reported, for example, because of lack of specification in the definition of supplements, no corrections could be made. Although supplement use was low in Greece, it is striking that none of the participants reported consumption of herbs/plant constituents. Some of the differences between the countries may be a consequence of the rather long period of data collection (5 years and 3 months in total), particularly if the increase in supplement use in Europe has taken place at different times or with different velocity in the participating countries. For example, the French 24-HDRs were completed

~2 years before those in Norway started. This does not, however, explain the 'extreme results'; data collection in Greece started as data collection ended in Denmark, but the intake was much lower in Greece than in Denmark (Riboli *et al.*, 2002; Slimani *et al.*, 2002).

As some medicines contain nutrients, for example, calcium in antacids, or consist of nutrients, for example, calcium for preventing osteoporosis, it was decided to include medicines with nutrients in the definition of supplements. Compared with other countries, the mean frequency of supplement use in France was higher because of their more comprehensive reporting of medicines. If categorization of supplements and medications differed among countries, it may have introduced bias.

A limitation of this study is that only one 24-HDR was available per subject, which means that investigation at the individual level was not possible as no appropriate reference period could be obtained for supplement use. This does not affect the estimates at the country level unless patterns of use are extremely different between countries, for example, if supplements in some countries are taken only on Mondays, whereas in other countries, consumption is spread equally over the week. However, it increases the variability in individual data, and makes it more difficult to observe clear trends. We do not know whether those we have labelled 'users' consumed supplements daily, weekly or even more infrequently. Furthermore, it is highly probable that some 'non-users' consumed supplements, just not every day. For supplements to affect nutritional status and health, in most cases, a relatively high frequency of use is necessary, and most supplements are designed for daily use. Other studies have found that supplement users differ from non-users in several identifiable and unidentifiable ways, including many health behaviours (Block *et al.*, 1994). It is likely that such differences exist not only for daily users but also for other regular users.

As the results regarding percentage of users in this study are similar to those reported in publications from local EPIC centres using baseline data, especially for men, the fact that only one recall was available does not seem to have limited our results much, although some discrepancies can be observed for Spain and Germany (Wallström *et al.*, 1996; Klipstein-Grobusch *et al.*, 1998; Pera *et al.*, 1999; Brustad *et al.*, 2004; Ocké *et al.*, 2005; Touvier *et al.*, 2006; Reinert *et al.*, 2007; Egeberg *et al.*, 2009). Moreover, in countries in which nationally representative data or other studies are available, the results are in the same range, although not all our participating cohorts were sampled from the general population (Johansson *et al.*, 1997; Food Standards Agency, 2002; Knudsen *et al.*, 2002; Ocké *et al.*, 2005). Consequently, it seems that differences in population sampling did not influence the representativeness of our results much. In some of the countries with a low mean frequency of use, very little literature exists with which to compare our results (e.g., Greece and Italy). Moreover, as noted earlier, a comparison between studies is very difficult because of different definitions and age ranges used. A confirmation of our results in a study representative of the general population, and with a longer frame of reference for supplement use would be welcome.

Conclusion

We presented a European comparison of dietary supplement use in an adult/elderly population using a common methodology across cohorts, and showed a clear north–south gradient in the mean percentage of dietary supplement use. In the United Kingdom, Denmark, Sweden and Norway, more than one-third of the participants had used supplements on the recalled day. Women had a higher consumption than men, and in most countries, the mean percentage of use was higher in older age groups. These results underline the need to combine information on nutrient intake from both foods and supplements in dietary research. In addition, as there was a considerable element of supplementation among foods in some of the countries, clear *a priori* definitions of what should be regarded as foods, supplements and medicines are needed for studies to obtain comparable results. We recommend that future studies include questions regarding dietary supplements in their food data collection, and attempt to quantify the risks and benefits for users of dietary supplements.

Conflict of interest

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