Dietary intakes and food sources of phenolic acids in the European Prospective Investigation into Cancer and Nutrition (EPIC) study

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Abstract

Phenolic acids are secondary plant metabolites that may have protective effects against oxidative stress, inflammation and cancer in experimental studies. To date, limited data exist on the quantitative intake of phenolic acids. We estimated the intake of phenolic acids and their food sources and associated lifestyle factors in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Phenolic acid intakes were estimated for 36 037 subjects aged 35–74 years and recruited between 1992 and 2000 in ten European countries using a standardised 24 h recall software (EPIC-Soft), and their food sources were identified. Dietary data were linked to the Phenol-Explorer database, which contains data on forty-five aglycones of phenolic acids in 452 foods. The total phenolic acid intake was highest in Aarhus, Denmark (1265·5 and 980·7 mg/d in men and women, respectively), while the intake was lowest in Greece (213·2 and 158·6 mg/d in men and women, respectively). The hydroxycinnamic acid subclass was the main contributor to the total phenolic acid intake, accounting for 84·6–95·3 % of intake depending on the region. Hydroxybenzoic acids accounted for 4·6–14·4 %, hydroxyphenylacetic acids 0·1–0·8 % and hydroxyphenylpropanoic acids ≤ 0·1 % for all regions. An increasing south–north gradient of consumption was also found. Coffee was the main food source of phenolic acids and accounted for 55·3–80·7 % of the total phenolic acid intake, followed by fruits, vegetables and nuts. A high heterogeneity in phenolic acid intake was observed across the European countries in the EPIC cohort, which will allow further exploration of the associations with the risk of diseases.

Key words: Phenolic acids: Dietary intakes: Food sources: European Prospective Investigation into Cancer and Nutrition

Phenolic acids are secondary plant metabolites widely spread throughout the plant kingdom[1]. Alongside the better-known flavonoids, they form one of the two major classes of dietary polyphenols. Chemically, phenolic acids are hydroxylated derivatives of benzoic, cinnamic, phenylacetic and phenylpropanoic acids. Hydroxycinnamic acids occur most frequently as simple esters with hydroxy carboxylic acids or sugars, whereas hydroxybenzoic acids are present mainly in glycosylated forms[2]. Most often, only low amounts of phenolic acids in the free form (aglycones) are found in foods. In nature, hundreds of phenolic acids have been identified, although only ninety (thirty-six aglycones) were found to be consumed by a French cohort[3]. They are most abundant in coffee, tea, red wine and some vegetables and fruits, especially berries[1].

Recent interest in phenolic acids stems from their potential protective role against oxidative stress, inflammation, diabetes and cancer in experimental studies[4–7]. However, very few epidemiological studies have evaluated the effects of dietary phenolic acids upon chronic diseases due to a lack of food composition data on these compounds[8]. Phenol-Explorer (www.phenol-explorer.eu) is a comprehensive food composition database (FCDB) on polyphenols, including phenolic acids, that has been available to the scientific community since 2009[9]. This FCDB enables researchers to more accurately assess the intake of phenols, their food sources and their potential effects on health, taking into account both the chemical structure of phenolic acids and their combination in glycosidic or ester forms.

To our knowledge, only three groups have assessed the dietary intake of phenolic acids. Using their own FCDB, German[10] and Finnish[11] studies estimated mean daily intakes of 222 and 641 mg of dietary phenolic acids (expressed as aglycones), respectively. Using Phenol-Explorer, the French cohort SUpplémentation en VItamines et Minéraux AntioXydants (SU.VI.MAX) estimated mean intakes of 599 mg/d (316 mg as aglycones/d) and 41 mg/d (40 mg as aglycones/d) for hydroxycinnamic acids and hydroxybenzoic acids, respectively[3]. It is difficult to determine whether these differences are due to different dietary and lifestyle patterns or to differences in the FCDB used. Therefore, the aim of the present study was to estimate the intake of phenolic acids and their main food sources across the ten European countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) study and across population subgroups using the same FCDB and dietary assessment tools.

Materials and methods

Study population

The EPIC is an ongoing multi-centre prospective cohort study involving twenty-three centres in ten European countries: Greece; Spain; Italy; France; Germany; The Netherlands; UK; Denmark; Sweden; Norway[12]. Over half a million subjects (29·5 % men) aged 20–85 years were enrolled between 1992 and 2000. Participants were mostly recruited from the general population within defined geographical areas, with some

exceptions: women who were members of a health insurance scheme for state school employees (France); women attending breast cancer screening (Utrecht, The Netherlands and Naples, Italy); mostly blood donors (some centres in Italy and Spain); mainly vegetarians (the 'health conscious' cohort in Oxford, UK). For the purpose of dietary analyses, the twenty-three administrative EPIC centres were redefined into twenty-seven geographical areas[13], of which nineteen included both male and female participants and eight recruited women only.

Data used in the present study were derived from the EPIC calibration study, in which a 24 h recall was administered. The cohort comprises an 8 % (*n* 36 994) age- and sex-stratified random sample, weighted according to the number of cancer cases expected over 10 years of follow-up[13]. After 957 exclusions due to an age restriction to 35–74 years or incomplete dietary information, 36 037 subjects were included in the present analysis. Approval for the study was obtained from ethical review boards of the International Agency for Research on Cancer (IARC) and from all local participating institutions. All participants provided written informed consent.

Dietary and lifestyle information

Dietary information was collected through a single 24 h recall using specialised software (EPIC-Soft)[14,15], which was developed to ensure standardisation of the interviews. All centres administered the interviews face to face, except in Norway where telephone interviews were conducted[16].

Data on other lifestyle factors, including educational level, anthropometry, physical activity (combining both occupation and leisure-time activities) and smoking history, were collected at baseline through standardised questionnaires and clinical examinations[12,13,17]. Data on age, as well as on body weight and height, were mostly self-reported by the participants during the 24 h recall interview. The mean time interval between these baseline measures and the 24 h recall interview varied by country, from 1 d to 3 years later[13].

Food composition database on phenolic acids

A food composition table was generated based on the mean content of individual phenolic acids in the Phenol-Explorer database and on the 24 h recall occurrences. Phenol-Explorer provides data on 502 polyphenol compounds in 452 plant-based foods[9], including data on 109 phenolic acids, of which forty-five are aglycones. They are distributed across four different subclasses: hydroxybenzoic acids (*n* 16); hydroxycinnamic acids (*n* 21); hydroxyphenylacetic acids (*n* 5); hydroxyphenylpropanoic acids (*n* 3). Total phenolic acid intake was calculated as the sum of the total intake of individual phenolic compounds using Phenol-Explorer food content values determined by chromatography without hydrolysis[9]. Intakes were expressed as aglycone equivalents (*n* 45) after the conversion of phenolic acid glycoside and ester contents into aglycone contents on the basis of their respective molecular weights. For phenolic acids linked to the food matrix, food content values obtained by chromatography after hydrolysis[9] were used; this applied to hydroxycinnamic acids in cereals, legumes and olives. In addition, when data obtained by chromatography without hydrolysis were unavailable, phenolic acid contents obtained by chromatography after hydrolysis were used.

Phenolic acid composition data for a small number of foods reported in the 24 h recall were absent from the Phenol-Explorer database and therefore obtained from scientific literature. These food items included honey, roasted chicory powder, orange and lemon peels, carob flour, mushrooms, okra seed pod, sweet potato, jujube, vanilla pod, seaweed and rose hip. A few more food items reported in the 24 h recall and expected to contain phenolic compounds (coconut, some liquors and spirits, hop, grapevine leaves, orgeat, pumpkin flower and some minor vegetable oils) were not available in the Phenol-Explorer database. However, the frequency of consumption or the polyphenol content of these foods was low and their contribution to phenolic acid intake was therefore considered minimal. Caffeic, ferulic, sinapic and *p*-coumaric acids in orange fruit were obtained by extrapolation from orange juice data. For some concentrated foods (e.g. tomato purée, tomato paste), dried foods (e.g. dried fruit, sun-dried tomato) and dehydrated foods (e.g. garlic and onion in powder) reported in the 24 h recall but not included in Phenol-Explorer, yield factors were applied to adjust for the gain or loss of moisture during food processing or cooking. The effect of cooking on phenolic acid content was not considered due to the paucity of data available. To estimate the phenolic acid contents of generic food items reported in the 24 h recall (e.g. fruit not specified), the profile of consumption of individual foods in that group and in each country was applied. Complex foods (e.g. cakes, sauces) were calculated as recipes taking into account the individual ingredients and their corresponding proportions as estimated from data available on the Internet.

Statistical analyses

Dietary phenolic acid intakes were calculated using generalised linear models and presented as means with their standard errors stratified by sex and the redefined centres, which are ordered geographically from south to north. These models were adjusted for age (continuous variable) and weighted by season and weekday of the 24 h recall to control for different distributions of participants across seasons and days of the recall. The contribution of each individual and subgroup of phenolic acids to the total intake was calculated as a percentage for each of the three European regions (south: all centres in Greece, Spain, Italy and the south of France; central: all centres in the north-east and north-west of France, Germany, The Netherlands and the UK; north: all centres in Denmark, Sweden and Norway). The contribution of each food group to the total phenolic acid intake by European region was also computed as a percentage.

Differences in phenolic acid intakes were compared using general linear models according to the categories of sex, age (35–44, 45–54, 55–64 and 65–74 years), BMI (<25, 25–30

and $> 30 \text{kg/m}^2$), European regions (south, central and north), educational level (none, primary completed, technical/professional, secondary school and university degree), smoking status (never smoker, current smoker and former smoker) and level of physical activity (inactive, moderately inactive, moderately active and active). All these models were adjusted for sex (categorical), age (years, continuous), centre (categorical), BMI (kg/m^2, continuous) and energy intake (kJ/d, continuous), and weighted by season and weekday. P values < 0.05 (two-tailed) were considered as significant. All analyses were conducted using SPSS Statistics software (version 19.0; SPSS, Inc.).

Results

Table 1 shows the centre-specific daily mean intakes of total and classes of phenolic acids, stratified by sex, adjusted for age and weighted for season and weekday of the 24 h recall. A south-to-north gradient in the mean intake of total phenolic acids and hydroxycinnamic acids was observed among the EPIC centres in both men and women. The highest total phenolic acid intake was observed in Aarhus, Denmark (1265·5 and 980·7 mg/d in men and women, respectively), whereas the lowest intake was in Greece (213·2 and 158·6 mg/d in men and women, respectively).

The main phenolic acid contributors were hydroxycinnamic acids (ranging from 84·6 % in the south region to 95·3 % in the north region), followed by hydroxybenzoic acids (ranging from 4·6 % in the north region to 14·4 % in the south region), hydroxyphenylacetic acids (ranging from 0·1 % in both central and north regions to 0·8 % in the south region) and, finally, hydroxyphenylpropanoic acids (≤ 0.1 % in all regions). The main hydroxybenzoic acid contributors were gallic acid, ellagic acid and 4-hydroxybenzoic acid. For hydroxycinnamic acids, the main contributors were caffeic acid and ferulic acid. Homovanillic and 4-hydroxyphenylacetic acids were the most abundant hydroxyphenylacetic acids, while the three hydroxyphenylpropanoic acid aglycones contributed in similar proportions.

Table 2 shows the evaluation of the relationship between sociodemographic, lifestyle and anthropometric characteristics and phenolic acid intakes adjusted for age, sex, centre, energy and BMI and weighted for season and weekday. Men had a statistically significant higher intake of total phenolic acids (540·2 *v.* 484·2 mg/d), hydroxycinnamic acids (491·8 *v.* 434·4 mg/d) and hydroxyphenylacetic acids (1·49 *v.* 1·14 mg/d) than women. There were no statistically significant differences in total hydroxybenzoic acid and hydroxyphenyl-propanoic acid intakes between sexes. Participants who were between 45 and 54 years had the highest intakes of total phenolic acids. A geographical gradient of increasing total phenolic acids, and hydroxycinnamic acids from south to north, was observed. The opposite geographical gradient was found for hydroxyphenylacetic acids and hydroxyphenyl-propanoic acids, whereas hydroxybenzoic acid intake was highest in the central region. Physically inactive individuals, current smokers, obese participants and those with a low level of education had higher intakes of phenolic acids and

hydroxycinnamic acids. However, for hydroxybenzoic acids, the opposite association was observed with BMI and level of education.

The main food sources of phenolic acid intake by European region were also studied (Table 3). Coffee was the most abundant food source of phenolic acids in all regions, with contributions ranging from 55 to 81 %. Other major food sources were fruits, nuts and seeds, some vegetables, and cereal and cereal products. For hydroxycinnamic acids, the main contributor was coffee, accounting for 67, 84 and 85 % in the south, central and north European regions, respectively. For hydroxybenzoic acids, the main food sources were tea in the central and north European regions, while in the south region, they were nuts and seeds. Other important contributors were wine, leafy vegetables and berries. For hydroxy-phenylacetic acids, the major food sources were olives, particularly in the south European region, beer and ciders, and wines. The most abundant sources of hydroxyphenylpro-panoic acids were olives and some condiments and sauces.

Table 4 shows the mean intakes of individual phenolic acids and their main food sources by European region, adjusted for sex and age and weighted by season and weekday. The most frequently consumed phenolic acids were caffeic acid (188·6–626·2 mg/d), ferulic acid (45·0–159·3 mg/d) and *p*-coumaric (11·7–17·9 mg/d) from coffee, gallic acid (15·8–33·5 mg/d) from tea and ellagic acid (3·7–12·8 mg/d) from nuts and berries.

Discussion

Estimating phenolic acid intake is the first step towards documenting the protective effects of these compounds against the risk of chronic diseases in epidemiological studies. This is the first study to assess the intake of phenolic acids across European countries. Moreover, the present study also shows the main food sources and associated factors of phenolic acid intakes using the same FCDB (Phenol-Explorer) and a common dietary assessment method (24 h recall).

Intake of total phenolic acids was the greatest in northern European countries, particularly Denmark, Sweden and Norway. In these countries, mean intake after adjustment was as much as five times higher than that of the lowest intake (Greece). Most of the phenolic acid intake in all regions was from hydroxycinnamic acids, in agreement with previous local studies[3,10,11]. The principal source of these in all regions was coffee, which contributes high levels of caffeic acid derived from as much as 150 mg chlorogenic acids/100 ml[18]. The high phenolic acid intake in Scandinavian and northern European countries is largely a consequence of high coffee consumption[19,20]. Southern European countries consume considerably less coffee, despite the apparent importance of coffee in Mediterranean culture. Ferulic acid, to a lesser extent, also contributes clearly to this difference in phenolic acid intake, with high intakes in the northern countries. As well as being present in coffee, this hydroxycinnamate is found complexed with hemicelluloses in high-fibre foods, and consequently, other important dietary sources are wheat bran, whole-grain flour and cereals[21]. Therefore,

Table 1. Adjusted* mean daily intakes of total and classes of phenolic acids by sex and centre ordered from south to north

(Mean values with their standard errors)

| | | Men | | | | | | | | | | | Women | | | | | | | | | | |
| | | Phenolic acids (mg/d) | | Hydroxy-benzoic acids (mg/d) | | Hydroxycin-namic acids (mg/d) | | Hydroxyphe-nylacetic acids (mg/d) | | Hydroxyphe-nylpropanoic acids (mg/d) | | | Phenolic acids (mg/d) | | Hydroxyben-zoic acids (mg/d) | | Hydroxycin-namic acids (mg/d) | | Hydroxyphe-nylacetic acids (mg/d) | | Hydroxyphe-nylpropanoic acids (mg/d) | |
Country and centre	n	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	n	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Greece	1314	213·2	12·4	29·8	2·9	175·6	12·2	7·11	0·19	0·70	0·03	1373	158·6	11·4	21·6	2·8	133·2	11·3	3·50	0·11	0·31	0·02
Spain																						
Granada	214	233·8	30·5	24·9	7·1	205·4	30·0	2·85	0·46	0·59	0·07	300	167·2	24·4	11·2	5·9	154·2	24·1	1·55	0·23	0·28	0·04
Murcia	243	229·3	28·6	40·8	6·6	181·6	28·2	5·95	0·43	0·92	0·07	304	196·1	24·3	23·2	5·9	169·2	23·9	3·12	0·23	0·53	0·04
Navarra	444	265·1	21·1	45·7	4·9	216·8	20·9	2·19	0·32	0·35	0·05	271	278·4	25·7	22·0	6·2	254·9	25·3	1·18	0·25	0·24	0·04
San Sebastian	490	227·1	20·3	45·4	4·7	179·4	20·0	1·91	0·30	0·31	0·05	244	259·7	27·1	27·6	6·5	231·1	26·7	0·80	0·26	0·20	0·05
Asturias	386	277·3	22·7	58·8	5·3	217·2	22·4	1·11	0·34	0·22	0·05	324	284·3	23·5	33·5	5·7	249·9	23·2	0·74	0·23	0·18	0·04
Italy																						
Ragusa	168	244·5	34·4	39·5	8·0	202·2	33·9	2·02	0·52	0·79	0·08	138	195·8	36·1	15·5	8·7	179·0	35·5	0·52	0·35	0·71	0·06
Naples												403	263·4	21·1	35·5	5·1	225·1	20·8	2·33	0·20	0·41	0·04
Florence	271	318·0	27·1	62·8	6·3	253·8	26·7	0·89	0·41	0·44	0·07	784	348·7	15·1	52·3	3·6	295·6	14·9	0·53	0·15	0·23	0·03
Turin	676	326·9	17·2	47·4	4·0	276·7	16·9	2·27	0·26	0·48	0·04	392	374·9	21·4	53·2	5·2	320·0	21·1	1·44	0·21	0·33	0·04
Varese	327	424·0	24·6	79·3	5·7	342·8	24·3	1·64	0·37	0·24	0·06	794	459·5	15·0	54·2	3·6	404·4	14·8	0·69	0·14	0·22	0·03
France																						
South coast												620	348·4	17·0	54·2	4·1	292·3	16·8	1·71	0·16	0·21	0·03
South												1425	367·3	11·2	67·4	2·7	299·2	11·1	0·66	0·11	0·09	0·02
North-east												2059	398·1	9·4	60·4	2·3	336·9	9·2	0·69	0·09	0·10	0·02
North-west												631	451·9	16·9	55·3	4·1	395·7	16·6	0·70	0·16	0·13	0·03
Germany																						
Heidelberg	1034	746·4	14·0	49·5	3·2	695·9	13·8	0·96	0·21	0·07	0·03	1087	647·4	13·0	49·1	3·1	597·7	12·8	0·52	0·12	0·12	0·02
Potsdam	1233	764·2	12·7	42·5	2·9	721·0	12·5	0·65	0·19	0·08	0·03	1061	642·5	13·0	30·8	3·1	611·5	12·9	0·23	0·13	0·04	0·02
The Netherlands																						
Bilthoven	1024	803·2	14·4	50·7	3·3	751·6	14·2	0·87	0·22	0·03	0·03	1086	674·7	13·1	45·9	3·1	628·4	12·9	0·39	0·13	0·03	0·02
Utrecht												1870	669·5	9·9	62·7	2·4	606·5	9·7	0·32	0·09	0·05	0·02
UK																						
General population	403	669·0	22·2	116·2	5·1	552·3	21·9	0·49	0·33	0·08	0·05	571	612·2	17·7	106·0	4·3	505·7	17·4	0·39	0·17	0·10	0·03
Health conscious	113	596·2	41·9	83·2	9·7	512·0	41·3	0·73	0·63	0·17	0·10	196	486·2	30·2	88·8	7·3	396·6	29·8	0·62	0·29	0·19	0·05
Denmark																						
Copenhagen	1356	1142·6	12·1	59·0	2·8	1082·3	11·9	1·14	0·18	0·12	0·03	1484	822·5	11·0	56·5	2·7	765·1	10·8	0·83	0·11	0·14	0·02
Aarhus	567	1265·5	18·7	52·1	4·3	1212·2	18·5	1·11	0·28	0·11	0·05	510	980·7	18·7	49·3	4·5	930·4	18·5	0·97	0·18	0·09	0·03
Sweden																						
Malmö	1421	861·4	12·5	30·9	2·9	829·9	12·3	0·44	0·19	0·12	0·03	1711	734·1	10·5	27·5	2·5	706·3	10·3	0·24	0·10	0·08	0·02
Umeå	1344	772·1	12·2	32·4	2·8	739·3	12·0	0·38	0·18	0·09	0·03	1574	635·3	10·7	28·9	2·6	605·8	10·5	0·42	0·10	0·09	0·02
Norway																						
South and east												1004	710·6	13·5	32·8	3·3	677·4	13·3	0·37	0·13	0·03	0·02
North and west												793	750·7	15·2	27·7	3·7	722·5	15·0	0·46	0·15	0·05	0·03

* Adjusted for age and weighted by season and day of recall.

Table 2. Adjusted* mean daily intakes of total and classes of phenolic acids by sex and selected characteristics

(Mean values with their standard errors)

Stratification variables	n	Phenolic acids (mg/d)			Hydroxybenzoic acids (mg/d)			Hydroxycinnamic acids (mg/d)			Hydroxyphenylacetic acids (mg/d)			Hydroxyphenylpropanoic acids (mg/d)		
		Mean	SE	P	Mean	SE	P	Mean	SE	P	Mean	SE	P	Mean	SE	P
Sex (n)				<0.001			0.213			<0.001			<0.001			0.259
Men	13 028	540.21	4.76		46.68	1.13		491.81	4.70		1.49	0.06		0.23	0.01	
Women	23 009	484.15	3.46		48.39	0.82		434.40	3.42		1.14	0.04		0.22	0.01	
Age (years)				<0.001			0.004			<0.001			0.001			<0.001
35−44	3335	520.59	7.94		41.44	1.89		477.52	7.85		1.36	0.10		0.28	0.02	
45−54	12 595	541.46	4.27		47.34	1.02		492.64	4.22		1.26	0.05		0.23	0.01	
55−64	14 940	501.10	4.08		48.16	0.97		451.47	4.03		1.26	0.05		0.21	0.01	
65−74	5167	463.47	6.88		49.96	1.64		411.67	6.81		1.61	0.08		0.24	0.01	
European region†				<0.001			<0.001			<0.001			<0.001			<0.001
South	11 285	289.21	4.26		43.67	0.99		242.75	4.20		2.42	0.05		0.36	0.01	
Central	12 988	632.59	4.06		55.16	0.94		576.61	4.00		0.73	0.05		0.09	0.01	
North	11 764	841.90	4.16		36.94	0.97		804.25	4.10		0.62	0.05		0.10	0.01	
BMI (kg/m²)				<0.001			<0.001			<0.001			0.075			0.156
< 25	16 854	497.96	4.09		49.56	0.97		446.86	4.04		1.31	0.05		0.23	0.01	
25 to <30	13 766	523.91	4.11		47.67	0.98		474.65	4.06		1.36	0.05		0.23	0.01	
≥ 30	5417	525.26	6.27		40.39	1.49		483.49	6.20		1.17	0.08		0.21	0.01	
Level of schooling				<0.001			<0.001			<0.001			0.011			0.176
None	1709	520.37	12.30		48.28	2.91		470.06	12.15		1.82	0.15		0.22	0.02	
Primary completed	10 469	538.93	4.87		42.83	1.15		494.58	4.81		1.30	0.06		0.21	0.01	
Technical/professional	8038	508.88	5.65		45.32	1.34		462.11	5.59		1.22	0.07		0.22	0.01	
Secondary school	7152	496.83	5.69		48.46	1.35		446.86	5.63		1.28	0.07		0.24	0.01	
University degree	8155	501.77	5.36		55.08	1.27		445.16	5.30		1.30	0.06		0.24	0.01	
Smoking status				<0.001			0.001			<0.001			<0.001			0.002
Never smoker	17 483	458.79	3.93		47.64	0.94		409.76	3.89		1.18	0.05		0.21	0.01	
Former smoker	10 288	498.97	4.63		49.94	1.11		447.35	4.58		1.43	0.06		0.25	0.01	
Current smoker	7726	641.57	5.26		44.21	1.26		595.72	5.20		1.41	0.06		0.23	0.01	
Physical activity				0.017			0.231			0.005			0.295			0.098
Inactive	7463	501.82	5.37		46.67	1.32		453.56	5.29		1.36	0.07		0.24	0.01	
Moderately inactive	11 969	493.68	4.37		49.84	1.07		442.28	4.31		1.34	0.05		0.23	0.01	
Moderately active	8400	484.38	5.15		49.52	1.27		433.30	5.08		1.32	0.06		0.24	0.01	
Active	6380	479.67	5.92		49.21	1.46		428.71	5.84		1.48	0.07		0.27	0.01	

* Adjusted for sex, age, energy intake and BMI and weighted by season and day of recall. P values are for overall differences in mean consumption by the general linear model among the sociodemographic, lifestyle and anthropometric subgroups.

† European region: south (all centres in Greece, Spain, Italy and the south of France); central (all centres in the north-east and north-west of France, Germany, The Netherlands and the UK); north (all centres in Denmark, Sweden and Norway).

Table 3. Major food sources of total and classes of dietary phenolic acids in the south, central and north European regions*†

Food groups and foods	Phenolic acids (%)			Hydroxybenzoic acids (%)			Hydroxycinnamic acids (%)			Hydroxyphenylacetic acids (%)			Hydroxyphenylpropanoic acids (%)		
	South	Central	North	South	Central	North	South	Central	North	South	Central	North	South	Central	North
Potatoes and other tubers	2·7	1·9	1·8	0·0	0·0	0·0	3·2	2·1	1·9	0·0	0·0	0·0	0·0	0·0	0·0
Vegetables	7·1	2·6	1·1	13·4	8·2	4·1	6·0	2·0	0·9	0·1	0·0	0·0	0·2	0·0	0·0
Leafy vegetables	3·1	1·3	0·0	9·4	5·7	0·2	2·1	0·9	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Fruiting vegetables	2·2	0·4	0·1	0·3	0·1	0·1	2·5	0·4	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Root vegetables	0·6	0·4	0·5	1·2	1·3	3·1	0·5	0·3	0·3	0·0	0·0	0·0	0·0	0·0	0·0
Cabbages	0·2	0·1	0·1	0·3	0·3	0·2	0·2	0·1	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Grain vegetables	0·2	0·1	0·1	0·0	0·0	0·0	0·2	0·1	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Onion, garlic	0·1	0·0	0·0	0·4	0·1	0·2	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Sprout vegetables	0·3	0·1	0·0	1·0	0·4	0·0	0·1	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Other vegetables	0·5	0·2	0·2	0·8	0·3	0·3	0·4	0·2	0·2	0·1	0·0	0·0	0·2	0·0	0·0
Legumes	1·3	0·2	0·1	0·1	0·0	0·0	1·5	0·2	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Fruits, nuts and seeds	18·0	4·8	2·0	49·1	19·7	8·9	11·6	3·2	1·6	90·6	60·0	50·4	77·1	62·2	38·1
Citrus fruit	1·2	0·3	0·2	0·1	0·1	0·1	1·3	0·3	0·2	0·0	0·0	0·0	0·0	0·0	0·0
Apple and pear	3·5	1·2	0·8	0·7	1·1	1·8	4·0	1·2	0·7	0·0	0·0	0·0	0·0	0·0	0·0
Grape	0·1	0·0	0·0	0·0	0·0	0·0	0·1	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Stone fruits	3·3	1·1	0·3	0·0	0·0	0·0	3·8	1·2	0·4	0·0	0·0	0·0	0·0	0·0	0·0
Berries	1·1	0·9	0·3	7·0	8·9	4·1	0·1	0·1	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Banana	0·0	0·0	0·0	0·2	0·4	0·7	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Kiwi	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Other fruits	0·1	0·0	0·0	0·1	0·0	0·0	0·1	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Nuts and seeds	5·4	0·9	0·2	34·5	8·5	1·2	0·2	0·2	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Olives	3·5	0·3	0·1	6·4	0·7	0·9	1·9	0·2	0·1	90·6	60·0	50·4	77·1	62·2	38·1
Dairy products	0·2	0·2	0·0	0·6	1·4	0·4	0·1	0·1	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Cereal and cereal products	4·7	5·5	8·7	0·9	2·5	8·6	5·4	5·8	8·7	0·2	0·1	0·0	3·5	0·0	17·1
Meat and meat products	0·0	0·0	0·0	0·0	0·0	0·1	0·0	0·0	0·0	0·0	0·0	0·0	0·5	2·0	6·5
Fish and shellfish	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Egg and egg products	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Fat	0·3	0·0	0·1	0·1	0·0	0·1	0·3	0·0	0·1	0·4	0·1	0·1	0·0	1·5	0·0
Sugar and confectionery	0·6	0·4	0·4	2·6	2·4	5·3	0·3	0·3	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Cakes and biscuits	1·2	0·7	0·3	2·7	1·6	1·8	0·9	0·6	0·3	0·0	0·0	0·0	0·0	0·0	1·1
Non-alcoholic beverages	58·2	81·3	83·7	13·5	52·2	51·5	66·9	84·3	85·4	0·0	0·3	0·0	0·0	0·0	0·0
Juices	0·5	1·1	0·4	0·1	2·2	0·1	0·6	0·9	0·4	0·0	0·3	0·0	0·0	0·0	0·0
Carbonated drinks	0·0	0·0	0·1	0·0	0·0	0·0	0·0	0·0	0·1	0·0	0·0	0·0	0·0	0·0	0·0
Coffee	55·3	75·0	80·7	0·4	0·9	1·9	65·8	82·5	84·6	0·0	0·0	0·0	0·0	0·0	0·0
Tea	2·2	5·0	2·6	13·0	49·1	49·4	0·3	0·6	0·3	0·0	0·0	0·0	0·0	0·0	0·0
Herbal tea	0·2	0·1	0·0	0·0	0·1	0·0	0·3	0·1	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Alcoholic beverages	4·9	2·0	1·7	15·6	11·0	18·4	3·0	1·1	0·9	7·0	39·1	46·7	0·0	0·0	0·0
Wine	4·6	1·1	1·1	14·4	6·0	11·1	2·8	0·6	0·6	6·1	14·1	19·9	0·0	0·0	0·0
Beer and ciders	0·3	0·8	0·6	1·1	4·7	7·0	0·2	0·4	0·3	0·8	24·4	26·4	0·0	0·0	0·0
Spirits	0·0	0·0	0·0	0·1	0·0	0·1	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0
Cocktails, punches	0·0	0·0	0·0	0·0	0·2	0·2	0·0	0·0	0·0	0·0	0·5	0·4	0·0	0·0	0·0
Condiments and sauces	0·4	0·1	0·1	0·6	0·2	0·3	0·3	0·1	0·1	1·7	0·3	2·7	18·1	20·6	16·8
Soups, bouillons	0·4	0·2	0·1	0·9	0·4	0·5	0·3	0·2	0·1	0·0	0·0	0·0	0·1	11·1	20·4
Soya products	0·0	0·0	0·0	0·0	0·1	0·0	0·0	0·0	0·0	0·1	0·0	0·0	0·5	2·7	0·0

* Values are percentages derived from models adjusted for centre, age and sex, and weighted by season and day of recall.
† European region: south (all centres in Greece, Spain, Italy and the south of France); central (all centres in the north-east and north-west of France, Germany, The Netherlands and the UK); north (all centres in Denmark, Sweden and Norway).

Table 4. Adjusted* intakes of individual phenolic acids (mg/d) in the European Prospective Investigation into Cancer and Nutrition cohort and their main food sources by European region†

(Mean values with their standard errors)

Classes and compounds	Region						Main food contributors (%)‡
	South		Central		North		
	Mean	SE	Mean	SE	Mean	SE	
Hydroxybenzoic acids							
2,3-Dihydroxybenzoic acid	0·069	0·001	0·041	0·001	0·055	0·001	Wine (97·8%), cocktails and punches (1·1%), fruit juices (0·6%), sauces (0·3%)
2,4-Dihydroxybenzoic acid	0·004	0·002	0·011	0·002	0·001	0·002	Fruit juices (60·2%), olives (28%), berries (10·3%), sauces (0·8%)
2,6-Dihydroxybenzoic acid	0·035	0·003	0·149	0·002	0·140	0·003	Beer and cider (99·5%), olives (0·5%)
2-Hydroxybenzoic acid	0·139	0·008	0·377	0·008	0·345	0·008	Beer and cider (77·7%), wine (14·2%), citrus fruit (4·2%), spices and herbs (1·4%)
3,5-Dihydroxybenzoic acid	0·011	0·001	0·049	0·001	0·046	0·001	Beer and cider (100%)
3-Hydroxybenzoic acid	0·011	0·001	0·049	0·001	0·044	0·001	Beer and cider (96·8%), fruit juices (2·7%), berries (0·5%)
4-Hydroxybenzoic acid	2·595	0·044	4·422	0·042	4·306	0·043	Beer and cider (24·8%), root vegetables (19·0%), berries (12·1%), coffee (9·0%)
Benzoic acid	0·003	0·178	1·175	0·170	0·080	0·175	Fruit juices (85·3%), berries (14·7%)
Gallic acid	15·847	0·478	33·512	0·458	22·739	0·471	Tea (72·6%), wine (11·5%), chestnuts (6·7%), leafy vegetables (4·2%)
Gentisic acid	0·902	0·018	0·975	0·017	0·907	0·017	Wine (78·7%), apple and pear (13·4%), beer and cider (4·1%), cocktails and punches 82·6%)
Protocatechuic acid	3·287	0·066	2·918	0·063	1·477	0·065	Leafy vegetables (35·4%), olives (%17·6), bread, crispbread and rusks (8·8%), wine (7·8%)
Syringic acid	3·427	0·065	1·815	0·062	2·118	0·064	Bread, crispbread and rusks (21·0%), leafy vegetables (19·8%), olives (%13·4), apple and pear (11·9%)
Vanillic acid	1·717	0·021	1·807	0·020	2·533	0·020	Bread, crispbread and rusks (33·3%), olives (%13·9), wine (12·2%), beer and cider (9·0%)
Ellagic acid	12·837	0·541	8·878	0·519	3·706	0·533	Chestnuts (29·5%), berries (29·2%), tree nuts (13·8%), jam and syrups (12·1%)
Valoneic acid dilactone	2·076	0·091	1·019	0·088	0·160	0·090	Tree nuts (90·2%), nuts and seeds n.s. (7·3%), cakes and pastries (2·5%)
Gallagic acid	0·000	0·000	0·000	0·000	0·000	0·000	
Hydroxycinnamic acids							
5-Caffeoylquinic acid	0·000	0·001	0·001	0·001	0·000	0·001	Fruit juices (100%)
Avenanthramide 2c	0·002	0·001	0·007	0·001	0·015	0·001	Flours and semolinas (47·9%), bread, crispbread and rusks (18·9%), soups (18·0%), pasta, rice, other grains (3·7%)
Avenanthramide 2p	0·002	0·001	0·007	0·001	0·012	0·001	Flours and semolinas (50·2%), bread, crispbread and rusks (17·5%), soups (16·2%), pasta, rice, other grains (4·1%)
Avenanthramide K	0·000	0·000	0·000	0·000	0·004	0·000	Soups (39·8%), bread, crispbread and rusks (32·8%), flours and semolinas (25·2%), non-chocolate confectionery (2·3%)
Caffeic acid	188·646	3·551	458·428	3·405	626·237	3·499	Coffee (90·1%), potatoes (2·8%), apple and pear (1·5%), stone fruits (1·2%)
Caffeoyl aspartic acid	0·124	0·010	0·124	0·010	0·236	0·009	Chocolates (52·9%), cream desserts and puddings (16·6%), chocolate milkshakes (14·4%), cakes and pastries (10·4%)
Cinnamic acid	0·735	0·054	0·244	0·052	0·160	0·053	Olives (61·9%), berries (14·7%), other fruits (8·1%), coffee (7·9%)
Hydroxycaffeic acid	0·001	0·000	0·000	0·000	0·000	0·000	Vegetable oils (68·6%), sauces (18·6%), bread, crispbread and rusks (4·5%), soups (2·0%)
m-Coumaric acid	0·382	0·008	0·119	0·008	0·094	0·008	Olives (85·8%), beer and cider (11·3%), sauces (1·5%), breakfast cereals (0·5%)
o-Coumaric acid	1·208	0·032	1·009	0·031	1·457	0·031	Breakfast cereals (30·8%), olives (29·5%), beer and cider (12·6%), grain and pod vegetables (8·4%)
p-Coumaric acid	11·685	0·118	16·079	0·113	17·877	0·116	Coffee (39·2%), wine (11·9%), stone fruits (6·1%), apple and pear (5·8%)
p-Coumaroyl tyrosine	0·000	0·000	0·000	0·000	0·000	0·000	
5-Feruloylquinic acid	0·000	0·000	0·001	0·000	0·001	0·000	Berries (76·3%), cakes and pastries (23·7%)

Table 4. *Continued*

Classes and compounds	South Mean	South SE	Central Mean	Central SE	North Mean	North SE	Main food contributors (%)‡
				Region			
Avenanthramide 2f	0·003	0·001	0·023	0·001	0·022	0·001	Cream desserts and puddings (31·7 %), bread, crispbread and rusks (30·5 %), flours and semolinas (20·8 %), soups (6·5 %)
Ferulic acid	44·990	0·778	106·287	0·746	159·258	0·766	Coffee (54·4 %), bread, crispbread and rusks (27·5 %), breakfast cereals (2·5 %), fruit juices (1·4 %)
Isoferulic acid	0·001	0·000	0·001	0·000	0·000	0·000	Sauces (58·2 %), condiments (40·4 %), cakes and pastries (0·2 %), fish and fish products (0·2 %)
Sinapic acid	3·336	0·044	2·616	0·042	2·593	0·043	Olives (19·4 %), beer and cider (14·7 %), cabbages (13·9 %), legumes (13·1 %)
5-5′-Dehydrodiferulic acid	0·209	0·012	0·107	0·012	0·107	0·012	Bread, crispbread and rusks (45·5 %), pasta, rice, other grains (42·1 %), cakes and pastries (3·1 %), flours and semolinas (2·9 %)
5-8′-Benzofuran dehydrodiferulic acid	0·149	0·011	0·151	0·011	0·372	0·011	Pasta, rice, other grains (59·1 %), bread, crispbread and rusks (25·4 %), cakes and pastries (4·2 %), flours and semolinas (3·8 %)
5-8′-Dehydrodiferulic acid	0·269	0·015	0·123	0·015	0·147	0·015	Bread, crispbread and rusks (54·1 %), pasta, rice, other grains (34·5 %), cream desserts and puddings (3·2 %), flours and semolinas (2·9 %)
8-*O*-4′-Dehydrodiferulic acid	0·255	0·018	0·232	0·018	0·715	0·018	Bread, crispbread and rusks (59·7 %), pasta, rice, other grains (29·9 %), flours and semolinas (2·5 %), cream desserts and puddings (2·5 %)
Hydroxyphenylacetic acids							
3,4-Dihydroxyphenylacetic acid	0·096	0·002	0·021	0·002	0·015	0·002	Olives (98·6 %), sauces (1·1 %), mixed salad (0·2 %), vegetable oils (0·1 %)
4-Hydroxyphenylacetic acid	0·366	0·005	0·255	0·005	0·253	0·005	Wine (45·4 %), olives (27·4 %), beer and cider (23·4 %), vegetable oils (1·1 %)
Homovanillic acid	1·913	0·043	0·500	0·041	0·378	0·042	Olives (92·2 %), beer and cider (5·8 %), sauces (1·8 %), vegetable oils (0·1 %)
Homoveratric acid	0·001	0·000	0·000	0·000	0·000	0·000	Olives (95·8 %), sauces (2·6 %), vegetable oils (1·2 %), cakes and pastries (0·2 %)
Methoxyphenylacetic acid	0·084	0·002	0·018	0·002	0·013	0·002	Olives (97·4 %), sauces (2·6 %)
Hydroxyphenylpropanoic acids							
3,4-Dihydroxyphenyl-2-oxypropanoic acid	0·078	0·005	0·035	0·005	0·058	0·005	Spices and herbs (48·4 %), soups (17·5 %), bread, crispbread and rusks (9·1 %), sauces (7·6 %)
Dihydrocaffeic acid	0·133	0·003	0·030	0·003	0·021	0·003	Olives (99·2 %), sauces (0·6 %), mixed salad (0·2 %)
Dihydro-*p*-coumaric acid	0·157	0·004	0·035	0·003	0·025	0·004	Olives (98·9 %), sauces (0·9 %), mixed salad (0·2 %)

n.s., Not specified.

* Adjusted for sex and age, and weighted by season and day of recall.

† European region: south (all centres in Greece, Spain, Italy and the south of France); central (all centres in the north-east and north-west of France, Germany, The Netherlands and the UK); north (all centres in Denmark, Sweden and Norway).

‡ Four main food sources for each phenolic acid; a lower number indicates the absence of other food sources.

another contributory factor could be the greater consumption of whole-grain bread, crisp bread and breakfast cereals in northern European countries than in southern Europe[22], which often contain a relatively high proportion of wheat bran. The third most consumed hydroxycinnamate was *p*-coumaric acid, primarily provided by fruits, nuts and spices, although its intake was minor in relation to that of caffeic and ferulic acids.

Even in southern European countries, hydroxycinnamic acids were by far the greatest contributor to the total phenolic acid intake, although the percentage contribution tended to be lower than that in northern Europe, due to lower coffee consumption[19]. Hydroxybenzoic acids, whose principal dietary sources are tea, wine and rosaceous fruits, constituted 14·4% of total phenolic acids in the southern region, yet the contribution of nuts, seeds and fruit vegetables to total hydroxybenzoic acids was the greatest here. Intake of hydroxyphenylacetic and hydroxyphenylpropanoic acids was higher in the southern region than in the northern and central regions. Hydrophenylacetic acids in the southern region were represented mainly by homovanillic acid (77·8%). This is found primarily in olives and olive oils, whose consumption is more frequent in southern European diets. Hydroxyphenylpropanoic acids were the least consumed phenolic acids in all regions, although significantly more were consumed in the southern region than in the northern and central regions. Again, this difference may be attributed to a greater consumption of olives and olive oils in the southern region.

Men from the EPIC cohort had higher phenolic acid intakes overall than women after adjustment for age, centre, energy and BMI, in agreement with the Finnish[11], but inconsistent with the findings of the German study[10]. A greater intake of hydroxycinnamic acids was largely responsible for the higher phenolic acid intake among men, which reflects a greater coffee consumption overall in European men than in women. Phenolic acid and hydroxycinnamic acid intakes were also related to health-detrimental lifestyle characteristics. Lack of exercise, smoking and obesity, as well as a low level of education, were linked to higher intakes among the study subjects. This is consistent with previous findings where coffee consumption was strongly associated with smoking and a less health-conscious lifestyle[23]. In sharp contrast, subjects who had consumed greater amounts of hydroxybenzoic acids (through main dietary sources such as tea, wine and fruit) tended to exercise more, smoke less and avoid obesity.

Over a decade ago, it was proposed that phenolic acids contributed approximately to one-third of total polyphenol intake[24], with flavonoids accounting for the remaining two-thirds. This was expected to vary considerably as a function of coffee consumption, with heavy coffee consumers ingesting a greater proportion of polyphenols as phenolic acids. As detailed databases on polyphenol composition were not available at this time, this hypothesis was generated by roughly estimating the flavonoid and phenolic acid contents of typical diets, based on the polyphenol compositions of commonly consumed food and beverage items. In the present study, the mean adjusted phenolic acid intake across all European countries was 512 mg/d. A recent study on the EPIC cohort,

using Phenol-Explorer food composition data, indicated a mean flavonoid intake of 372 mg/d in Europe[25]. Therefore, we can estimate that 58% of polyphenols are ingested as phenolic acids on average across Europe. Again, this proportion varies along the north–south axis from 44% in countries bordering the Mediterranean Sea to 66% in the northern and central European countries.

To date, this is the largest study describing phenolic acid intake across several countries of diverse dietary habits. The use of a single FCDB and a standardised 24 h recall allowed reliable comparisons among countries to be drawn. However, as not all the EPIC cohorts are representative of their respective countries, the observed level of intake cannot be extrapolated to the general population of each region. In addition, for some demographic groups, profiles of phenolic acid intake could be very different from those observed in the EPIC. For example, phenolic acid intake would be quite different for children, as well as for adults who consume little or no tea and coffee. Another limitation of the present study could be possible inaccuracies in estimations due to the variation in the methods of preparation of some foods between countries. In the case of coffee, larger volumes are undoubtedly consumed in northern Europe, but the strength of a typical brew is thought to vary considerably from country to country and larger volumes might be offset by a weaker average brew[26,27]. Moreover, Phenol-Explorer contains data on raw foods only, although many processes, such as cooking and peeling, can cause variable losses in the concentrations of polyphenols[2,28]. Therefore, vegetables and cereals might overestimate their contribution to phenolic acid intake, although these were not the most important food sources in the present study. Further underestimation may arise due to the omission of dietary supplements in this analysis. However, there are few consumers of herb or plant supplements in the present study (up to 5% in Denmark, the highest consumer country) and supplements containing phenolic acid are not commonly consumed[29]. Despite these limitations, Phenol-Explorer is currently the most extensive FCDB on phenolic acids. A compilation of new data on the effects of food processing and cooking on polyphenol content in foods is in progress, and these data should further enrich the Phenol-Explorer database and the accuracy of polyphenol intake estimations. Therefore, the present estimations of phenolic acid intake might be revised when more data become available.

In conclusion, the present study presents the most extensive description so far of both total and individual phenolic acid intakes and their food sources across the ten European countries. Phenolic acids account for the major fraction of the total polyphenols ingested through Western diets in all European countries examined. Coffee is the main food source of phenolic acids. Differences in the nature and amount of the individual phenolic acids consumed are observed between countries along a north–south gradient, mainly due to the differences found in the consumption of phenolic acid-rich foods, particularly coffee. These differences were shown to be related to sociodemographic, anthropometric and lifestyle factors. More epidemiological studies on

phenolic acids should be undertaken to explore links with the risk of chronic diseases.

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