British Journal of Nutrition (2012), **108**, 1095–1108 doi:10.1017/S0007114511006386

Intake estimation of total and individual flavan-3-ols, proanthocyanidins and theaflavins, their food sources and determinants in the European Prospective Investigation into Cancer and Nutrition (EPIC) study

Viktoria Knaze[1], Raul Zamora-Ros[1]*, Leila Luján-Barroso[1], Isabelle Romieu[2], Augustin Scalbert[2], Nadia Slimani[2], Elio Riboli[3], Caroline T. M. van Rossum[4], H. Bas Bueno-de-Mesquita[4,5], Antonia Trichopoulou[6,7], Vardis Dilis[6,7], Konstantinos Tsiotas[6], Guri Skeie[8], Dagrun Engeset[8], J. Ramón Quirós[9], Esther Molina[10,11], José María Huerta[11,12], Francesca Crowe[13], Elisabet Wirfäl[14], Ulrika Ericson[14], Petra H. M. Peeters[3,15], Rudolf Kaaks[16], Birgit Teucher[16], Gerd Johansson[17], Ingegerd Johansson[18], Rosario Tumino[19], Heiner Boeing[20], Dagmar Drogan[20], Pilar Amiano[11,21], Amalia Mattiello[22], Kay-Tee Khaw[23], Robert Luben[23], Vittorio Krogh[24], Eva Ardanáz[11,25], Carlotta Sacerdote[26], Simonetta Salvini[27], Kim Overvad[28], Anne Tjønneland[29], Anja Olsen[29], Marie-Christine Boutron-Ruault[30,31], Guy Fagherazzi[30,31], Florence Perquier[30,31] and Carlos A. González[1]

[1]*Unit of Nutrition, Environment and Cancer, Cancer Epidemiology Research Programme, Catalan Institute of Oncology (ICO-IDIBELL), Avda Gran Via 199-203 08907 L'Hospitalet de Llobregat, Barcelona, Spain*
[2]*Dietary Exposure Assessment Group, International Agency for Research on Cancer (IARC), Lyon, France*
[3]*Department of Epidemiology and Biostatistics, School of Public Health, Faculty of Medicine, Imperial College London, London, UK*
[4]*National Institute of Public Health and the Environment (RIVM), Bilthoven, The Netherlands*
[5]*Department of Gastroenterology and Hepatology, University Medical Center Utrecht (UMCU), Utrecht, The Netherlands*
[6]*WHO Collaborating Center for Food and Nutrition Policies, Department of Hygiene, Epidemiology and Medical Statistics, University of Athens Medical School, Athens, Greece*
[7]*Hellenic Health Foundation, Athens, Greece*
[8]*Department of Community Medicine, University of Tromsø, Tromsø, Norway*
[9]*Public Health and Health Planning Directorate, Asturias, Spain*
[10]*Andalusian School of Public Health, Granada, Spain*
[11]*CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain*
[12]*Department of Epidemiology, Murcia Regional Health Authority, Murcia, Spain*
[13]*Cancer Epidemiology Unit, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK*
[14]*Department of Clinical Sciences in Malmö, Nutrition Epidemiology, Lund University, Malmö, Sweden*
[15]*Julius Center, University Medical Center Utrecht, Utrecht, The Netherlands*
[16]*Department of Cancer Epidemiology, German Cancer Research Center, Heidelberg, Germany*
[17]*Department of Clinical Medicine and Public Health/Nutritional Research, Umeå University, Umeå, Sweden*
[18]*Department of Odontology/Cariology, Umeå University, Umeå, Sweden*
[19]*Cancer Registry and Histopathology Unit, "Civile M.P. Arezzo" Hospital, Ragusa, Italy*
[20]*Department of Epidemiology, German Institute of Human Nutrition Potsdam-Rehbrücke, Nuthetal, Germany*
[21]*Public Health Division of Gipuzkoa, Institute Investigation BioDonostia, Basque Government, San Sebastian, Spain*
[22]*Department of Clinical and Experimental Medicine, Federico II University, Naples, Italy*
[23]*School of Clinical Medicine, University of Cambridge, Cambridge, UK*
[24]*Nutritional Epidemiology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*
[25]*Navarre Public Health Institute, Pamplona, Spain*
[26]*Center for Cancer Prevention (CPO-Piemonte), and Human Genetic Foundation (HuGeF), Torino, Italy*
[27]*Molecular and Nutritional Epidemiology Unit, ISPO Cancer Prevention and Research Institute, Florence, Italy*

Abbreviations: 24-HDR, 24 h dietary recall; EPIC, European Prospective Investigation into Cancer and Nutrition; FCDB, food composition database; MED, Mediterranean; PA, proanthocyanidins; USDA, US Department of Agriculture.

* **Corresponding author:** R. Zamora-Ros, fax +34 932607787, email rzamora@iconcologia.net

[28]*Department of Epidemiology, School of Public Health, Aarhus University, Aarhus, Denmark*
[29]*Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen, Denmark*
[30]*INSERM, Centre for Research in Epidemiology and Population Health, U1018, Institut Gustave Roussy, F-94805 Villejuif, France*
[31]*Paris South University, UMRS 1018, F-94805 Villejuif, France*

(Submitted 27 July 2011 – Final revision received 13 October 2011 – Accepted 22 October 2011 – First published online 20 December 2011)

Abstract

Epidemiological studies suggest health-protective effects of flavan-3-ols and their derived compounds on chronic diseases. The present study aimed to estimate dietary flavan-3-ol, proanthocyanidin (PA) and theaflavin intakes, their food sources and potential determinants in the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration cohort. Dietary data were collected using a standardised 24 h dietary recall software administered to 36 037 subjects aged 35–74 years. Dietary data were linked with a flavanoid food composition database compiled from the latest US Department of Agriculture and Phenol-Explorer databases and expanded to include recipes, estimations and retention factors. Total flavan-3-ol intake was the highest in UK Health-conscious men (453·6 mg/d) and women of UK General population (377·6 mg/d), while the intake was the lowest in Greece (men: 160·5 mg/d; women: 124·8 mg/d). Monomer intake was the highest in UK General population (men: 213·5 mg/d; women: 178·6 mg/d) and the lowest in Greece (men: 26·6 mg/d in men; women: 20·7 mg/d). Theaflavin intake was the highest in UK General population (men: 29·3 mg/d; women: 25·3 mg/d) and close to zero in Greece and Spain. PA intake was the highest in Asturias (men: 455·2 mg/d) and San Sebastian (women: 253 mg/d), while being the lowest in Greece (men: 134·6 mg/d; women: 101·0 mg/d). Except for the UK, non-citrus fruits (apples/pears) were the highest contributors to the total flavan-3-ol intake. Tea was the main contributor of total flavan-3-ols in the UK. Flavan-3-ol, PA and theaflavin intakes were significantly different among all assessed groups. This study showed heterogeneity in flavan-3-ol, PA and theaflavin intake throughout the EPIC countries.

Key words: **Flavan-3-ols: Proanthocyanidins: Theaflavins: Intake: European Prospective Investigation into Cancer and Nutrition-Europe**

Flavan-3-ols or flavanols, terms used interchangeably, are compounds that belong to a polyphenol subclass called flavonoids, which share a common C6–C3–C6 skeleton. Flavan-3-ols are perhaps the most structurally complex in the flavonoid subclass ranging from simple monomers (such as catechin and its isomer epicatechin) to oligomers (from dimers to decamers), polymers ($>$10mers) and other derived compounds (e.g. theaflavins and thearubigins). The oligo and polymers of flavan-3-ols are also referred to as condensed tannins or proanthocyanidins (PA), named for their ability to yield anthocyanidins when heated in acidic media[1]. Enzymatic and non-enzymatic oxidation of (gallo)catechins, reactions characteristic of green tea fermentation, results in flavanol-derived compounds: theaflavins and high-molecular-weight thearubigins[1,2]. Being much larger molecules, PA and flavanol-derived compounds tend to be less bioavailable and have different functional properties; therefore they are often considered as separate groups of flavonoids[1,3]. Although their average degree of polymerisation can be estimated, the structures of some high-molecular weight polymers of PA and of most of the thearubigins have not been well defined due to inadequate analytical methods[1].

Flavan-3-ol monomers are found ubiquitously in plants as secondary metabolites[4]. Flavan-3-ol monomers are most abundant in fruits (e.g. berries, apples/pears, stone fruits), barley, cocoa beans, nuts[5] and their derived products[6]. Gallocatechins are found, almost exclusively, in green tea infusions[2,7] while flavanol-derived compounds, theaflavins and thearubigins, are abundant in fermented black and oolong teas[2]. Common PA-rich foods are cocoa, berries, nuts and some raw beans[5,8]. Transformations and losses of some flavonoid compounds during processing and cooking are common and vary for different subclasses and even for the individual compounds[9–11].

Total and individual compounds of flavan-3-ols have been studied extensively *in vitro* for their antioxidant, anti-inflammatory, immunomodulator and anti-carcinogenic effects[12–14]. A plethora of human intervention studies currently available strongly suggests beneficial effects on human health, particularly the effects of flavan-3-ol-rich foods, such as tea, cocoa and chocolate[7,15,16]. Intervention studies involving various PA-rich sources such as red wine, grape, pomegranate, chocolate and cranberry juice showed numerous positive effects on antioxidant, CVD and endothelial maintenance biomarkers[3]. Given the limited reported bioavailability of PA, particularly those having a high degree of polymerisation ($>$3)[17], the observed action of PA-rich foods in the body, with the exception of perhaps the intestinal lumen, may be attributed to flavan-3-ol monomers, which are systematically associated to PA and comprise 5–25 % in these foods, or to other yet unidentified PA[3,18]. Furthermore, PA may also exert their action after their degradation by the colonic microbiota and subsequent absorption[19]. Indeed, two Italian case–control studies suggested inverse associations between PA, but not flavan-3-ol monomer, intake and gastric and colorectal cancers[20,21]. Furthermore, the inverse association augmented with increasing degrees of polymerisation of PA in colorectal cancer cases[20] despite their observed

British Journal of Nutrition

decrease in absorption. Further research, particularly in prospective studies, on individual flavan-3-ol and PA compounds is clearly needed to clarify and confirm these potential effects.

Total intake of any nutrients is usually related to sex, cultural, lifestyle and socio-economic factors that may affect accessibility to and habitual consumption of health-promoting foods. Studies in European Prospective Investigation into Cancer and Nutrition (EPIC) Spain and the USA found significant differences in total flavonoid intake between sexes and among different age groups, socio-economic levels and ethnic groups[22,23]. Therefore, these factors need to be taken into consideration when looking into associations of these compounds and their dietary sources in disease prevention. To our knowledge, there are few data on individual flavan-3-ol intakes in the European population. The present study aims to evaluate total, subclasses and individual dietary intake of flavan-3-ols and their main food sources by EPIC centre and geographical region, while taking into account lifestyle, anthropometric and socio-demographic factors.

Materials and methods

Study population

EPIC is an ongoing prospective cohort study designed to investigate the associations between diet, lifestyle and cancer throughout ten Western European countries: Denmark, France, Germany, Greece, Italy, Norway, Spain, Sweden, The Netherlands and UK[24]. The cohort includes approximately 366 000 women and 153 000 men, most of them aged 35–74 years, who were enrolled between 1992 and 2000 by twenty-three centres. Some differences in methods of recruitment exist between centres. Part of the Oxford (UK) cohort was recruited from subjects who consumed a vegetarian-type diet. This was designated a 'Health-conscious' group and shall be distinguished from the UK General population cohort which is a combined group of the UK Cambridge and UK Oxford general population. The female part of the cohort in Florence (Italy) and Utrecht (The Netherlands) is composed of women who underwent breast cancer screening. The French cohorts recruited women only, but from the members of the health insurance scheme for the state-school employees. The centres in Italy and Spain recruited mostly blood donors. For the purpose of dietary consumption patterns analysis, the initial twenty-three centres were later redefined by geographical areas into twenty-seven centres[25]. The calibration subsample of the EPIC cohort study composed of 36 994 subjects (8 % of the whole EPIC cohort), who were recruited to be a random sample stratified by age, sex and centre, and weighted for expected cancer cases in each stratum of the main EPIC cohort study, was considered herein. After exclusion of 945 subjects under 35 or over 74 years of age because of low participation in these age categories, and sixteen subjects without baseline dietary data, a total of 36 037 subjects were included. Approval for the study was obtained from the ethical review boards of all local recruiting research institutions. All participants provided written informed consent.

Measurements of diet and other lifestyle factors

Dietary intake was measured with a standardised 24 h dietary recall (24-HDR) administered via a computerised interview programme (EPIC-SOFT) developed specifically for the EPIC calibration study[25,26]. The 24-HDR was administered in a face-to-face interview, except in Norway where it was obtained by telephone[27]. A detailed description of the rationale and methodology of the 24-HDR calibration study in the EPIC cohort has been described elsewhere[24,28–30]. Data on socio-demographic and lifestyle factors, including educational level, physical activity and smoking history were collected at baseline through standardised questionnaires and clinical examinations for the calibration sample[31–34]. Age as well as body weight and height were self-reported by the participants during the 24-HDR interview. The mean time interval between these baseline questionnaire measures and the 24-HDR interview varied by country, from 1 d to 3 years[24].

Flavonoid Food Composition Database

The US Department of Agriculture (USDA) released a PA database in 2004 and an updated flavonoid database in 2007, with more analytical values for raw, cooked, canned and commercially processed foods[35,36]. In the process of combining the two USDA databases, we observed data duplicity of the monomers. Since flavan-3-ols monomers (USDA database on flavonoids)[35] and PA monomers (USDA database on PA)[36] are the same molecules, the PA monomer data was removed. We expanded these databases with analytical values from the Phenol-Explorer database released in 2009[37]. Approximately, 6·5 and 0·6 % of our database came from USDA and Phenol-Explorer, respectively. Thus far, these databases are the most complete and updated databases on flavonoids/polyphenols and they evaluate and compile the most worldwide food composition data published. We further expanded our EPIC-specific food composition database (FCDB) by estimating values for foods not present in either of the two databases, but that had occurred in the 24-HDR. Therefore, for our FCDB, we calculated estimated values (92·9 %) including logical zeros (25·3 %), estimations based on similar food items (22·5 %), application of retention factors (27·7 %) and recipes (17·3 %). When there were no analytical data provided for cooked foods by either USDA or Phenol-Explorer, retention factors were applied. The retention factors reported in various foods were between 42 and 74 % for catechins and 0 and 95 % for tannins[38]. Therefore, to simplify and homogenise the calculations, we used the same retention factors for all flavonoids, as in our previous studies[23,39,40]. They were 70, 35 and 25 % after frying, cooking in a microwave oven and boiling, respectively[41]. The final FCDB created contained a total of 1877 food items. The unknown composition values, without any analytical or estimated data, were calculated as a zero by default and ranged from 2 % (theaflavin gallates) to 16 % (epicatechin-3-gallates). Finally, the 24-HDR food items were linked with the expanded flavonoid FCDB using an *ad hoc* SQL (Structured Query Language) application.

Statistical methods

General linear modelling was used for the calculation of the adjusted daily mean (least squared) intake and standard error using SPSS (version 17.0.0, SPSS, Inc.) for total flavan-3-ols, their individual compounds and subgroups. The mean intake was adjusted for age, weighted by season and day of 24-HDR and stratified by EPIC centre and age. Flavan-3-ol monomers as aglycones included: catechin, epigallocatechin, epicatechin, epicatechin-3-gallate, epigallocatechin-3-gallate, gallocatechin and catechin-3-gallate. PA were divided into the following subgroups: dimers, trimers, 4–6mers, 7–10mers and >10mers (polymers). Theaflavins included compounds: theaflavin, theaflavin-3,3′-digallate, theaflavin-3′-gallate and theaflavin-3-gallate. Although present in the USDA database, due to the extensive limitations in analytical methods currently employed to identify and quantify thearubigins, we did not include them in our analysis of total flavan-3-ols[1,41]. Epigallocatechin, epicatechin-3-gallate, epigallocatechin-3-gallate, gallocatechin and catechin-3-gallate were later combined into a single group called '(epi)gallocatechins' due to the resemblance among the chemical structures. Flavan-3-ol monomer, PA and theaflavin intakes are calculated as the sum of the individual compounds or subgroups and expressed in mg/100 g of fresh weight. During the analysis of the related factors and of the main food sources, EPIC centres were combined by geographical regions into a Mediterranean (MED) region (Greece, Italy, Spain and South of France) and non-MED (non-MED) region (France other than the South centre, Germany, The Netherlands, Norway, Denmark and Sweden). The UK General population cohort and the Health-conscious cohort presented similar intakes for flavan-3-ols and their food sources but markedly different from all others; therefore, in the socio-demographic analysis they were kept as a separate UK region. The contribution of each food and food group to the total and individual intake of flavan-3-ols was calculated as a percentage. The general linear modelling was also used in the comparison of the mean intakes by socio-demographic, anthropometric and lifestyle factors, adjusting for age, region, energy intake and BMI, and weighted for season and day of 24-HDR. P values $<0{\cdot}05$ indicated significance.

Results

A south-to-north gradient in the daily mean intake of total and monomers of flavan-3-ols and of theaflavins was observed among EPIC centres in both men and women (Table 1). The highest total flavan-3-ol intake was observed in the UK Health-conscious men (453·6 mg/d) and in women of the UK General population cohort (377·6 mg/d). The lowest total intake was observed in Greek men (160·5 mg/d) and women (124·8 mg/d). Flavan-3-ol monomer intake was the highest in the UK General population (213·5 mg/d in men, 178·6 mg/d in women) and the lowest in Greece (26·6 mg/d in men, 20·7 mg/d in women). Theaflavin intake was the highest in the UK General population for both men (29·3 mg/d) and women (25·3 mg/d). Daily theaflavin intake was close to 0 mg in Greece and in Spanish and southern Italian centres (Ragusa, Naples and Florence). In contrast, daily intake of total PA was the highest in Spanish centres (455·2 mg in men from Asturias and 237·9 mg in women from San Sebastian), followed by men in Turin (Italy) and women in Asturias (Spain), respectively. However, PA intake was the lowest in Greece (134·6 mg/d in men and 101·0 mg/d in women). Intake amounts of the individual flavan-3-ols, theaflavins and of PA subgroups are presented in Annexes 1 and 2. PA subclass, particularly the group of polymers (>10mers), was the highest contributor to the total flavan-3-ol intake (Table 2). Flavan-3-ol monomers were the second highest contributors to the total intake, providing contribution of between 18·6 % in the MED region and 44·9 % in the UK. Catechins and epicatechins, equally, were the main single-compound contributors in the MED region, while in the non-MED and UK regions it was the epigallocatechin-3-gallate monomers. Theaflavins were the lowest contributors to the total flavan-3-ol intake. The four theaflavin compounds contributed almost equally to the total theaflavins in all three regions.

Non-citrus fruit, particularly apples/pears, was the most important food source of total flavan-3-ols in the MED (56·2 %) and non-MED (34·1 %) regions (Table 3). Wine and then tea were the other two major sources of flavan-3-ols in these two regions. On the other hand, tea (51·3 %) was the most prominent source of total flavan-3-ols in the UK, followed by non-citrus fruit (19·9 %) and wine (6·1 %). The major food sources of catechins and epicatechins in all three regions were tea, non-citrus fruits and wine; however, chocolate candy/bars were also noteworthy dietary contributors. Tea was the lone source of theaflavins and a major source of (epi)gallocatechins in all three regions (77·7 % in the MED, 90·5 % in the non-MED and 95·1 % in the UK region). The principal dietary source of total PA in the MED region was non-citrus fruit (62·3 %) followed by wine (17·3 %) and chocolate candy/bars (4·6 %). Non-citrus fruits were also the main source of PA in the non-MED and UK regions, but their contributions were smaller (48·0 and 37·2 %, respectively). In the non-MED region, wine was the second most important source (12·6 %), followed by chocolate/candy (6·6 %) and tea (5·0 %). Whereas in the UK region, the secondary sources of PA were tea (15·0 %), wine (10·0 %), cakes/pies/pastries/puddings (7·6 %) and pulses (7·1 %).

Sex-stratified analysis of the related factors showed similar results; therefore the data are presented for men and women combined (Table 4). Total flavan-3-ol intake and also the intake stratified by monomers, PA and theaflavins were shown to significantly vary between the geographical regions. The intake of flavan-3-ol monomers and theaflavins in the UK region was almost 4-fold and over 16-fold that of the MED region, respectively. Conversely, PA intake was significantly higher in the MED region (217·2 mg/d) compared to the non-MED (177·9 mg/d) and the UK (198·4 mg/d) regions. After adjusting for BMI and energy, women had significantly higher intakes of total flavan-3-ols and their subclasses. The intake of total flavan-3-ols and their subclasses was significantly different between the age groups, being the highest

Table 1. Adjusted* daily mean intakes (mg/d) of total and subgroups of flavan-3-ols in men and women by European Prospective Investigation into Cancer and Nutrition centre ordered from south to north

(Mean values with their standard errors)

	Men									Women								
		Total flavan-3-ols		Monomers†		PA		Theaflavins‡			Total flavan-3-ols		Monomers†		PA		Theaflavins‡	
Country and centre	*n*	Mean	SE	Mean	SE	Mean	SE	Mean	SE	*n*	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Greece	1314	160·5	7·6	26·6	3·0	134·6	6·9	0·3	0·3	1373	124·8	7·4	20·7	2·9	101·0	6·5	0·6	0·3
Spain																		
Granada	214	279·4	18·7	41·7	7·3	221·8	22·7	0·6	1·1	300	151·7	15·8	20·5	6·2	132·3	15·4	0·1	0·8
Murcia	243	279·9	17·5	43·3	6·9	235·8	18·9	0·3	0·9	304	184·2	15·7	24·6	6·2	159·3	18·1	0·2	0·9
Navarra	444	286·2	13·0	40·1	5·1	235·2	15·5	0·0	0·8	271	180·6	16·6	21·1	6·5	164·1	18·2	0·0	0·9
San Sebastian	490	422·9	12·4	49·1	4·9	357·3	15·5	0·0	0·8	244	267·8	17·5	30·6	6·9	237·9	18·9	0·5	0·9
Asturias	386	498·3	13·9	54·7	5·5	455·2	14·9	0·1	0·7	324	286·3	15·2	33·6	6·0	236·8	15·6	0·3	0·8
Italy																		
Ragusa	168	317·5	21·1	53·9	8·3	239·6	28·8	0·4	1·4	138	235·4	23·3	37·3	9·2	193·7	27·1	0·4	1·4
Naples										403	217·4	13·6	36·9	5·4	204·6	14·4	0·4	0·7
Florence	271	382·7	16·6	61·1	6·5	325·5	18·4	0·7	0·9	784	264·3	9·8	54·5	3·8	209·5	11·3	1·0	0·6
Turin	676	435·3	10·5	73·6	4·1	370·8	11·9	0·6	0·6	392	303·6	13·8	66·6	5·4	228·2	19·4	1·5	1·0
Varese	327	379·9		77·2	5·9	258·7	23·5	1·4	1·2	794	276·4	9·7	70·4	3·8	192·4	9·9	1·7	0·5
France																		
South coast										620	251·5	11·0	66·1	4·3	181·6	9·3	5·2	0·5
South										1425	290·7	7·2	82·6	2·8	201·5	6·3	8·0	0·3
North-East										2059	290·2	6·0	78·6	2·4	210·0	5·3	7·3	0·3
North-West										631	281·4	10·9	83·7	4·3	185·9	9·8	8·8	0·5
Germany																		
Heidelberg	1034	301·6	8·5	88·3	3·3	207·6	15·9	6·6	0·8	1087	321·9	8·4	107·5	3·3	175·9	21·7	4·1	1·1
Potsdam	1233	277·1	7·8	72·0	3·1	209·7	8·7	4·3	0·4	1061	261·5	8·4	59·9	3·3	187·8	12·2	2·9	0·6
The Netherlands																		
Bilthoven	1024	220·6	8·6	77·8	3·4	128·1	20·8	10·4	1·0	1086	233·8	8·4	85·9	3·3	118·2	20·5	11·4	1·0
Utrecht										1870	286·8	6·3	114·6	2·5	159·0	5·4	16·0	0·3
UK																		
General population	403	439·6	13·6	213·5	5·4	217·1	12·8	29·3	0·6	571	377·6	11·4	178·6	4·5	172·9	10·5	25·3	0·5
Health-conscious	113	453·6	25·7	156·1	10·1	277·6	25·9	27·4	1·3	196	368·9	19·5	148·8	7·7	201·4	19·2	21·1	1·0
Denmark																		
Copenhagen	1356	325·5	7·4	96·0	2·9	229·6	11·2	9·7	0·6	1484	319·4	7·1	102·1	2·8	205·4	10·2	11·0	0·5
Aarhus	567	312·7	11·5	85·7	4·5	295·7	23·7	5·6	1·2	510	347·7	12·1	92·5	4·8	218·5	22·8	8·9	1·1
Sweden																		
Malmö	1421	242·3	7·4	103·9	2·9	143·7	7·4	3·1	0·4	1711	235·3	6·7	98·9	2·6	140·7	5·6	3·1	0·3
Umeå	1344	287·4	7·5	113·9	2·9	171·8	7·8	3·7	0·4	1574	271·3	6·9	108·9	2·7	160·7	6·6	3·7	0·3
Norway																		
South and East										1004	298·9	8·7	85·2	3·4	218·2	8·7	6·6	0·4
North and West										793	289·2	9·8	70·5	3·8	232·0	9·9	4·9	0·5

PA, proanthocyanidins.
* Adjusted for age and weighted by season and day of recall.
† Sum of catechin, epicatechin and epicatechin 3-gallate, epigallocatechin 3-gallate, gallocatechin and catechin-3-gallate.
‡ Sum of theaflavin, theaflavin-3′-gallate, theaflavin-3 gallate and theaflavin-3,3′-digallate.

Table 2. Percentage contribution* of individual and subclasses of flavan-3-ols to subclass and total intake in the European Prospective Investigation into Cancer and Nutrition cohort by European region

	Region					
	MED countries		Non-MED countries		UK	
Class and compound	Class (%)	Total (%)	Class (%)	Total (%)	Class (%)	Total (%)
Flavan-3-ol monomers	100·0	18·6	100·0	32·9	100·0	44·9
(+)-Catechin	30·0	5·6	17·6	5·8	12·4	5·6
(−)-Epigallocatechin	9·4	1·7	13·8	4·5	17·5	7·9
(−)-Epicatechin	30·1	5·6	17·8	5·8	12·6	5·7
(−)-Epicatechin 3-gallate	7·4	1·4	11·9	3·9	13·6	6·1
(−)-Epigallocatechin 3-gallate	17·0	3·2	26·8	8·8	21·2	9·5
(+)-Gallocatechin	1·7	0·3	3·0	1·0	4·7	2·1
(+)-Catechin 3-gallate	4·3	0·8	9·1	3·0	18·1	8·1
PA or condensed tannins	100·0	80·8	100·0	64·8	100·0	48·8
PA dimers	19·1	15·4	20·7	13·4	28·9	14·1
PA trimers	6·8	5·5	7·2	4·7	7·8	3·8
PA 4–6mers	22·5	18·2	20·6	13·4	19·0	9·2
PA 7–10mers	16·7	13·5	15·0	9·7	13·6	6·6
PA polymers (>10mers)	34·9	28·2	36·4	23·6	30·7	15·0
Theaflavins	100·0	0·6	100·0	2·4	100·0	6·4
Theaflavin	26·0	0·2	26·0	0·6	25·9	1·6
Theaflavin-3,3′-digallate	29·1	0·2	29·2	0·7	29·2	1·9
Theaflavin-3′-gallate	22·7	0·1	22·6	0·5	22·7	1·4
Theaflavin-3-gallate	22·2	0·1	22·2	0·5	22·3	1·4

MED, Mediterranean; Non-MED, non-Mediterranean; PA, proanthocyanidins.
* Values are percentages derived from models adjusted for sex, age and weighted by season and day of recall.

in the 55- to 64-year-olds. It also increased with the level of education completed and the level of physical activity. On the other hand, current smokers and obese participants (BMI $\geq 30\,kg/m^2$) had the lowest intakes of total flavan-3-ols and their subclasses.

Discussion

To our knowledge, this is the only study thus far assessing the intake of total and flavan-3-ol monomers, PA and flavan-3-ol-derived compounds as well as their food sources and associated factors in all twenty-seven EPIC centres of ten European countries using a common expanded flavonoid FCDB and dietary assessment method (24-HDR). Our results show a wide range of total flavan-3-ol intakes following a south-to-north geographical gradient. When stratified by regions, total flavan-3-ol intake in the UK was about 2-fold that of the MED region. This relatively steep gradient in flavan-3-ol intake was mainly due to higher intakes of theaflavins and epigallocatechins in northern EPIC cohorts; indeed the main source of these subclasses of flavan-3-ols was found to be tea. On the other hand, PA intake was found to be statistically higher in the MED region, although large differences were also noted among centres within the same region. The main source of PA in the MED region was non-citrus fruit, chiefly apples and pears, followed by wine, similar to what was previously reported for the EPIC Spanish cohort[23]. Furthermore, the almost-nil intake of theaflavins in Greece, Spain and southern Italy indicates minimal consumption of tea in these countries. Even so, the major sources identified for the total and individual flavanols, PA and theaflavins were quite similar except in the UK where pulses also formed a considerable food source of PA.

A well-established inverse geographical gradient of CVD mortality exists[42], which may seem paradoxical with the north-to-south gradient for flavan-3-ol intake and the observed beneficial effects of these compounds and flavonoid-rich foods against CVD[13,15,16]. Though far-fetched at this point to imply that flavan-3-ols have a significant role in CVD, a few factors could be considered to help elucidate this. Despite their higher observed antioxidant activity *in vitro*[43,44], galloylated flavan-3-ol monomers (mainly found in fermented/black teas) have lower bioavailability than non-galloylated monomers[3,44] (found more commonly in non-citrus fruit, green tea and cocoa). However, it is more likely that other risk factors of CVD may be more prevalent in the northern countries, such as high intake of SFA[45], low intake of MUFA[46], low intake of fruits and vegetables[47], low wine consumption[48], sedentary lifestyle[49,50] and social class influences[51].

The present study also demonstrated that statistical differences exist in flavan-3-ol intakes among groups with different socio-demographic, anthropometric and lifestyle characteristics. Consumption of total flavan-3-ols, monomers and PA increased with age up to about 64 years of age and then it fell slightly. Similar results were seen in Spanish-EPIC[23], US[8,22] and Australian[52] studies in adults. The intakes were significantly higher in former and never smokers. Since the major sources were tea and fruits, respectively, this suggests possible interaction between the consumption of these food sources and smoking habits[53,54]. Additionally, two case–control studies suggested that a flavonoid-rich diet may protect against pancreatic and lung cancer in smokers only[55,56]. Total flavan-3-ol intakes have been shown to be significantly associated with a slower increase of BMI in women in The Netherlands Cohort Study after adjusting for confounders

Table 3. Major food sources of dietary flavan-3-ols, their monomers, proanthocyanidins (PA) and theaflavins in the Mediterranean (MED), non-Mediterranean (non-MED) and UK regions*

	Total flavan-3-ols (%)			Monomers (%)			Catechins (%)			Epicatechins (%)			EGC (%)†			PA (%)			Theaflavins (%)‡		
Food groups and foods	MED	Non-MED	UK	MED	Non-MED	UK	MED	Non-MED	UK	MED	Non-MED	UK	MED	Non-MED	UK	Med	Non-MED	UK	MED	Non-MED	UK
Coffee, tea, herbal teas	8·2	28·8	51·8	36·5	69·2	83·7	5·8	19·4	47·7	7·7	26·1	41·8	81·9	93·7	96·4	1·2	5·0	15·0	100·0	100·0	100·0
Coffee	0·0	0·2	0·1	0·2	0·5	0·3	0·0	0·0	0·0	0·4	1·4	1·3	0·3	0·4	0·2	0·0	0·0	0·0	0·0	0·0	0·0
Tea	7·9	28·0	51·3	34·7	66·8	82·6	5·6	19·1	47·5	7·3	24·7	40·4	77·7	90·5	95·1	1·2	5·0	15·0	100·0	100·0	100·0
Herbal tea	0·3	0·6	0·4	1·6	1·9	0·8	0·1	0·3	0·2	0·0	0·1	0·0	4·0	2·8	1·1	0·0	0·0	0·0	0·0	0·0	0·0
Wine	17·4	10·2	6·1	18·1	6·3	2·8	41·0	24·5	15·8	18·6	11·4	7·7	0·8	0·2	0·1	17·3	12·6	10·0	0·0	0·0	0·0
Beer, cider	3·4	3·1	3·2	2·1	3·6	1·3	5·9	16·5	3·9	0·9	2·5	0·6	0·2	0·6	1·0	3·7	3·0	5·5	0·0	0·0	0·0
Milk beverages	0·0	0·1	2·4	0·0	0·0	2·3	0·0	0·1	4·2	0·0	0·1	12·4	0·0	0·0	0·3	0·0	0·1	2·9	0·0	0·0	0·0
Fruit and vegetable juices	0·5	2·3	0·9	0·3	1·4	0·4	0·3	2·0	0·7	0·6	6·0	2·5	0·0	0·0	0·1	0·5	2·8	1·5	0·0	0·0	0·0
Carbonated/soft/isotonic drinks, diluted syrups	0·0	2·2	0·2	0·0	0·2	0·0	0·0	0·7	0·1	0·0	0·3	0·1	0·0	0·1	0·0	0·0	3·3	0·3	0·0	0·0	0·0
Fruit	56·2	34·1	19·9	31·8	10·2	4·8	38·1	24·2	18·9	54·9	29·1	17·9	9·0	1·6	0·5	62·3	48·0	37·2	0·0	0·0	0·0
Apple and pear	33·0	21·8	11·5	17·2	5·7	2·1	11·1	6·0	2·0	38·2	22·6	13·5	5·4	1·0	0·3	36·8	31·0	22·0	0·0	0·0	0·0
Stone fruits	13·9	4·7	2·7	8·8	1·4	0·6	15·1	4·0	2·4	11·3	3·4	1·7	2·2	0·2	0·1	15·2	6·6	5·1	0·0	0·0	0·0
Grape	5·0	2·3	2·0	3·5	0·9	0·5	5·8	2·6	2·3	4·4	1·9	1·7	1·0	0·2	0·1	5·4	3·1	3·7	0·0	0·0	0·0
Berries	3·1	3·4	2·0	0·7	0·6	0·3	1·6	2·6	1·5	0·3	0·7	0·4	0·3	0·1	0·1	3·7	4·9	3·9	0·0	0·0	0·0
Banana	0·3	0·7	0·8	1·2	1·4	1·2	3·9	8·3	10·0	0·0	0·0	0·0	0·0	0·0	0·0	0·1	0·4	0·6	0·0	0·0	0·0
Citrus fruit	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	0·0	0·0	0·0	0·0	0·0	0·0
Kiwi	0·2	0·1	0·1	0·1	0·0	0·0	0·0	0·0	0·0	0·2	0·1	0·1	0·0	0·0	0·0	0·3	0·2	0·1	0·0	0·0	0·0
Other fruits	0·7	1·1	0·8	0·3	0·2	0·1	0·6	0·6	0·7	0·5	0·4	0·4	0·1	0·0	0·0	0·7	1·7	1·7	0·0	0·0	0·0
Chocolate candy/bars, paste, confetti	4·7	5·7	3·2	5·6	4·2	1·3	3·5	4·6	2·1	9·2	12·2	5·7	4·3	2·0	0·5	4·6	6·6	5·5	0·0	0·0	0·0
Cakes, sweet pies, pastries, puddings	2·3	3·1	3·4	2·4	1·9	1·3	1·7	3·1	2·9	5·0	8·3	7·5	2·2	1·3	0·8	3·1	5·8	7·6	0·0	0·0	0·0
Pulses	1·8	0·5	3·5	0·2	0·0	0·1	0·5	0·2	0·7	0·1	0·0	0·1	0·0	0·0	0·0	2·2	0·7	7·1	0·0	0·0	0·0
Cereal and cereal products	0·1	0·6	1·1	0·1	0·1	0·2	0·1	0·4	0·7	0·1	0·3	0·5	0·0	0·0	0·0	2·1	3·8	3·5	0·0	0·0	0·0
Soups	0·0	2·8	0·0	0·0	0·3	0·0	0·0	1·1	0·0	0·0	0·4	0·0	0·0	0·0	0·0	0·0	4·3	0·0	0·0	0·0	0·0
Other foods and beverages	5·4	6·5	4·3	2·9	2·6	1·8	3·0	3·3	2·2	2·9	3·4	3·2	1·5	0·6	0·4	3·0	3·9	3·9	0·0	0·0	0·0

EGC, (epi)gallocatechins.
* Values are percentages derived from models adjusted for centre, age and sex, and weighted by season and day of recall.
† Sum of epigallocatechin, epicatechin 3-gallate, epigallocatechin 3-gallate, gallocatechin and catechin-3-gallate.
‡ Sum of theaflavin, theaflavin-3′-gallate, theaflavin-3 gallate and theaflavin-3,3′-digallate.

British Journal of Nutrition

Table 4. Socio-demographic, lifestyle and anthropometric determinants of intake (mg/d) of total flavan-3-ols and their subgroups*
(Mean values with their standard errors)

		Total flavan-3-ols			Monomers†			Proanthocyanidins			Theaflavins‡		
	n	Mean	SE	*P*§	Mean	SE	*P*§	Mean	SE	*P*§	Mean	SE	*P*§
Region				< 0·001			< 0·001			< 0·001			< 0·001
Mediterranean countries	11 285	268·8	2·6		50·0	1·0		217·2	2·2		1·6	0·1	
Non-Mediterranean countries	23 469	274·7	1·9		90·2	.7		177·9	1·5		6·5	0·1	
UK	1283	406·6	7·6		182·4	3·0		198·4	6·3		25·9	0·3	
Sex				< 0·001			0·002			< 0·001			0·019
Male	13 028	280·7	3·0		73·6	1·2		201·6	2·5		5·5	0·1	
Female	23 009	296·5	2·2		78·1	0·9		212·5	1·8		5·9	0·1	
Age (years)				< 0·001			0·004			< 0·001			0·340
35–44	3335	262·6	5·0		72·2	2·0		185·0	4·1		5·4	0·2	
45–54	12 595	274·9	2·7		73·9	1·1		195·2	2·2		5·7	0·1	
55–64	14 940	302·5	2·6		78·1	1·0		218·7	2·1		5·7	0·1	
65–74	5167	298·3	4·3		76·7	1·7		215·7	3·6		5·9	0·2	
Education level completed				< 0·001			< 0·001			< 0·001			< 0·001
None	1709	267·4	7·7		69·6	3·0		192·5	6·4		5·4	0·3	
Primary	10 469	258·0	3·0		59·4	1·2		194·1	2·5		4·4	0·1	
Technical/professional	8038	281·1	3·5		72·0	1·4		204·0	2·9		5·1	0·1	
Secondary school	7152	303·1	3·5		82·1	1·4		215·1	2·9		6·0	0·1	
Post-secondary	8155	329·6	3·3		96·3	1·3		225·7	2·8		7·7	0·1	
Smoking status				< 0·001			< 0·001			< 0·001			< 0·001
Never	17 483	295·5	2·5		79·8	1·0		209·8	2·0		6·0	0·1	
Former	10 288	301·4	2·9		80·2	1·2		215·0	2·4		6·2	0·1	
Smoker	7726	256·1	3·3		62·4	1·3		189·3	2·7		4·5	0·1	
Physical activity				< 0·001			< 0·001			< 0·001			0·002
Inactive	7463	274·5	3·2		71·9	1·3		197·3	2·6		5·3	0·1	
Moderately inactive	11 969	283·8	2·6		75·0	1·1		203·1	2·1		5·7	0·1	
Moderately active	8400	299·1	3·1		79·0	1·3		214·1	2·5		6·1	0·1	
Active	6380	304·5	3·5		79·1	1·5		219·6	2·8		5·8	0·2	
BMI (kg/m^2)				< 0·001			< 0·001			0·012			< 0·001
< 25	16 854	297·1	2·6		81·6	1·0		209·3	2·1		6·3	0·1	
25 to < 30	13 766	285·2	2·6		72·5	1·0		207·3	2·1		5·4	0·1	
> 30	5417	270·0	3·9		66·8	1·6		198·4	3·2		4·7	0·2	

* General linear model adjusted for age, sex, region, BMI (whenever not stratified for the respective variables) and energy intake, and weighted by season and day of recall.
† Sum of catechins, epicatechins and (epi)gallocatechins.
‡ Sum of theaflavin, theaflavin-3′-gallate, theaflavin-3 gallate and theaflavin-3,3′-digallate.
§ *P* values are for overall differences in mean consumption by general linear model among the socio-demographic, lifestyle and anthropometric subgroups.

including dieting, and some healthy habits such as fruit and vegetable intake[57]. Our study showed that the intakes of total and subclasses of flavan-3-ols were lower in obese subjects and, in addition, higher in physically active subjects. Further investigation explaining the association between all these factors and their role in obesity is needed. In our study, intakes of PA increased with higher level of education, and were found to be considerably low in the group without formal schooling. In line with our findings, consumption of fruits, fruit juice, wine and tea has been previously associated with higher socio-economic status[58]. These factors should be taken into consideration when looking at disease prevention, planning of healthy diets within a specific population and may also be instrumental when establishing ‘lifespan essential’ dietary reference intakes for flavan-3-ols, PA and theaflavins in different populations, and in subgroups with unfavourable lifestyle factors[59].

Major differences in total flavan-3-ol intake can be observed between our study and other descriptive studies (Table 5). Our estimates of total flavan-3-ol intake were much higher than those reported in other countries and the main reason being that some individual compounds or subclasses of flavan-3-ols were not included in the total estimation of flavan-3-ols in those studies. Comparison of the subclasses (monomers, PA and theaflavins) may therefore be preferable. Even then, the intakes may vary because of other important factors involved in the estimation, such as different methodologies used to assess dietary intake of cohorts (FFQ, 24-HDR, diet history, etc); compositional data of the compounds may come from different sources or from older versions of the USDA database[23,60], or the median intake reported rather than the mean. The latter is particularly the case in the Greek EPIC study[61]. Finally, cohort characteristics, especially those that are associated with flavan-3-ol consumption (e.g. age and sex) may vary considerably. All these are to be kept in mind when making comparisons. Flavan-3-ol monomer intake reported recently for the UK and Ireland by Beking & Vieira[62] and based on food balance sheets was about one-third that of our reported intake for the UK region. The monomer intake reported in an elderly Dutch cohort[63] as closer but still slightly lower than our estimates for the Dutch cohorts of Bilthoven and Utrecht even though, in our study, intakes were found to be higher in older age groups. Monomer intakes reported recently in Italy[21] and for Spanish[23] and Greek[61] EPIC cohorts were within our ranges for those countries. As for other countries known to have a tea culture,

Table 5. Previously estimated daily flavan-3-ol intakes (mg) in adults in several countries*

Country	Total flavan-3-ols (mg/d)	Compounds included in the total flavan-3-ols	Flavan-3-ol monomers (mg/d)	C (mg/d)	EC (mg/d)	EGC (mg/d)	PA (mg/d)	Theaflavins (mg/d)	Source of compositional data	Study population (sample size/age (years)/sex)	Dietary assessment method
Finland[66]	128	C, EC, PA	12	ns	ns	–	116	–	National Finnish database	2007/25–64/both	48DR
Ireland[62]	47	C, EC, EGC	47	ns	ns	ns	–	–	USDA 2007 and various other	ns/ns/ns	Food balance sheets
UK[62]	52	C, EC, EGC	52	ns	ns	ns	–	–	USDA 2007 and various other	ns/ns/ns	Food balance sheets
UK[64]†	154	C, EC, EGC, PA	119	7	25	88	34	–	Various	404/32–88/both	FFQ
Denmark[52]	148	C, EC, EGC, theaflavins, thearubigins	ns	ns	ns	ns	–	ns	USDA 2003	ns/ns/both	Dietary history
The Netherlands[52]	145	C, EC, EGC, theaflavins, thearubigins	ns	ns	ns	ns	–	ns	USDA 2003	6200/1–92/both	2 d dietary record
The Netherlands[63]	72	C, EC, EGC	72	ns	ns	ns	–	–	Own data	1266/65–84/men	1-month dietary history
France[65]	338	C, EC, EGC, PA	87	ns	ns	ns	227	9	Phenol-Explorer	13 017/35–60/both	24DR
Italy[21]	343	C, EC, EGC, PA, theaflavins, thearubigins	53	ns	ns	ns	290	ns	USDA 2003, 2004	547/22–80/both	FFQ
Spain EPIC[23]	221	C, EC, EGC, theaflavins, thearubigins	30	13	11	6	189	0	USDA 2004, 2007	40 683/35–64/both	FFQ
Greece EPIC[61]‡	89	C, EC, ECG, PA	13	6	6	1	75	–	USDA 2004, 2007	28 572/30–76/both	FFQ
USA[22,67]	251	(C, EC, theaflavins, thearubigins), PA	ns	ns	ns	ns	95	ns	USDA 2004, 2007	8809/19 + /both	24DR
Australia[52]	422	C, EC, EGC, theaflavins, thearubigins	188	9	17	162	–	22	USDA 2003	17 326/19 + /both	24DR
Japan[60]	380	C, EC, EGC	380	ns	ns	ns	–	–	National Japanese database	514/40 + /women	24 h dietary record

C, catechins; EC, epicatechins; EGC, (epi)gallocatechins; PA, proanthocyanidins; ns, not specified; –, value not provided by the original study; DR, dietary recall; USDA, US Department of Agriculture.

* Where applicable and when not provided by the study, total flavan-3-ols were calculated as the sum of the subgroups.

† Median values given instead of the mean.

‡ Total flavan-3-ols were calculated as the sum of the values in Rossi *et al.*[21] for C, EC, theaflavins and thearubigins combined and in Wang *et al.*[67] for PA.

Otaki *et al.*[60] have estimated monomer intake in Japanese women to be around 380 mg/d, more than double the value we reported for the UK region. This is probably because of higher consumption of non-fermented tea, such as green tea, in Japan. Green tea is a rich source of flavan-3-ol monomers but not a source of theaflavins, which was found exclusively in black tea, the tea more commonly consumed in the UK. In contrast, monomer intake (188 mg/d) reported in Australia was comparable to our value in the UK region. PA intake for Spain in our study is slightly higher than previously reported for the EPIC Spain cohort; however, the previous study used dietary history questionnaires and only the USDA food composition values in their estimation of flavan-3-ols[23]. A recent Italian case–control study assessed the mean PA intake to be around 290 mg/d which is within the range of the Italian values in our study[21]. However, most PA estimations have been done in case–control studies, which assess small groups of controls and not always all the subgroups of PA were included[20,21,64]. Surprisingly, Greece being a MED country had the lowest intake of PA of all EPIC centres. Among the other previously mentioned factors for this difference, this finding is also supported by the lower consumption of fruit in Greece compared to Italy and Spain reported previously in EPIC studies[47]. Perez-Jimenez *et al.*[65] reported intakes of flavan-3-ol monomers (114 mg/d), PA (191 mg/d) and theaflavins (16 mg/d) in French women that are within the range of our values for the French EPIC centres. A limited number of descriptive studies is available on PA to facilitate a comparison with non-EPIC countries. Using their own composition database, Ovaskainen *et al.*[66] reported lower PA intakes for a Finnish population compared to the northern EPIC countries such as Sweden and Norway. The sources of PA in northern EPIC countries were found to be similar to those in Finland, with the exception of berries, which were not singled out in our study but were an important source of PA in Finland. These differences in intake and food sources compared to our study are most probably due to the varying study variables already exposed earlier. Finally, Wang *et al.*[67] recently estimated PA intake for the US population to be about 95 mg/d. This is still slightly lower than the lowest intakes found in our study (Greek cohorts). Clearly, more consistent methods of intake estimation between and within countries are needed. Parallel to that, improved methods for identification and quantification of some flavan-3-ol compounds, such as thearubigins, are needed to allow for more exhaustive flavonoid composition databases.

The use of a common expanded flavonoid database provided us with greater coverage of foods representative of the EPIC countries while allowing for comparisons of results across the countries. Despite the fact that we applied retention factors to foods prepared by cooking, we estimated higher intakes than in the previous studies. Moreover, our values are likely to be underreported due to spices and herbs often not accounted for during diet assessment and because a small proportion (2–16 %) of flavan-3-ol analytical values in our study was still missing. The underestimation of intakes is also probably due to the omission of dietetic supplements in this analysis. However, few consumers of herb/plant supplements participated in this study (the highest was 5 % reported in Denmark)[68].

To our knowledge, this is the largest study to date describing flavan-3-ol and PA intake across several European countries. Since not all the EPIC cohorts are representative of the population, the observed level of intake cannot be extrapolated to the general population of each region.

In summary, this study provides total and individual flavan-3-ol, PA and theaflavin intakes for ten EPIC countries by sex and EPIC centre. The major dietary contributors of these flavonoid subclasses are described by the MED, non-MED and UK regions. In addition, we show that socio-demographic, anthropometric and lifestyle factors associated with differential consumption of flavan-3-ols, PA and theaflavins exist. Combined with more elucidated information on the bioavailability of these compounds, these descriptive data will be valuable in future evaluations of total and individual flavan-3-ols and their role in health and disease in the European population.

Acknowledgements

The present work was carried out with the financial support of the European Commission: Public Health and Consumer Protection Directorate 1993–2004; Research Directorate-General 2005; Ligue contre le Cancer, Institut Gustave Roussy, Mutuelle Générale de l'Education Nationale, Institut National de la Santé et de la Recherche Médicale (INSERM, France); German Cancer Aid; German Cancer Research Centre; German Federal Ministry of Education and Research; Danish Cancer Society: Health Research Fund (FIS) of the Spanish Ministry of Health (RTICC (DR06/0020); the participating regional governments and institutions of Spain; Cancer Research UK; Medical Research Council, UK; the Stroke Association, UK; British Heart Foundation; Department of Health, UK; Food Standards Agency, UK; the Wellcome Trust, UK; Hellenic Ministry of Health; the Stavros Niarchos Foundation and the Hellenic Health Foundation; Italian Association for Research on Cancer; Compagnia San Paolo, Italy; Dutch Ministry of Public Health, Welfare and Sports; Dutch Ministry of Health; Dutch Prevention Funds; LK Research Funds; Dutch ZON (Zorg Onderzoek Nederland); World Cancer Research Fund (WCRF); Swedish Cancer Society; Swedish Scientific Council; Regional Government of Skane, Sweden; Nordforsk – Centre of Excellence programme. Some authors are partners of ECNIS, a network of excellence of the 6FP of the EC. R Z.-R. is thankful for a post-doctoral programme Fondo de Investigación Sanitaria (FIS; no. CD09/00133) from the Spanish Ministry of Science and Innovation. The authors thank Raul M. García for developing an application to link the FCDB and the 24-HDR. The authors declare that there are no conflicts of interest. The authors' contributions are as follows: R. Z.-R. and C. A. G. designed the research; V. K. and R. Z.-R. conducted the research; V. K. and L. L.-B. performed the statistical analysis; V. K. and R. Z.-R. wrote the manuscript. V. K., R. Z.-R., L. L.-B., I. R., A. S., N. S., E. R., C. T. M. v. R., H. B. B.-d. M., A. T., V. D., K. T., G. S.,

D. E., J. R. Q., E. M., J. M. H., F. C., E. W., U. E., P. H. M. P, R. K., B. T., G. J., I. J., R. T., H. B., D. D., P. A., A. M., K.-T. K., R. L., V. Kr., E. A., C. S., S. S., K. O., A. T., A. O., M.-C. B.-R., G. F., F. P. and C. A. G. read, critically reviewed and approved the final manuscript.

References

1. Santos-Buelga C & Scalbert A (2000) Proanthocyanidins and tannin-like compounds – nature, occurence, dietary intake and effects on nutrition and health. *J Sci Food Agric* **80**, 1094–1117.
2. Laura A de la Rosa, E Alvarez-Parrilla and GA González-Aguilar (editors) (2010) *Fruit and Vegetable Phytochemicals*, 1st ed. Ames, IA: Blackwell Publishing.
3. Manach C, Williamson G, Morand C, *et al.* (2005) Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies. *Am J Clin Nutr* **81**, 230S–242S.
4. Aron PM & Kennedy JA (2007) Compositional investigation of phenolic polymers isolated from *Vitis vinifera* L. Cv. Pinot noir during fermentation. *J Agric Food Chem* **55**, 5670–5680.
5. Hellstrom JK, Torronen AR & Mattila PH (2009) Proanthocyanidins in common food products of plant origin. *J Agric Food Chem* **57**, 7899–7906.
6. Auger C, Al-Awwadi N, Bornet A, *et al.* (2004) Catechins and procyanidins in Mediterranean diets. *Food Res Int* **37**, 233–245.
7. Williamson G & Manach C (2005) Bioavailability and bioefficacy of polyphenols in humans. *Am J Clin Nutr* **81**, 243S–255S.
8. Gu L, Kelm MA, Hammerstone JF, *et al.* (2004) Concentrations of proanthocyanidins in common foods and estimations of normal consumption. *J Nutr* **134**, 613–617.
9. Crozier A, Lean MEJ, McDonald MS, *et al.* (1997) Quantitative analysis of the flavonoid content of commercial tomatoes, onions, lettuce, and celery. *J Agric Food Chem* **45**, 590–595.
10. Rickman JC, Barrett DM & Bruhn CM (2007) Nutritional comparison of fresh, frozen and canned fruits and vegetables. Part 1. Vitamins C and B and phenolic compounds. *J Sci Food Agric* **87**, 930–944.
11. Beecher GR (2003) Overview of dietary flavonoids: nomenclature, occurrence and intake. *J Nutr* **133**, 3248S–3254S.
12. Ramiro-Puig E & Castell M (2009) Cocoa: antioxidant and immunomodulator. *Br J Nutr* **101**, 931–940.
13. Suzuki J, Isobe M, Morishita R, *et al.* (2009) Tea polyphenols regulate key mediators on inflammatory cardiovascular diseases. *Mediators Inflamm* **2009**, article ID 494928; Epublication 19 July 2009.
14. Yang CS, Wang X, Lu G, *et al.* (2009) Cancer prevention by tea: animal studies, molecular mechanisms and human relevance. *Nat Rev Cancer* **9**, 429–439.
15. Hooper L, Kroon PA, Rimm EB, *et al.* (2008) Flavonoids, flavonoid-rich foods, and cardiovascular risk: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* **88**, 38–50.
16. Williamson G, Sies H, Heber D, *et al.* (2009) Functional foods for health promotion: state-of-the-science on dietary flavonoids. Extended abstracts from the 12th Annual Conference on Functional Foods for Health Promotion, April 2009. *Nutr Rev* **67**, 736–743.
17. Cos P, de Bruyne T, Hermans N, *et al.* (2004) Proanthocyanidins in health care: current and new trends. *Curr Med Chem* **11**, 1345–1359.
18. Schroeter H, Heiss C, Balzer J, *et al.* (2006) (−)-Epicatechin mediates beneficial effects of flavanol-rich cocoa on vascular function in humans. *Proc Natl Acad Sci U S A* **103**, 1024–1029.
19. Monagas M, Urpi-Sarda M, Sánchez-Patán F, *et al.* (2010) Insights into the metabolism and microbial biotransformation of dietary flavan-3-ols and the bioactivity of their metabolites. *Food Funct* **1**, 233–253.
20. Rossi M, Negri E, Parpinel M, *et al.* (2010) Proanthocyanidins and the risk of colorectal cancer in Italy. *Cancer Causes Control* **21**, 243–250.
21. Rossi M, Rosato V, Bosetti C, *et al.* (2010) Flavonoids, proanthocyanidins, and the risk of stomach cancer. *Cancer Causes Control* **21**, 1597–1604.
22. Chun OK, Chung SJ & Song WO (2007) Estimated dietary flavonoid intake and major food sources of U.S. adults. *J Nutr* **137**, 1244–1252.
23. Zamora-Ros R, Andres-Lacueva C, Lamuela-Raventós RM, *et al.* (2010) Estimation of dietary sources and flavonoid intake in a Spanish adult population (EPIC-Spain). *J Am Diet Assoc* **110**, 390–398.
24. Slimani N, Kaaks R, Ferrari P, *et al.* (2002) European Prospective Investigation into Cancer and Nutrition (EPIC) calibration study: rationale, design and population characteristics. *Public Health Nutr* **5**, 1125–1145.
25. Slimani N, Ferrari P, Ocke M, *et al.* (2000) Standardization of the 24-hour diet recall calibration method used in the European Prospective Investigation into Cancer and Nutrition (EPIC): general concepts and preliminary results. *Eur J Clin Nutr* **54**, 900–917.
26. Slimani N, Deharveng G, Charrondiere RU, *et al.* (1999) Structure of the standardized computerized 24-h diet recall interview used as reference method in the 22 centers participating in the EPIC project. European Prospective Investigation into Cancer and Nutrition. *Comput Methods Programs Biomed* **58**, 251–266.
27. Brustad M, Skeie G, Braaten T, *et al.* (2003) Comparison of telephone vs face-to-face interviews in the assessment of dietary intake by the 24 h recall EPIC SOFT program – the Norwegian calibration study. *Eur J Clin Nutr* **57**, 107–113.
28. Kaaks R, Plummer M, Riboli E, *et al.* (1994) Adjustment for bias due to errors in exposure assessments in multicenter cohort studies on diet and cancer: a calibration approach. *Am J Clin Nutr* **59**, 245S–2250.
29. Kaaks R, Riboli E & van Staveren W (1995) Calibration of dietary intake measurements in prospective cohort studies. *Am J Epidemiol* **142**, 548–556.
30. Kaaks R & Riboli E (1997) Validation and calibration of dietary intake measurements in the EPIC project: methodological considerations. European Prospective Investigation into Cancer and Nutrition. *Int J Epidemiol* **26**, Suppl. 1, S15–S25.
31. Haftenberger M, Schuit AJ, Tormo MJ, *et al.* (2002) Physical activity of subjects aged 50–64 years involved in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Public Health Nutr* **5**, 1163–1176.
32. Haftenberger M, Lahmann PH, Panico S, *et al.* (2002) Overweight, obesity and fat distribution in 50- to 64-year-old participants in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Public Health Nutr* **5**, 1147–1162.
33. Riboli E, Hunt KJ, Slimani N, *et al.* (2002) European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. *Public Health Nutr* **5**, 1113–1124.
34. Slimani N, Fahey M, Welch AA, *et al.* (2002) Diversity of dietary patterns observed in the European Prospective

Investigation into Cancer and Nutrition (EPIC) project. *Public Health Nutr* **5**, 1311–1328.
35. United States Department of Agriculture (2007) *USDA Database for the Flavonoid Content of Selected Foods*, release 2.1 ed. Beltsville, MD: USDA.
36. United States Department of Agriculture (2004) *USDA Database for the Proanthocyanidin Content of Selected Foods*. Beltsville, MD: USDA.
37. Neveu V, Perez-Jimenez J & Vos F, *et al.* (2010) Phenol-Explorer: an online comprehensive database on polyphenol contents in food. *Database (Oxf),* version 1.5.2. http://www.phenol-explorer.eu
38. Arts IC, van de Putte B & Hollman PC (2000) Catechin contents of foods commonly consumed in The Netherlands. 1. Fruits, vegetables, staple foods, and processed foods. *J Agric Food Chem* **48**, 1746–1751.
39. Zamora-Ros R, Knaze V, Lujan-Barroso L, *et al.* (2011) Estimation of the intake of anthocyanidins and their food sources in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Br J Nutr* **106**, 1090–1099.
40. Zamora-Ros R, Knaze V, Lujan-Barroso L, *et al.* (2011) Estimated dietary intakes of flavonols, flavanones and flavones in the European Prospective Investigation into Cancer and Nutrition (EPIC) 24 hour dietary recall cohort. *Br J Nutr* **106**, 1915–1925.
41. Rechner AR, Wagner E, van Buren L, *et al.* (2002) Black tea represents a major source of dietary phenolics among regular tea drinkers. *Free Radic Res* **36**, 1127–1135.
42. Levi F, Chatenoud L, Bertuccio P, *et al.* (2009) Mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world: an update. *Eur J Cardiovasc Prev Rehabil* **16**, 333–350.
43. Henning SM, Niu Y, Lee NH, *et al.* (2004) Bioavailability and antioxidant activity of tea flavanols after consumption of green tea, black tea, or a green tea extract supplement. *Am J Clin Nutr* **80**, 1558–1564.
44. Auger C, Mullen W, Hara Y, *et al.* (2008) Bioavailability of polyphenon E flavan-3-ols in humans with an ileostomy. *J Nutr* **138**, 1535S–1542S.
45. Linseisen J, Welch AA, Ocke M, *et al.* (2009) Dietary fat intake in the European Prospective Investigation into Cancer and Nutrition: results from the 24-h dietary recalls. *Eur J Clin Nutr* **63**, Suppl. 4, S61–S80.
46. Lopez-Miranda J, Perez-Jimenez F, Ros E, *et al.* (2010) Olive oil and health: summary of the II international Aconference on olive oil and health consensus report, Jaén and Córdoba (Spain) 2008. *Nutr Metab Cardiovasc Dis* **20**, 284–294.
47. Agudo A, Slimani N, Ocke MC, *et al.* (2002) Consumption of vegetables, fruit and other plant foods in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohorts from 10 European countries. *Public Health Nutr* **5**, 1179–1196.
48. Vidavalur R, Otani H, Singal PK, *et al.* (2006) Significance of wine and resveratrol in cardiovascular disease: French paradox revisited. *Exp Clin Cardiol* **11**, 217–225.
49. Thorp AA, Healy GN, Owen N, *et al.* (2010) Deleterious associations of sitting time and television viewing time with cardiometabolic risk biomarkers: Australian Diabetes, Obesity and Lifestyle (AusDiab) study 2004–2005. *Diabetes Care* **33**, 327–334.
50. Jakes RW, Day NE, Khaw KT, *et al.* (2003) Television viewing and low participation in vigorous recreation are independently associated with obesity and markers of cardiovascular disease risk: EPIC-Norfolk population-based study. *Eur J Clin Nutr* **57**, 1089–1096.
51. McFadden E, Luben R, Wareham N, *et al.* (2008) Occupational social class, risk factors and cardiovascular disease incidence in men and women: a prospective study in the European Prospective Investigation of Cancer and Nutrition in Norfolk (EPIC-Norfolk) cohort. *Eur J Epidemiol* **23**, 449–458.
52. Johannot L & Somerset SM (2006) Age-related variations in flavonoid intake and sources in the Australian population. *Public Health Nutr* **9**, 1045–1054.
53. Whichelow MJ, Erzinclioglu SW & Cox BD (1991) A comparison of the diets of non-smokers and smokers. *Br J Addict* **86**, 71–81.
54. Dauchet L, Montaye M, Ruidavets JB, *et al.* (2010) Association between the frequency of fruit and vegetable consumption and cardiovascular disease in male smokers and non-smokers. *Eur J Clin Nutr* **64**, 578–586.
55. Cui Y, Morgenstern H, Greenland S, *et al.* (2008) Dietary flavonoid intake and lung cancer – a population-based case–control study. *Cancer* **112**, 2241–2248.
56. Bobe G, Weinstein SJ, Albanes D, *et al.* (2008) Flavonoid intake and risk of pancreatic cancer in male smokers (Finland). *Cancer Epidemiol Biomarkers Prev* **17**, 553–562.
57. Hughes LA, Arts IC, Ambergen T, *et al.* (2008) Higher dietary flavone, flavonol, and catechin intakes are associated with less of an increase in BMI over time in women: a longitudinal analysis from the Netherlands Cohort Study. *Am J Clin Nutr* **88**, 1341–1352.
58. Hulshof KF, Brussaard JH, Kruizinga AG, *et al.* (2003) Socio-economic status, dietary intake and 10 y trends: the Dutch National Food Consumption Survey. *Eur J Clin Nutr* **57**, 128–137.
59. Williamson G & Holst B (2008) Dietary reference intake (DRI) value for dietary polyphenols: are we heading in the right direction? *Br J Nutr* **99**, Suppl. 3, S55–S58.
60. Otaki N, Kimira M, Katsumata S, *et al.* (2009) Distribution and major sources of flavonoid intakes in the middle-aged Japanese women. *J Clin Biochem Nutr* **44**, 231–238.
61. Dilis V & Trichopoulou A (2010) Antioxidant intakes and food sources in Greek adults. *J Nutr* **140**, 1274–1279.
62. Beking K & Vieira A (2011) An assessment of dietary flavonoid intake in the UK and Ireland. *Int J Food Sci Nutr* **62**, 17–19.
63. Arts IC, Hollman PC, Feskens EJ, *et al.* (2001) Catechin intake might explain the inverse relation between tea consumption and ischemic heart disease: the Zutphen Elderly Study. *Am J Clin Nutr* **74**, 227–232.
64. Kyle JA, Sharp L, Little J, *et al.* (2010) Dietary flavonoid intake and colorectal cancer: a case–control study. *Br J Nutr* **103**, 429–436.
65. Perez-Jimenez J, Fezeu L, Touvier M, *et al.* (2011) Dietary intake of 337 polyphenols in French adults. *Am J Clin Nutr* **93**, 1220–1228.
66. Ovaskainen ML, Torronen R, Koponen JM, *et al.* (2008) Dietary intake and major food sources of polyphenols in Finnish adults. *J Nutr* **138**, 562–566.
67. Wang Y, Chung SJ, Song WO, *et al.* (2011) Estimation of daily proanthocyanidin intake and major food sources in the U.S. diet. *J Nutr* **141**, 447–452.
68. Skeie G, Braaten T, Hjartaker A, *et al.* (2009) Use of dietary supplements in the European Prospective Investigation into Cancer and Nutrition calibration study. *Eur J Clin Nutr* **63**, Suppl. 4, S226–S238.

Annex 1. Adjusted* mean daily intakes (mg/d) of flavan-3-ol monomer compounds by European Prospective Investigation into Cancer and Nutrition centre ordered from south to north

(Mean values with their standard errors)

		Flavan-3-ol monomers													
		(+)-Catechin		(−)-Epicatechin		(−)-Epigallocatechin		(−)-Epicatechin 3-gallate		(−)-Epigallocatechin 3-gallate		(+)-Gallocatechin		(+)-Catechin 3-gallate	
Country and centre	*n*	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Greece	2687	8·21	0·27	9·63	0·31	1·26	0·37	1·40	0·31	1·58	0·92	0·50	0·08	1·07	0·28
Spain															
Granada	514	13·25	0·63	11·97	0·71	1·89	0·85	1·88	0·72	1·37	2·13	0·26	0·18	0·46	0·64
Murcia	547	15·67	0·61	12·59	0·68	1·92	0·82	1·86	0·69	1·18	2·05	0·33	0·17	0·40	0·61
Navarra	715	14·46	0·54	12·50	0·61	1·67	0·73	0·79	0·62	0·88	1·83	0·16	0·15	0·15	0·55
San Sebastian	734	17·69	0·55	16·60	0·62	2·35	0·75	1·26	0·63	1·41	1·87	0·24	0·16	0·33	0·56
Asturias	710	17·85	0·53	19·25	0·59	2·64	0·72	1·48	0·60	2·35	1·79	0·21	0·15	0·33	0·54
Italy															
Ragusa	306	15·04	0·81	14·74	0·91	4·28	1·09	2·47	0·92	8·09	2·73	0·44	0·23	0·55	0·82
Naples	403	10·34	0·70	11·46	0·79	3·64	0·95	2·45	0·80	8·05	2·37	0·40	0·20	0·56	0·71
Florence	1055	16·43	0·50	17·22	0·56	5·81	0·67	3·92	0·56	12·54	1·67	0·79	0·14	1·09	0·50
Turin	1068	21·84	0·45	20·31	0·50	6·44	0·60	4·61	0·51	14·57	1·51	0·93	0·13	1·38	0·45
Varese	1121	18·87	0·46	18·36	0·52	7·67	0·62	6·10	0·53	19·86	1·56	1·13	0·13	1·80	0·47
France															
South coast	620	14·53	0·56	17·26	0·63	7·63	0·76	7·19	0·64	10·71	1·91	1·84	0·16	6·96	0·57
South	1425	15·41	0·37	18·37	0·42	11·01	0·50	9·79	0·42	14·63	1·26	2·76	0·11	10·62	0·38
North-East	2059	15·80	0·31	18·44	0·35	10·07	0·42	8·86	0·35	13·62	1·05	2·45	0·09	9·32	0·31
North-West	631	14·83	0·56	17·54	0·63	11·68	0·76	9·85	0·64	15·31	1·89	2·99	0·16	11·49	0·57
Germany															
Heidelberg	2121	18·94	0·31	20·42	0·35	13·12	0·42	13·03	0·35	22·91	1·04	2·43	0·09	7·04	0·31
Potsdam	2294	16·16	0·29	15·73	0·33	7·27	0·40	8·76	0·34	11·45	1·00	1·63	0·08	4·98	0·30
The Netherlands															
Bilthoven	2110	14·77	0·31	13·98	0·35	12·32	0·42	9·77	0·36	15·22	1·06	3·36	0·09	12·45	0·32
Utrecht	1870	14·46	0·33	16·50	0·37	19·40	0·44	15·25	0·37	23·61	1·10	5·18	0·09	20·24	0·33
UK															
General population	974	22·76	0·46	23·91	0·51	35·07	0·62	26·44	0·52	42·61	1·55	9·30	0·13	35·96	0·46
Health-conscious	309	19·87	0·83	20·06	0·93	26·18	1·12	21·93	0·94	31·08	2·81	6·82	0·24	26·53	0·84
Denmark															
Copenhagen	2840	23·27	0·26	19·09	0·30	12·92	0·36	10·65	0·30	16·46	0·89	3·69	0·08	12·93	0·27
Aarhus	1077	21·85	0·43	20·99	0·48	10·50	0·58	8·98	0·49	13·87	1·45	2·92	0·12	10·01	0·44
Sweden															
Malmö	3132	12·27	0·26	13·83	0·29	14·30	0·35	12·01	0·30	43·44	0·88	2·10	0·07	3·42	0·27
Umeå	2918	11·15	0·26	14·09	0·29	16·33	0·35	13·63	0·30	49·99	0·88	2·35	0·07	3·89	0·27
Norway															
South and East	1004	13·39	0·45	15·81	0·50	12·17	0·61	10·70	0·51	22·04	1·52	2·57	0·13	8·48	0·45
North and West	793	11·70	0·50	14·68	0·57	9·46	0·68	8·93	0·57	17·75	1·70	1·88	0·14	6·09	0·51

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

British Journal of Nutrition

Annex 2. Adjusted* mean daily intakes (mg/d) of proanthocyanidin (PA) and theaflavin subgroups by European Prospective Investigation into Cancer and Nutrition centre ordered from south to north (Mean values with their standard errors)

		PA										Theaflavins							
		PA dimers		PA trimers		PA 4–6mers		PA 7–10mers		PA >10mers		Theaflavin		Theaflavin-3,3′-digallate		Theaflavin-3′-gallate		Theaflavin-3-gallate	
Country and centre	*n*	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Greece	2687	17·9	0·8	7·7	0·3	24·8	0·9	19·0	0·7	48·9	2·3	0·13	0·06	0·12	0·05	0·12	0·05	0·11	0·05
Spain																			
Granada	514	36·4	1·8	12·7	0·7	41·9	2·1	30·0	1·6	63·1	5·4	0·07	0·13	0·06	0·11	0·06	0·11	0·06	0·11
Murcia	547	38·7	1·7	14·2	0·7	46·9	2·0	33·2	1·5	64·8	5·2	0·06	0·13	0·05	0·11	0·05	0·11	0·05	0·11
Navarra	715	39·1	1·5	13·1	0·6	45·9	1·8	34·1	1·4	70·4	4·6	0·01	0·11	0·01	0·10	0·01	0·10	0·01	0·10
San Sebastian	734	56·1	1·6	20·3	0·6	69·8	1·8	53·3	1·4	105·7	4·7	0·06	0·11	0·05	0·10	0·05	0·10	0·05	0·10
Asturias	710	61·7	1·5	25·7	0·6	83·0	1·8	63·0	1·3	114·6	4·5	0·05	0·11	0·04	0·10	0·04	0·10	0·04	0·09
Italy																			
Ragusa	306	44·3	2·3	15·5	0·9	52·6	2·7	38·3	2·1	79·6	6·9	0·13	0·17	0·11	0·15	0·11	0·15	0·11	0·14
Naples	403	31·1	2·0	13·3	0·8	43·5	2·3	30·6	1·8	61·5	6·0	0·14	0·15	0·12	0·13	0·12	0·13	0·11	0·13
Florence	1055	50·1	1·4	18·5	0·6	60·9	1·6	44·7	1·3	90·6	4·2	0·22	0·10	0·19	0·09	0·19	0·09	0·19	0·09
Turin	1068	61·7	1·3	19·9	0·5	67·3	1·5	49·5	1·1	100·1	3·8	0·26	0·09	0·22	0·08	0·22	0·08	0·21	0·08
Varese	1121	53·4	1·3	17·0	0·5	56·0	1·5	41·4	1·2	85·1	3·9	0·37	0·10	0·32	0·08	0·32	0·08	0·31	0·08
France																			
South coast	620	36·7	1·6	12·2	0·6	40·1	1·9	28·0	1·4	62·8	4·8	1·40	0·12	1·23	0·10	1·23	0·10	1·20	0·10
South	1425	40·8	1·1	13·9	0·4	44·1	1·2	31·3	0·9	69·6	3·2	2·14	0·08	1·88	0·07	1·88	0·07	1·84	0·07
North-East	2059	41·9	0·9	14·8	0·4	46·2	1·0	32·0	0·8	69·5	2·6	1·88	0·06	1·64	0·06	1·64	0·06	1·61	0·06
North-West	631	40·5	1·6	13·6	0·6	42·8	1·9	30·8	1·4	61·0	4·8	2·31	0·12	2·03	0·10	2·03	0·10	1·99	0·10
Germany																			
Heidelberg	2121	45·5	0·9	17·2	0·4	43·9	1·0	32·4	0·8	69·4	2·6	1·39	0·06	1·20	0·06	1·20	0·06	1·19	0·06
Potsdam	2294	33·1	0·8	14·9	0·3	44·4	1·0	32·8	0·8	74·5	2·5	0·92	0·06	0·80	0·05	0·80	0·05	0·79	0·05
The Netherlands																			
Bilthoven	2110	29·6	0·9	10·6	0·4	29·9	1·0	21·0	0·8	44·4	2·7	2·52	0·07	2·20	0·06	2·20	0·06	2·16	0·06
Utrecht	1870	36·1	0·9	12·1	0·4	33·7	1·1	24·3	0·8	50·1	2·8	4·10	0·07	3·59	0·06	3·59	0·06	3·52	0·06
UK																			
General population	974	58·5	1·3	14·8	0·5	34·3	1·5	23·9	1·2	52·7	3·9	7·32	0·10	6·41	0·08	6·41	0·08	6·29	0·08
Health-conscious	309	51·9	2·3	18·0	1·0	46·8	2·8	36·1	2·1	85·2	7·1	5·37	0·17	4·70	0·15	4·70	0·15	4·62	0·15
Denmark																			
Copenhagen	2840	58·9	0·7	15·1	0·3	43·5	0·9	30·4	0·7	65·5	2·3	2·62	0·05	2·30	0·05	2·30	0·05	2·25	0·05
Aarhus	1077	57·9	1·2	17·7	0·5	51·7	1·4	36·6	1·1	69·3	3·7	2·02	0·09	1·77	0·08	1·77	0·08	1·74	0·08
Sweden																			
Malmö	3132	26·3	0·7	10·1	0·3	28·2	0·9	19·4	0·7	50·3	2·2	0·83	0·05	0·72	0·05	0·72	0·05	0·69	0·05
Umeå	2918	23·4	0·7	10·3	0·3	28·2	0·9	21·8	0·7	80·7	2·2	0·95	0·05	0·82	0·05	0·82	0·05	0·79	0·05
Norway																			
South and East	1004	32·2	1·3	12·0	0·5	35·6	1·5	28·5	1·1	98·8	3·8	1·73	0·09	1·50	0·08	1·50	0·08	1·48	0·08
North and West	793	31·1	1·4	12·6	0·6	37·1	1·7	29·5	1·3	103·7	4·3	1·23	0·10	1·07	0·09	1·07	0·09	1·06	0·09

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