Public Health Nutrition: 16(8), 1454–1462 doi:10.1017/S1368980012003904

Intakes and sources of isoflavones, lignans, enterolignans, coumestrol and soya-containing foods in the Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk), from 7 d food diaries, using a newly updated database

Angela A Mulligan[1,*], Gunter GC Kuhnle[2], Marleen AH Lentjes[1], Veronica van Scheltinga[1], Natasha A Powell[1], Alison McTaggart[1], Amit Bhaniani[1] and Kay-Tee Khaw[1,3]

[1]European Prospective Investigation of Cancer, Department of Public Health and Primary Care, University of Cambridge, Strangeways Research Laboratory, Worts Causeway, Cambridge CB1 8RN, UK: [2]Department of Food and Nutritional Sciences, University of Reading, Reading, UK: [3]EPIC, Department of Gerontology, Addenbrooke's Hospital, School of Clinical Medicine, University of Cambridge, Cambridge, UK

Submitted 27 March 2012: Final revision received 27 June 2012: Accepted 5 July 2012: First published online 3 September 2012

Abstract

Objective: A diet rich in phyto-oestrogens has been suggested to protect against a variety of common diseases but UK intake data on phyto-oestrogens or their food sources are sparse. The present study estimates the average intakes of isoflavones, lignans, enterolignans and coumestrol from 7 d food diaries and provides data on total isoflavone, lignan and phyto-oestrogen consumption by food group.

Design: Development of a food composition database for twelve phyto-oestrogens and analysis of soya food and phyto-oestrogen consumption in a population-based study.

Setting: Men and women, aged 40–79 years, from the general population participating in the Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk) between 1993 and 1997, with nutrient and food data from 7 d food diaries.

Subjects: A subset of 20 437 participants.

Results: The median daily phyto-oestrogen intake for all men was 1199 μg (interquartile range 934–1537 μg; mean 1504 μg, SD 1502 μg) and 888 μg for all women (interquartile range 710–1135 μg; mean 1205 μg, SD 1701 μg). In soya consumers, median daily intakes were higher: 2861 μg in men (interquartile range 1304–7269 μg; mean 5051 μg, SD 5031 μg) and 3142 μg in women (interquartile range 1089–7327 μg; mean 5396 μg, SD 6092 μg). In both men and women, bread made the greatest contribution to phyto-oestrogen intake – 40·8 % and 35·6 %, respectively. In soya consumers, vegetable dishes and soya/goat's/sheep's milks were the main contributors – 45·7 % and 21·3 % in men and 38·4 % and 33·7 % in women, respectively.

Conclusions: The ability to estimate phyto-oestrogen intake in Western populations more accurately will aid investigations into their suggested effects on health.

Keywords
Phyto-oestrogens
Soya
EPIC-Norfolk

Phyto-oestrogens are a group of non-steroidal, polyphenolic plant metabolites that induce biological responses and can mimic or modulate the action of endogenous oestrogens, often by binding to oestrogen receptors[1]. The bioactivity of phyto-oestrogens is based on their structural similarity to 17β-oestradiol[2] and their ability to bind to the oestrogen receptor[3]. Due to their bioactivity, these compounds are associated with potentially beneficial effects on a wide range of human conditions, such as cancer[4–6], CVD[7,8], osteoporosis[9], menopausal symptoms[10,11], obesity and type 2 diabetes[12,13]. The occurrence of many of these conditions is much lower in traditional Asian societies, where phyto-oestrogen-rich foods form an important component of the diet. Estimates suggest that the average isoflavone intake in Japan ranges from 25 to 100 mg/d[1].

*Corresponding author: Email angela.mulligan@phpc.cam.ac.uk

The major phyto-oestrogen classes are isoflavones, found predominantly in legumes and soya foods; lignans, found in cereals, linseed, fruits and vegetables; and coumestans, found in young sprouting legumes, such as clover and alfalfa sprouts. Colonic microflora metabolise plant lignans into enterolignans, enterolactone and enterodiol[14]. Daidzein, an isoflavone, is metabolised to equol in some individuals[15]. Traditional soya foods rich in isoflavones, such as tofu, tempeh and miso, are seldom consumed in the UK; instead soya dairy alternatives, such as soya milk, cheese, yoghurts, and textured vegetable protein (TVP)/tofu burgers are more commonly eaten. However a number of commercial products, such as bread, biscuits and breakfast cereals, contain soya ingredients as food additives and these also contribute to phyto-oestrogen intake[16,17].

A number of detailed studies have previously been carried out to measure the phyto-oestrogen content of food items in the UK[18–20], Finland[21], the USA[17,22], the Netherlands[23] and Canada[24]. To date, there are few data available on soya and/or phyto-oestrogen intakes in the UK and most intake data have been mainly on isoflavones.

The present paper investigates the intakes, distributions and sources of phyto-oestrogen-containing foods in a population-based cohort study, the Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk), as recorded by a 7 d food diary (7dFD), using a newly in-filled phyto-oestrogen database.

Methods

The EPIC-Norfolk study

EPIC-Norfolk is a prospective cohort study of over 25 000 free-living men and women, aged between 40 and 75 years, studying the effects of nutrition and other lifestyle factors on health[25]. The study was approved by the Norwich District Health Authority Ethics Committee, and all participants gave signed informed consent. Participants completed a 7dFD between 1993 and 1998, of which 92 % were returned. Of these, 20 437 were entered and available for statistical analysis.

Dietary data

The 7dFD is an A5, 45-page booklet in which the description, preparation and amounts of foods and drinks consumed at main meals, snacks and between meals are recorded over a week[26]. A trained nurse instructed each participant on how to fill in the diary. As part of this instruction, the nurse asked the participant to recall the previous day's intake and this description was written into the first day.

The diary data were entered using DINER (Data Into Nutrients for Epidemiological Research), a data-entry system specifically created for EPIC-Norfolk[27]. The DINER program contains nutrient data derived from the 5th edition of *McCance and Widdowson's The Composition of Foods* and associated supplements[28–37]. Although there are approximately 4500 food items available from these sources, the nutrient data of only 2704 of these food items are appropriate as DINER only contains foods in an edible state. More than 8000 items, so-called 'new foods', have been added to DINER in an attempt to cover the wide range of foods and drinks available in the UK. The nutrient data of these 'new foods' is obtained by matching known nutrient composition, e.g. using manufacturers' data, with between one and four of the aforementioned 2704 items, in order to obtain the best possible match of nutrient analyses. These 'new foods' also contain approximately 2300 non-specific (n.s.) items, which are used when the data recorded in a food diary are minimal or missing, e.g. 'bread n.s.', 'milk n.s.', etc.

Selection of foods for analysis

Primarily single food items, called 'basic foods', were chosen for analysis (e.g. banana, rice, flour, peas). Foods to be analysed were selected on the basis of their frequency of consumption, calculated from the entry of more than 14 500 7dFD from EPIC-Norfolk. However, soya-containing foods (e.g. soya mince, soya and linseed bread) were also analysed, in addition to foods previously thought not to contain any phyto-oestrogens (e.g. meat, fish) and foods where there was uncertainty regarding the presence of phyto-oestrogens (e.g. milk, tea, coffee, alcohol). Of the 2704 foods, 349 were analysed for phyto-oestrogen content (13 %); values have been reported for cereals and cereal-based foods[38], fruits and vegetables[39], beverages, nuts, seeds and oils[40] and foods from animal origin[41].

Analysis of foods

The phyto-oestrogens analysed included the isoflavones: biochanin A, daidzein, genistein, glycitein and formononetin; the lignans: matairesinol, secoisolariciresinol and shonanin; the enterolignans: enterodiol and enterolactone; and equol and coumestrol. Foods were analysed as described previously[42]. In brief, foods were prepared, freeze-dried and extracted with 10 % aqueous methanol by volume. After deconjugation with *Helix pomatia* juice, samples were prepared by solid-phase extraction and analysed by LC–MS/MS with triply ^{13}C-labelled internal standards. The reproducibility of this method is better than 15 % (relative CV) and the detection limit is 1·5 μg/100 g.

Development of the phyto-oestrogen database

The remaining basic foods were in-filled using one of three methods: copying, calculating using a conversion factor or calculating using a recipe.

Values from similar food items were copied and assigned to 295 basic foods (11 %). Copying of values was carried out: (i) where there were two or more foods of a similar classification, but the analysis for only one of these was available (e.g. analysis of roast chicken breast used

for grilled chicken breast without skin, fresh lemon juice used for fresh lime juice); (ii) where commercial products were analysed but similar types were not (e.g. analysis of commercial trifle used for frozen commercial trifle and frozen, boiled petit pois used for canned petit pois); and (iii) where recipe foods needed to be calculated without the availability of a recipe (e.g. values of homemade mayonnaise used for commercial mayonnaise, fresh chocolate éclair used for frozen chocolate éclair).

The foods that were analysed contained the edible part only. Therefore foods that included skin, bone/fat and peel had to be calculated accordingly, as did foods where the phyto-oestrogen content changed due to water uptake during cooking or water loss during drying. Values for 175 basic food items were calculated using a conversion factor in this way (6·5 %). Examples include toasted brown bread and avocado weighed with skin and stone.

Only a limited number of meats were analysed so values for other meats had to be in-filled from these data, many of which were calculated from separately analysed lean and fat samples. For example, 'beef, topside, roasted, well done, lean and fat' was calculated using the analysed values of 'beef, topside, roasted, well done, lean' (87 %) and 'beef fat, roasted' (13 %).

Of the aforementioned 2704 foods, 1056 had their phyto-oestrogen content assigned using the recipe calculation method (39 %), using basic food analyses and recipes mainly available in the 5th edition of *McCance and Widdowson's The Composition of Foods* and associated supplements[28–37]. Examples of recipe foods include vegetable lasagne, egg custard tart and banana cake.

Remaining foods had different types of missing value assigned. The phyto-oestrogen content was assumed zero (e.g. salt, water); or amount unknown but may be significant (e.g. cocoa/hot chocolate powders, some cheeses, herbs and spices, less commonly consumed fruits and vegetables, some fish, some fats and oils, some meats, chocolate and savoury snacks).

Categorisation of soya foods and consumers

In the DINER system, similar foods are grouped together, such as tea and coffee, fruits, vegetables, breakfast cereals, etc. These food groups have been utilised to study food group sources of total lignans, total isoflavones and total phyto-oestrogens between 'soya consumers' (SC) and 'non-soya consumers' (NSC). SC were identified as those who had consumed any foods related to 'soya', 'tofu', 'TVP', 'tempeh' and/or 'miso', of which there were 134 in the DINER program. NSC did not consume any of these foods.

Statistical analyses

The data were analysed using the statistical software packages SAS version 9 and STATA version 10. Mean, standard deviation, median and interquartile range (IQR) were calculated to describe the distribution of intakes for two groups: SC and NSC, stratified by sex. Differences in means between these groups were tested using two-sided *t* tests and further adjusted for energy intake using linear regression analyses.

Results

Absolute phyto-oestrogen intake

Table 1 describes anthropometric data and average daily coumestrol, total enterolignan, isoflavone, lignan, phyto-oestrogen and energy intakes in 9326 NSC men and 354 SC men. The mean daily intakes of total isoflavones ($P < 0{\cdot}0001$), lignans ($P < 0{\cdot}001$) and phyto-oestrogens ($P < 0{\cdot}0001$) were significantly higher in SC men than in NSC men; mean daily total phyto-oestrogen intake was 5051 (SD 5031) μg in SC men but only 1369 (SD 942) μg in NSC men. NSC men were significantly older and heavier and had a significantly greater BMI (all $P < 0{\cdot}05$).

Data for 10 274 NSC and 483 SC women are shown in Table 2. The mean daily intakes of total isoflavones, lignans and phyto-oestrogens (all $P < 0{\cdot}0001$) were significantly

Table 1 Average daily intakes of coumestrol, total enterolignans, total isoflavones, total lignans, total phyto-oestrogens and energy in non-soya-consuming (NSC) men (*n* 9326) and soya-consuming (SC) men (*n* 354), as measured by a 7 d food diary, and anthropometric data. Men aged 40–79 years, Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk), 1993–1997

	NSC men (*n* 9326)				SC men (*n* 354)						
Variable	Mean	SD	Median	IQR	Mean	SD	Median	IQR	MD	CI of MD	*P* value
Coumestrol (μg)	7	9	5	4–8	8	7	6	4–9	−0·5	−1·2, 0·3	0·25
Total enterolignans (μg)	19	9	18	13–24	18	9	17	12–24	0·9	−0·1, 1·8	0·07
Total isoflavones (μg)	1033	871	858	633–1155	4664	4973	2413	998–6845	−3631	−4152, −3111	<0·0001
Total lignans (μg)	311	178	273	209–364	361	230	309	237–422	−50	−75, −26	<0·001
Total phyto-oestrogens (μg)	1369	942	1185	926–1502	5051	5031	2861	1304–7269	−3681	−4208, −3155	<0·0001
Energy (kJ)	9366	2206	9283	7878–10 717	9417	2042	9275	8004–10 653	−50	−268, 168	0·65
Age (years)	61·1	9·0	61·8	53·6–68·7	59·7	9·3	59·6	51·9–67·7	1·4	0·4, 2·4	<0·05
Weight (kg)*	80·4	11·5	79·4	72·8–87·2	78·4	11·3	77·9	70·8–84·8	1·9	0·7, 3·1	<0·005
Height (cm)†	173·7	6·6	173·7	169·3–178·1	173·7	6·3	173·8	169·1–177·8	0·0	−0·6, 0·7	0·96
BMI (kg/m^2)‡	26·6	3·3	26·3	24·4–28·5	26·0	3·3	25·7	23·9–27·8	0·6	0·3, 1·0	<0·001

IQR, interquartile range; MD, difference between means.
*NSC men (*n* 9320).
†NSC men (*n* 9315).
‡NSC men (*n* 9311).

Table 2 Average daily intakes of coumestrol, total enterolignans, total isoflavones, total lignans, total phyto-oestrogens and energy in non-soya-consuming (NSC) women (*n* 10 274) and soya-consuming (SC) women (*n* 483), as measured by a 7 d food diary, and anthropometric data. Women aged 40–79 years, Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk), 1993–1997

	NSC women (*n* 10 274)				SC women (*n* 483)						
Variable	Mean	SD	Median	IQR	Mean	SD	Median	IQR	MD	CI of MD	*P* value
Coumestrol (μg)	6	8	5	3–7	7	10	5	4–8	−1·0	−1·9, −0·1	0·02
Total enterolignans (μg)	16	8	16	11–21	16	8	15	10–20	0·9	0·2, 1·6	0·02
Total isoflavones (μg)	734	597	615	457–819	5055	6054	2830	779–6938	−4322	−4863, −3780	<0·0001
Total lignans (μg)	251	141	229	180–293	318	212	276	215–351	−67	−86, −48	<0·0001
Total phyto-oestrogens (μg)	1008	652	877	703–1105	5396	6092	3142	1089–7327	−4389	−4934, −3844	<0·0001
Energy (kJ)	7100	1649	7076	5961–8128	7443	1635	7422	6291–8568	−344	−493, −194	<0·0001
Age (years)	60·4	9·3	60·7	52·3–68·3	57·9	9·0	57·4	50·2–64·9	2·5	1·7, 3·4	<0·0001
Weight (kg)*	68·2	11·9	66·6	60·0–74·4	65·1	10·6	63·0	58·0–70·8	3·1	2·2, 4·1	<0·0001
Height (cm)†	160·7	6·2	160·7	156·6–164·9	161·8	6·8	161·2	157·6–166·2	−1·1	−1·7, −0·5	<0·001
BMI (kg/m^2)‡	26·4	4·4	25·7	23·4–28·7	24·8	3·8	24·1	22·2–26·9	1·6	1·2, 1·9	<0·0001

IQR, interquartile range; MD, difference between means.
*NSC women (*n* 10 256); SC women (*n* 482).
†NSC women (*n* 10 255); SC women (*n* 482).
‡NSC women (*n* 10 247); SC women (*n* 482).

higher in SC women than in NSC women; mean daily total phyto-oestrogen intake was 5396 (SD 6092) μg in SC women but only 1008 (SD 652) μg in NSC women. NSC women consumed significantly less energy than SC women ($P < 0·0001$). However, the results from the energy-adjusted means did not differ from the unadjusted means. SC women were significantly younger, lighter and taller, and therefore also had a significantly lower BMI ($P < 0·0001$ for all except height, where $P < 0·001$).

The mean daily total phyto-oestrogen intake was higher in SC women than in SC men, 5396 μg *v.* 5051 μg, but this difference was not significant. However, average daily intakes of total lignans ($P < 0·05$) and total enterolignans ($P < 0·0 0 1$) were significantly higher in SC men than in SC women.

The intakes of coumestrol, total enterolignans, isoflavones, lignans and phyto-oestrogens were slightly higher in all men than in all women and these differences were significant ($P < 0·0001$). The mean total daily phyto-oestrogen intake was 1504 μg in men (SD 1502 μg; median 1199 μg, IQR 934–1537 μg) and 1205 μg in women (SD 1701 μg; median 888 μg, IQR 710–1135 μg; data not shown). Total enterolignan intake was low in both men and women and was significantly related to milk and milk products intake ($P < 0·0001$).

Table 3 illustrates total mean daily phyto-oestrogen intake, by 10-year age bands, for NSC and SC, stratified by sex. There was a small significant linear decrease ($P < 0·0001$) in intake for both NSC men and women, as well as for SC men, with increasing age; this linear decrease was not as significant in SC women ($P < 0·05$). When the data were adjusted for energy, similar trends were observed (Table 3).

Sources of phyto-oestrogen intake

Data on percentage food group sources of total phyto-oestrogens, total isoflavones and total lignans in men and women are shown in Table 4, but only where food groups contribute 5% or more to the intake of each phyto-oestrogen group. In all men and women, bread and bread rolls made the greatest contribution to phyto-oestrogen intake – 40·8% and 35·6%, respectively. When SC were excluded, the contribution made by bread and bread rolls rose to 45·1% in men and 42·4% in women. However, in SC men and women, foods contributing to total phyto-oestrogen intake were very different, with vegetable dishes and soya/goat's/sheep's milk being the main contributors, accounting for a combined total of approximately 67% of intake in men and 72% in women.

Bread and bread rolls also made the greatest contribution to total isoflavone intake in all men and women – 51·3% and 45·2%, respectively. In SC, vegetable dishes and soya/goat's/sheep's milk were the main contributors, accounting for approximately 66% of intake in men and 72% in women.

Tea and coffee were the main contributors to total lignan intakes, accounting for 32·8% of intake in men and 37·3% in women. These values are very similar to those found in NSC men and women (33·0% and 37·8%, respectively). This food group was also the greatest contributor to lignan intake in SC: 26·9% in men and 29·4% in women. The consumption of alcohol also contributed to lignan intake: approximately 7% of intake in all women from wine and 21% in all men from wine, beer and lager.

Figure 1a illustrates the percentage contribution of food groups to the daily intake of total phyto-oestrogens in NSC. Bread and bread rolls made the greatest contribution (43%), followed by breakfast cereals (12%) and tea and coffee (6%). In SC, vegetable dishes were the highest contributor (41%), followed by soya/goat's/sheep's milk (25%) and bread and bread rolls (11%) (Fig. 1b).

Food choices of soya consumers and non-soya consumers

Mean average daily intakes (in grams) of the food groups listed in Table 4 were compared between SC and NSC, stratified by sex, using a two-sample *t* test. In men, these

Table 3 Unadjusted (U) mean daily intakes (and standard deviation) and energy-adjusted (A) mean daily intakes (and standard error of the mean, SEM) of total phyto-oestrogens (μg) in non-soya-consuming (NSC) and soya-consuming (SC) men and women, by age band. Men and women aged 40–79 years (*n* 20 437), Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk), 1993–1997

		NSC men			SC men			NSC women			SC women		
Age band (years)	U/A	*n*	Mean	SD or SEM	*n*	Mean	SD or SEM	% SC by age band	*n*	Mean	SD or SEM	*n*	Mean	SD or SEM	% SC by age band
39–49	U	1331	1515	963	72	6420	5761	5	1777	1079	721	115	6251	7112	6
	A		1433	19		6642	473			1030	12		6000	466	
50–59	U	2750	1444	1023	110	5969	5133	4	3116	1034	664	172	5457	5484	5
	A		1394	11		5544	289			1016	7		5532	288	
60–69	U	3372	1331	883	113	4022	4305	3	3417	985	602	137	5003	5691	4
	A		1355	10		4446	302			1001	7		5064	344	
70+	U	1873	1225	881	59	3638	4485	3	1964	941	640	59	4465	6459	3
	A		1316	17		3348	496			986	11		4597	569	
P for age trend	U		<0·0001			<0·0001				<0·0001			<0·05		
	A		<0·0001			<0·0001				<0·05			0·11		

were all significantly different ($P<0{\cdot}0001$ for all food groups except wine, where $P<0{\cdot}05$). NSC men had significantly higher intakes of vegetables, fruits, nuts and seeds, meat products, wine and beer and lager; intakes of bread and bread rolls, breakfast cereals, tea and coffee, vegetable dishes and soya/goat's/sheep's milk were higher in SC men.

In women, mean average daily intakes of most food groups listed were significantly different between SC and NSC ($P<0{\cdot}0001$ for all food groups, with the exception of wine and soya/goat's/sheep's milk where $P<0{\cdot}05$). NSC women had significantly higher intakes of vegetables, fruits, nuts and seeds, meat products, soya/goat's/sheep's milk and beer and lager; intakes of bread and bread rolls, breakfast cereals, tea and coffee, wine and vegetable dishes were higher in SC women.

Discussion

The aim of the present study was to investigate the average intake and distribution of soya-containing foods, coumestrol, total isoflavones, lignans, enterolignans and phyto-oestrogens, using a newly in-filled phyto-oestrogen database. This data set of phyto-oestrogen intake data is one of the largest to be investigated to date. The isoflavone intake data are similar to the intake of the vegetarian group (7·4 mg/d) in a recent UK study[43]. Data from the 1998 UK Total Diet Study estimated average daily intake of 3 mg of the combined isoflavone aglycones (daidzein, genistein and glycitein)[44]. Exposure estimates of total isoflavones for SC and soya-containing foods in UK adults based on the National Diet and Nutrition Survey (1986–1987) and the Dietary Survey of Vegetarians (1994–1995) were 0·6 and 2·6 mg/person per d respectively[45].

These data on daily isoflavone intake are higher than those from a previous study of EPIC-Norfolk participants[46]; 0·84 mg in all men (IQR 0·39–0·82 mg) and 0·77 mg in all women (IQR 0·30–0·64 mg). The differences in intake can mainly be attributed to the inclusion of the phyto-oestrogen analysis of certain foods in the database, foods which had not previously been analysed in the UK, such as tea, coffee, meat, fish, milk and dairy products[40,41], as well as changes in the isoflavone content of isoflavone-rich foods, such as soya flour, soya yoghurt, tofu/soyabean curd, tofu burgers and soyabean burgers. These foods were previously taken from published values[47] but recently analysed in the UK[38,41] and a 30–85 % reduction in their isoflavone content was found. Some commonly consumed foods, including brown and wholemeal breads, were also found to contain 20–30 % less isoflavones than previously estimated. The phyto-oestrogen content in plants is variable and depends on genetic, environmental, growth, harvesting and processing factors. A recent investigation into the variability of the phyto-oestrogen content in nine foods from different sources has shown that the phyto-oestrogen

Table 4 Percentage (%) contribution to total phyto-oestrogens (TOT PE), total isoflavones (TOT ISO) and total lignans (TOT LIG) from food groups, in all men and women, and non-soya-consuming (NSC) and soya-consuming (SC) men and women, ordered by percentage contribution in all men. Men and women aged 40–79 years (*n* 20 437), Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk), 1993–1997

Food group	PE group	All men	NSC men	SC men	All women	NSC women	SC women
Bread and bread rolls*	TOT PE	40·8	45·1	9·5	35·6	42·4	6·8
	TOT ISO	51·3	58·0	13·9	45·2	56·7	9·9
	TOT LIG	–	–	5·5	–	–	6·0
Breakfast cereals*	TOT PE	11·3	12·0	6·2	10·3	11·2	6·3
	TOT ISO	13·2	14·5	6·3	11·6	13·2	6·7
	TOT LIG	5·8	5·7	8·0	5·3	5·2	6·7
Tea and coffee	TOT PE	8·7	9·6	1·7	10·2	12·2	1·7
	TOT ISO	–	–	–	–	–	–
	TOT LIG	32·8	33·0	26·9	37·3	37·8	29·4
Vegetable dishes*	TOT PE	7·5	2·3	45·7	9·6	2·8	38·4
	TOT ISO	9·3	–	45·7	12·7	–	41·0
	TOT LIG	–	–	5·8	–	–	6·0
Meat products	TOT PE	5·0	5·5	0·6	3·9	4·8	–
	TOT ISO	6·3	7·3	–	5·0	6·5	–
	TOT LIG	–	–	–	–	–	–
Milk, soya/goat's/sheep's*	TOT PE	2·5	–	21·3	6·4	–	33·7
	TOT ISO	–	–	20·5	7·7	–	31·1
	TOT LIG	–	–	–	–	–	–
Beer and lager	TOT PE	–	–	–	–	–	–
	TOT ISO	–	–	–	–	–	–
	TOT LIG	12·1	12·3	8·8	–	–	–
Vegetables	TOT PE	–	–	–	–	–	–
	TOT ISO	–	–	–	–	–	–
	TOT LIG	9·4	9·5	8·4	11·7	11·7	11·3
Wine	TOT PE	–	–	–	–	–	–
	TOT ISO	–	–	–	–	–	–
	TOT LIG	8·9	8·9	8·3	7·3	7·4	7·0
Fruits	TOT PE	–	–	–	–	–	–
	TOT ISO	–	–	–	–	–	–
	TOT LIG	5·4	5·3	7·3	9·1	9·1	10·3
Nuts and seeds*	TOT PE	–	–	–	–	–	–
	TOT ISO	–	–	–	–	–	–
	TOT LIG	–	–	–	–	–	6·0

–, % contribution <5·0 %.
*Contain soya/textured vegetable protein/tofu/tempeh foods.

content varied on average by a factor of 2·8, with a CV of 39 % for isoflavones and 33 % for lignans[48].

Food group sources of total lignans, total isoflavones and total phyto-oestrogens were analysed separately. The richest food group source of both total isoflavones and phyto-oestrogens was bread and bread rolls. This is due to the soya flour added to bread in large-scale bread manufacture which produces 80 % of the UK's bread. In EPIC-Norfolk, 96–97 % of bread is commercially produced. Data from Italy and Ireland have estimated that over 90 % of total isoflavone intake comes from bread[49].

Recipes from *McCance and Widdowson's The Composition of Foods*, 5th edition and its associated food supplements[28–37] were used in calculating the phyto-oestrogen content of most food products and dishes. However, some of these foods were analysed in the 1980s (e.g. croissants, jam tarts, scones, apple pies), and soya is not listed as an ingredient. In the DINER system[27], commercial items sometimes receive the same nutrient composition as homemade items in the absence of reliable analyses. Therefore underestimation of phyto-oestrogen content is likely as it has been estimated that 60 % of commercially processed foods contain soya[17].

Regarding food group sources of phyto-oestrogens in SC, vegetable dishes and soya/goat's/sheep's milk were the main contributors. Soya product consumption in ten countries participating in the EPIC study consisting of 35 955 subjects, as measured by a 24 h dietary recall interview, found that soya product consumption is low in Western European countries. Of the seven subgroups of soya products, soya dairy products were consumed in the highest quantities: 1200 mg/d for men and 1900 mg/d for women[50].

A number of the findings relating to the food group choices made by SC and NSC were somewhat unexpected. In both NSC men and women, intakes of vegetables, fruit, nuts and seeds were significantly higher, whereas intakes of bread and bread rolls, breakfast cereals, tea and coffee and vegetable dishes were significantly higher in SC. However the differences found were small and could have been due to the large sample size. A more detailed food group classification is required to more accurately assess choices made by SC and NSC.

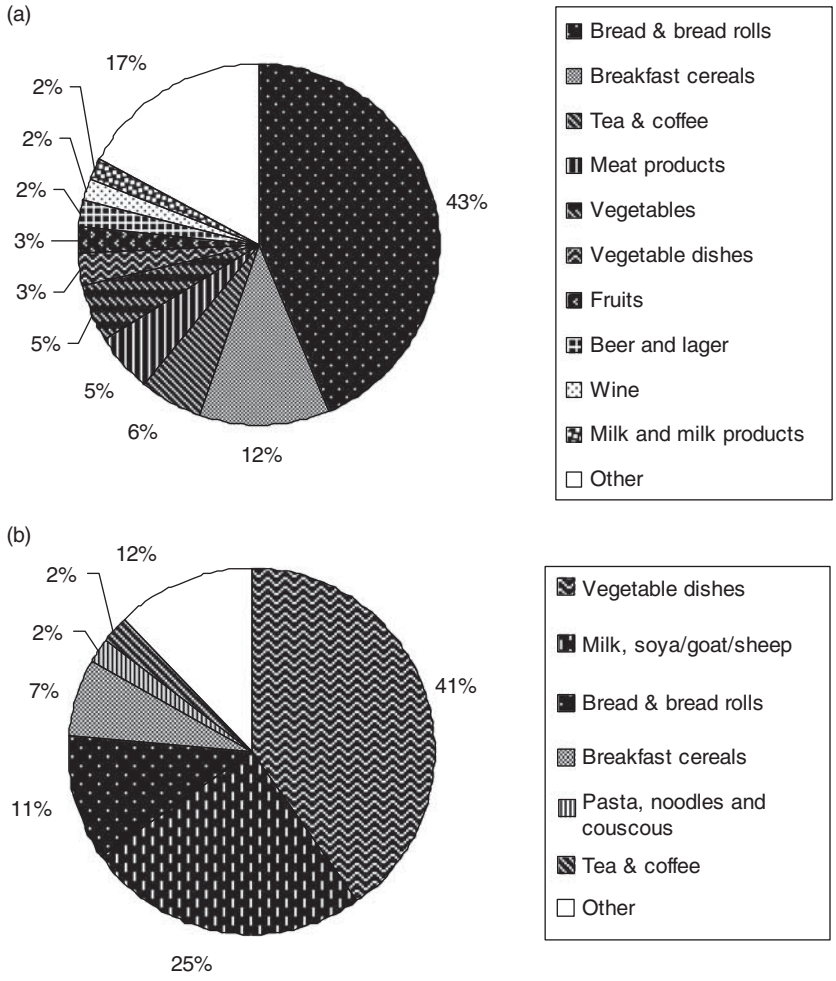

Fig 1 Percentage contribution of food groups to the daily intake of total phyto-oestrogens in (a) non-soya consumers and (b) soya consumers. Men and women aged 40–79 years (*n* 20 437), Norfolk arm of the European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk), 1993–1997

The ability to more accurately estimate phyto-oestrogen and soya intake in Western populations will enable investigations into the suggested beneficial effects of soya on health to be carried out, in the absence of biomarker data.

Acknowledgements

Source of funding: This study was supported by research grants from the Food Standards Agency (T05028), the Medical Research Council (G0500300, G1000143) and Cancer Research UK (C864/A8257). *Conflicts of interest:* The authors declare that they have no conflict of interest. *Authors' contribution:* A.A.M. oversaw the development of the database, conducted the statistical analyses and drafted the manuscript. M.A.H.L., K.-T.K. and G.G.C.K. assisted in writing and revising the manuscript. M.A.H.L., V.v.S., N.A.P. and A.M. assisted in the development of the database. A.B. created the programs for the database. All authors read and approved the final manuscript. *Acknowledgements:* The authors would like to thank all participants of the EPIC-Norfolk study and the EPIC staff for their help with this work.

References

1. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (2003) *Phytoestrogens and Health*. London: Food Standards Agency.
2. Setchell KDR & Adlercreutz H (1988) Mammalian lignans and phytoestrogens. In *The Role of the Gut Flora in Toxicity and Cancer*, pp. 315–346 [IR Rowland, editor]. London: Academic Press.
3. Shutt DA & Cox RI (1972) Steroid and phyto-oestrogen binding to sheep uterine receptors *in vitro*. *J Endocrinol* **52**, 299–310.
4. Peeters PHM, Keinan-Boker L, van der Schouw YT *et al.* (2003) Phytoestrogens and breast cancer risk. Review of the epidemiological evidence. *Breast Cancer Res Treat* **77**, 171–183.
5. Buck K, Zaineddin AK, Vrieling A *et al.* (2010) Meta-analyses of lignans and enterolignans in relation to breast cancer risk. *Am J Clin Nutr* **92**, 141–153.

6. Ward HA, Kuhnle GG, Mulligan AA *et al.* (2010) Breast, colorectal and prostate cancer risk in the European Prospective Investigation into Cancer and Nutrition-Norfolk in relation to phytoestrogen intake derived from an improved database. *Am J Clin Nutr* **91**, 440–448.
7. Anthony MS (2002) Phytoestrogens and cardiovascular disease: where's the meat? *Arterioscler Thromb Vasc Biol* **22**, 1245–1247.
8. Bhupathy P, Haines CD & Leinwand LA (2010) Influence of sex hormones and phytoestrogens on heart disease in men and women. *Womens Health (Lond Engl)* **6**, 77–95.
9. Lagari VS & Levis S (2010) Phytoestrogens and bone health. *Curr Opin Endocrinol Diabetes Obes* **17**, 546–553.
10. Krebs EE, Ensrud KE, MacDonald R *et al.* (2004) Phytoestrogens for treatment of menopausal symptoms: a systematic review. *Obstet Gynecol* **104**, 824–836.
11. Tousen Y, Ezaki J, Fujii Y *et al.* (2011) Natural *S*-equol decreases bone resorption in postmenopausal, non-equol-producing Japanese women: a pilot randomized, placebo-controlled trial. *Menopause* **18**, 563–574.
12. Bhathena SJ & Velasquez MT (2002) Beneficial role of dietary phytoestrogens in obesity and diabetes. *Am J Clin Nutr* **76**, 1191–1201.
13. Cederroth CR, Vinciguerra M, Gjinovci A *et al.* (2008) Dietary phytoestrogens activate AMP-activated protein kinase with improvement in lipid and glucose metabolism. *Diabetes* **57**, 1176–1185.
14. Borriello SP, Setchell KD, Axelson M *et al.* (1985) Production and metabolism of lignans by the human faecal flora. *J Appl Bacteriol* **58**, 37–43.
15. Rowland IR, Wiseman H, Sanders TAB *et al.* (2000) Interindividual variation in metabolism of soy isoflavones and lignans: influence of habitual diet on equol production by the gut microflora. *Nutr Cancer* **36**, 27–32.
16. US Department of Agriculture (2002) USDA–Iowa State University Database on the Isoflavone Content of Foods. http://www.nal.usda.gov/fnic/foodcomp/Data/isoflav/isoflav.html (accessed November 2010).
17. the ENDS report (1996) Supermarkets demand segregation of genetically modified soya. *ENDS Report* issue 258, 26.
18. Liggins J, Bluck LJ, Runswick S *et al.* (2000) Daidzein and genistein contents of vegetables. *Br J Nutr* **84**, 717–725.
19. Liggins J, Bluck LJ, Runswick S *et al.* (2000) Daidzein and genistein content of fruits and nuts. *J Nutr Biochem* **11**, 326–331.
20. Liggins J, Mulligan A, Runswick S *et al.* (2002) Daidzein and genistein content of cereals. *Eur J Clin Nutr* **56**, 961–966.
21. Valsta LM, Kilkkinen A, Mazur W *et al.* (2003) Phyto-oestrogen database of foods and average intake in Finland. *Br J Nutr* **89**, Suppl. 1, S31–S38.
22. Horn-Ross PL, Barnes S, Lee M *et al.* (2000) Assessing phytoestrogen exposure in epidemiologic studies: development of a database (United States). *Cancer Causes Control* **11**, 289–298.
23. Milder IEJ, Arts ICW, Van De Putte B *et al.* (2005) Lignan contents of Dutch plant foods: a database including lariciresinol, pinoresinol, secoisolariciresinol and matairesinol. *Br J Nutr* **93**, 393–402.
24. Thompson LU, Boucher BA, Liu Z *et al.* (2006) Phytoestrogen content of foods consumed in Canada, including isoflavones, lignans and coumestan. *Nutr Cancer* **54**, 184–201.
25. Day N, Oakes S, Luben R *et al.* (1999) EPIC-Norfolk: study design and characteristics of the cohort. *Br J Cancer* **80**, 95–103.
26. Bingham SA, Welch AA, McTaggart A *et al.* (2001) Nutritional methods in the European Prospective Investigation of Cancer in Norfolk. *Public Health Nutr* **4**, 847–858.
27. Welch AA, McTaggart A, Mulligan AA *et al.* (2001) DINER (Data Into Nutrients for Epidemiological Research) – a new data-entry program for nutritional analysis in the EPIC-Norfolk cohort and the 7-day diary method. *Public Health Nutr* **4**, 1253–1265.
28. Holland B, Unwin ID & Buss DH (1988) *Cereals and Cereal Products. Third Supplement to McCance and Widdowson's The Composition of Foods*, 4th ed. Cambridge: Royal Society of Chemistry.
29. Holland B, Unwin ID & Buss DH (1989) *Milk Products and Eggs. Fourth Supplement to McCance and Widdowson's The Composition of Foods*, 4th ed. Cambridge: Royal Society of Chemistry.
30. Holland B, Welch AA, Unwin ID *et al.* (1991) *McCance and Widdowson's The Composition of Foods*, 5th ed. Cambridge: Royal Society of Chemistry.
31. Holland B, Unwin ID & Buss DH (1991) *Vegetables, Herbs and Spices. Fifth Supplement to McCance and Widdowson's The Composition of Foods*, 4th ed. Cambridge: Royal Society of Chemistry.
32. Holland B, Unwin ID & Buss DH (1992) *Fruit and Nuts. First Supplement to McCance and Widdowson's The Composition of Foods*, 5th ed. Cambridge: Royal Society of Chemistry.
33. Holland B, Welch AA & Buss DH (1992) *Vegetable Dishes. Second Supplement to McCance and Widdowson's The Composition of Foods*, 5th ed. Cambridge: Royal Society of Chemistry.
34. Holland B, Brown JB & Buss DH (1993) *Fish and Fish Products. Third Supplement to McCance and Widdowson's The Composition of Foods*, 5th ed. Cambridge: Royal Society of Chemistry.
35. Chan W, Brown JB & Buss DH (1994) *Miscellaneous Foods. Fourth Supplement to McCance and Widdowson's The Composition of Foods*, 5th ed. Cambridge: Royal Society of Chemistry.
36. Chan W, Brown J, Lee SM *et al.* (1995) *Meat, Poultry and Game. Fifth Supplement to McCance and Widdowson's The Composition of Foods*, 5th ed. Cambridge: Royal Society of Chemistry.
37. Chan W, Brown J, Church SM *et al.* (1996) *Meat Products and Dishes. Sixth Supplement to McCance and Widdowson's The Composition of Foods*, 5th ed. Cambridge: Royal Society of Chemistry.
38. Kuhnle GGC, Dell'aquila C, Aspinall SM *et al.* (2009) Phytoestrogen content of cereals and cereal-based foods consumed in the UK. *Nutr Cancer* **61**, 302–309.
39. Kuhnle GG, Dell'Aquila C, Aspinall SM *et al.* (2009) Phytoestrogen content of fruits and vegetables commonly consumed in the UK based on LC–MS and ^{13}C-labelled standards. *Food Chem* **116**, 542–554.
40. Kuhnle GGC, Dell'Aquila C, Aspinall SM *et al.* (2008) Phytoestrogen content of beverages, nuts, seeds, and oils. *J Agric Food Chem* **56**, 7311–7315.
41. Kuhnle GGC, Dell'Aquila C, Aspinall SM *et al.* (2008) Phytoestrogen content of foods of animal origin: dairy products, eggs, meat, fish, and seafood. *J Agric Food Chem* **56**, 10099–10104.
42. Kuhnle GGC, Dell'Aquila C, Low YL *et al.* (2007) Extraction and quantification of phytoestrogens in foods using automated solid-phase extraction and LC/MS/MS. *Anal Chem* **79**, 9234–9239.
43. Ritchie MR, Cummings JH, Morton MS *et al.* (2006) A newly constructed and validated isoflavone database for the assessment of total genistein and daidzein intake. *Br J Nutr* **95**, 204–213.
44. Clarke DB & Lloyd AS (2004) Dietary exposure estimates of isoflavones from the 1998 UK Total Diet Study. *Food Addit Contam* **21**, 305–316.
45. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (2001) *Working Group on*

Phytoestrogen Paper PEG/2001/24: Amendment to the Isoflavone Intake Assessment. London: Food Standards Agency.
46. Mulligan AA, Welch AA, McTaggart AA *et al.* (2007) Intakes and sources of soya foods and isoflavones in a UK population cohort study (EPIC-Norfolk). *Eur J Clin Nutr* **61**, 248–254.
47. Kiely M, Faughnan M, Wahala K *et al.* (2003) Phytoestrogen levels in foods: the design and construction of the VENUS database. *Br J Nutr* **89**, 19–23.
48. Kuhnle GGC, Dell'Aquilla C, Runswick SA *et al.* (2009) Variability of phytoestrogen content in foods from different sources. *Food Chem* **113**, 1184–1187.
49. Van Erp-Baart MAJ, Brants HAM, Kiely M *et al.* (2003) Isoflavone intake in four different European countries: the VENUS approach. *Br J Nutr* **89**, Suppl. 1, S25–S30.
50. Keinan-Boker L, Peeters PHM, Mulligan AA *et al.* (2002) Soy product consumption in 10 European countries: the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Public Health Nutr* **5**, 1217–1226.