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European Prospective Investigation into Cancer and Nutrition (EPIC) calibration study: rationale, design and population characteristics

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Abstract

The European Prospective Investigation into Cancer and Nutrition (EPIC), which covers a large cohort of half a million men and women from 23 European centres in 10 Western European countries, was designed to study the relationship between diet and the risk of chronic diseases, particularly cancer. Information on usual individual dietary intake was assessed using different validated dietary assessment methods across participating countries. In order to adjust for possible systematic over- or underestimation in dietary intake measurements and correct for attenuation bias in relative risk estimates, a calibration approach was developed. This approach involved an additional dietary assessment common across study populations to re-express individual dietary intakes according to the same reference scale. A single 24-hour diet recall was therefore collected, as the EPIC reference calibration method, from a stratified random sample of 36 900 subjects from the entire EPIC cohort, using a software program (EPIC-SOFT) specifically designed to standardise the dietary measurements across study populations. This paper describes the design and populations of the calibration sub-studies set up in the EPIC centres. In addition, to assess whether the calibration sub-samples were representative of the entire group of EPIC cohorts, a series of subjects' characteristics known possibly to influence dietary intakes was compared in both population groups. This was the first time that calibration sub-studies had been set up in a large multi-centre European study. These studies showed that, despite certain inherent methodological and logistic constraints, a study design such as this one works relatively well in practice. The average response in the calibration study was 78.3% and ranged from 46.5% to 92.5%. The calibration population differed slightly from the overall cohort but the differences were small for most characteristics and centres. The overall results suggest that, after adjustment for age, dietary intakes estimated from calibration samples can reasonably be interpreted as representative of the main cohorts in most of the EPIC centres.

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Compared with retrospective case–control or ecological studies, large multi-centre prospective studies offer major advantages for investigating the relationship between diet and other lifestyle factors and risk of chronic diseases[1–3]. These studies are designed to increase the statistical power to detect an association between diet and disease by including large study populations varying both in the type of dietary patterns and cancer incidence rates, thus increasing the heterogeneity of both exposure and disease outcomes[4]. However, multi-centre studies also raise relatively new statistical and methodological issues for the comparison and pooled analysis of dietary intake data collected from large heterogeneous populations with wide differences in food consumption, language and socio-cultural characteristics. In particular, the inherent difficulty of estimating and comparing individuals' usual dietary intakes is amplified in large multi-centre studies, where dietary questionnaires often differ across study populations in order to capture the specific local diets[5]. The magnitude and nature of systematic and random errors in dietary intake measurements may thus vary across study populations and distort the estimation and interpretation of the overall relationship between diet and disease when all cohorts are combined.

Several authors[6–10] have proposed the use of a calibration approach in large nutritional studies. The purpose of such calibration studies is twofold: first, at the population level, to adjust for systematic over- and underestimation of the true mean dietary intakes in each centre; second, at the individual level, to attempt to correct for attenuation bias in relative risk due to random errors in dietary measurements. For calibration at the population level, where emphasis is on unbiased estimates of mean intake, calibration can be achieved by applying, in addition to the dietary questionnaires, a second highly standardised dietary method in a representative sub-sample from each cohort as a common reference measurement across study populations. In its simplest definition, calibration means re-expressing the individual dietary measurements by means of centre-specific scaling factors. At the individual level, correction for regression dilution can only be fully achieved if the measurement errors of the second dietary assessment instrument are independent from the errors of the main instrument used in the entire cohort.

Although this complex study design initiates a new generation of large nutritional cohorts with nested calibration sub-studies, there is still little experience on how to set up such studies in practice[11,12]. This paper describes the design of the calibration sub-studies within the European Prospective Investigation into Cancer and Nutrition (EPIC), a network of prospective cohort studies involving 23 European centres from 10 Western European countries (France, Italy, Spain, the UK, Germany, The Netherlands, Greece, Sweden, Denmark and Norway). Among the most important features of EPIC are its size, geographical distribution and heterogeneity of the dietary patterns and other lifestyle and socio-cultural characteristics of the study populations. Information on usual diet, lifestyle, environmental factors and anthropometry was collected from each individual at baseline, as well as one blood sample. Information on usual individual dietary intakes was assessed using different dietary history questionnaires, food-frequency questionnaires or a modified dietary history[13] developed and validated in each participating country[14–16]. More details on the EPIC study design, the study cohort populations, the individual information collected and the EPIC biological bank are given elsewhere in this supplement[17].

In addition, a single 24-hour dietary recall (24-HDR) was collected from a sub-sample of 36 900 individuals, to be used as the EPIC reference calibration method. Computerised 24-hour dietary recall interview software (EPIC-SOFT) was developed to standardise dietary intakes reported across the EPIC centres and increase the likelihood that measurement errors will be of a similar magnitude and nature in all study centres. The concept of standardisation and the structure of the EPIC-SOFT software are described in detail by Slimani *et al.*[18,19].

This paper describes the design and populations of the calibration sub-studies set up in the centres participating in the EPIC study. In addition, in order to assess whether the calibration sub-samples were representative of the overall group of EPIC cohorts, a series of subjects' characteristics known possibly to influence dietary intakes was compared in both population groups.

Study protocol

Sampling procedures

The EPIC study populations were not chosen to provide representative samples. Recruitment was determined by practical and logistic considerations in order to obtain high participation and long-term follow-up from the study participants[17]. These study populations represent heterogeneous groups and were population-based (Bilthoven, The Netherlands; Greece; Germany; Sweden; Denmark; Norway; Cambridge and a small part of the Oxford cohort from the UK; Spain; Italy) or participants in breast screening (Utrecht, The Netherlands; Florence, Italy) or teachers and school workers in France. In Oxford, most of the cohort (~87%) was recruited among subjects with an interest in health and/or vegetarian eating habits who were either self-defined vegans (i.e. consumed no animal products), ovo-lacto vegetarians, fish eaters (i.e. consumers of fish but not meat) or meat eaters. Blood donors were also recruited in different proportions in certain Italian and Spanish centres. In France, Norway, Utrecht (The Netherlands) and Naples (Italy) only women were recruited.

The calibration population was defined as a random sample from each of these cohorts, weighted according to

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the cumulative numbers of cancer cases expected over 10 years of follow-up per gender and 5-year age stratum. The sample sizes were chosen to provide calibration at both the individual and population level, even though it was recognised that the 24-hour dietary recall and the main dietary assessment instrument would not have fully independent error structures. A total of about 4000 24-hour dietary recalls, equivalent to a single, large random sample drawn from each *full* country cohort, was recommended per country, according to calculations detailed elsewhere[20]. This sample size was achieved in most countries, except in the UK (1117), Norway (1819) and Greece (2930), and represents, according to the age distribution and size of the cohort, between 5% and 12% of the study population in each national cohort, except in the UK (~1.5%). In Norway, the calibration sample size requirement was smaller because lower numbers of cancers are expected from the relatively young cohort of women only. In Greece, a 10% representative sample of the entire cohort (28 572) was recruited all over Greece including Athens. In the UK, the sample size of 1117 was chosen to provide population-level calibration, i.e. the sample size was calculated to give a sufficiently accurate estimation of mean intakes. Much of the UK cohort has already completed a second dietary instrument, a 7-day diet diary that included an interviewed 24-hour recall as a component, which could be used for (within-cohort) individual-level calibration should it be required.

In certain countries, the calibration population was sampled strictly at random, particularly when the age distributions were quite narrow, as in Norway (e.g. 49.3 ± 4.3 years). In France, where the study population was scattered all over the country and it was not possible to interview subjects living far from large urban areas, cluster sampling was used: contiguous, sparsely populated administrative regions were grouped into seven geographical areas in which the subjects could more easily be sampled randomly and approached for home visits or invited to a local centre for the 24-HDR interview. Using cluster sampling, a higher probability of being sampled was given to clusters with a higher number of subjects and vice versa.

In addition, the sampling procedures were defined as having an equal distribution of season and day of interview, to control for possible day-to-day and seasonal variations in dietary consumption. Although in Spain, for example, the response rates obtained during the pilot phase were as high for interviews on Saturdays as for the other days of the week, other countries such as France and The Netherlands experienced high refusal rates for Saturday interviews. In addition, certain examination centres were closed or interviewers did not work during the weekends (e.g. Denmark, The Netherlands). Because of these constraints, alternative methods were considered to approach and interview the subjects during the weekend (i.e. to recall the Saturdays and Fridays). In some instances, interviews on Fridays and Saturdays were collected 48 hours later instead of the following day, and interviews at home were proposed to increase the participation rate. Such methods were rarely used for other days of the week, unless it was impossible to interview on the given sampled day or perform the interview at the examination centre.

Logistics used to set up the EPIC calibration sub-studies

The EPIC calibration fieldwork was conducted over a 5-year period between March 1995 and June 2000. A pilot phase was started initially in France (Rhône-Alpes), Spain (Basque Country) and The Netherlands in order to test the first version of EPIC-SOFT and the overall logistics. It was then extended to the other countries/centres according to the availability of country-specific EPIC-SOFT versions and the date of entry in EPIC. In order to have representative calibration sub-populations, the calibration study lasted until the end of the EPIC baseline recruitment. Depending on the country, it took between 10 and 31 months to collect the interviews sampled to cover both day-to-day and seasonal variations. Overall it took longer to perform the required dietary interviews in countries where several local, geographically distant centres were involved (e.g. France, Italy or Spain), where total population coverage was attempted (Greece) and where different study populations, study designs and recruitment methods were used. The time required for conducting the calibration fieldwork was not strictly related to the total number of interviews, because at least 1 year was needed to cover all seasons. It is also interesting to note, for example, that the Nordic countries, which joined EPIC later, benefited from more advanced methodology (i.e. the overall logistics and EPIC-SOFT programs were fully developed and tested), which allowed them to complete the interviews more quickly than other countries.

Table 1 summarises the methods of recruitment and the localisation of the 24-HDR interviews performed in the EPIC centres. Whenever possible, subjects were recruited to the calibration study 'by surprise', when they came for their first baseline examination. The dietary interview was then performed 30–40 minutes immediately after their baseline examination. It was anticipated that this recruitment approach would give a higher participation rate, as subjects would not have to return to the examination centres. This method was used for 84–100% of the subjects in Paris and the surrounding area (Ile-de-France), Potsdam (Germany), The Netherlands and Denmark, and to a lesser extent in other French centres (i.e. Rhône-Alpes, 36%; Bretagne/Pays-de-Loire, 28%), Heidelberg (Germany; 62%) and Ragusa (Italy; 42%).

In the other centres, the subjects had either been enrolled before joining EPIC or had already been invited for the baseline examination when the calibration study was started. The subjects randomly selected to participate

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Table 1 Methods of recruitment of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and related issues

	Study period covered	Number of subjects approached	Recruitment method used (%)			Number of reminders	Type of reminders used (+/ −)			Location of interviews (%)			
			Letter	Telephone	Centre		None	Letter	Telephone	Centre	Home	Elsewhere	Unknown/missing
Greece	05/97–06/99	5406	–	100	–	2	–	–	+	–	–	100‡	–
Spain		3741								99.4	0.2	0.2	0.2
Granada	12/95–10/96	722	–	100	–	0	+	–	–	100	–	–	–
Murcia	10/95–09/96	591	2	98	–	0	+	–	–	98.9	0.2	–	0.9
Navarra	02/96–01/97	850	–	100	–	0	+	–	–	100	–	–	–
San Sebastian	07/95–06/96	806	100*	100*	–	0	+	–	–	98.1	0.7	0.8	0.4
Asturias	02/96–01/97	772	–	100	–	0	+	–	–	100	–	–	–
Italy		4418								93.7	6.3	–	–
Ragusa	04/96–07/98	348	46	12	42	1	–	–	+	92.0	8.0	–	–
Naples	04/96–03/98	482	–	99	1	0	+	–	–	99.0	1.0	–	–
Florence	05/96–08/98	1155	–	99	1	0	+	–	–	92.0	8.0	–	–
Turin	04/96–03/98	1172	–	99	1	0	+	–	–	87.0	13.0	–	–
Varese	04/96–06/98	1261	–	99	1	0	+	–	–	97.0	3.0	–	–
France		6456								29.5	19.9	45.9	4.7
Languedoc/Roussillon	10/95–04/97	869	100	–	–	2–3	–	+	–	–	22.4	73.1	4.5
Aquitaine	10/95–02/97	803	100	–	–	2–3	–	+	–	26.6	16.5	55.1	1.8
Rhône-Alpes	03/95–03/97	623	64	–	36	2	–	+	–	–	33.8	62.5	3.7
Bretagne/Pays-de-Loire	01/96–04/97	665	72	–	28	1–2	–	+	–	0.2	30.1	69.5	0.2
Ile-de-France	01/96–07/97	1575	16	–	84	0	–	–	–	23.4	24.5	41.5	10.6
Alsace-Lorraine	10/95–02/97	1343	100	–	–	1–2	–	+	–	84.0	8.0	7.5	0.5
Nord-Pas-de-Calais	10/95–07/97	578	100	–	–	2–3	–	+	–	0.2	19.7	67.5	12.6
Germany		4693								81.1	18.5	0.2	0.2
Heidelberg	06/96–10/98	2349	–	38†	62†	0	+	–	–	61.7	37.3	0.5	0.5
Potsdam	06/96–04/98	2344	–	–	100	0	+	–	–	98.9	1.1	–	–
The Netherlands		5642								67.0	31.9	0.1	0.9
Bilthoven	04/95–12/97	3411	–	–	100	0	+	–	–	96.3	2.1	0.0	1.6
Utrecht	04/95–12/97	2231	–	–	100	0	+	–	–	24.8	74.8	0.3	0.1
United Kingdom		1900								99.4	0.6	–	–
Cambridge	03/97–04/98	905	100	–	–	1–4	–	+	+	98.7	1.3	–	–
Oxford	02/97–07/98	995	100	–	–	0	+	–	–	100	–	–	–
Denmark		4511								96.1	3.9	–	0.1
Copenhagen	07/96–05/97	3268	–	–	100	0	–	–	–	94.6	5.4	–	0.1
Aarhus	08/96–05/97	1243	–	–	100	0	–	–	+	100	–	–	–
Sweden		8413								100	–	–	–
Malmö	03/96–07/97	4064	100	–	–	2	–	+	+	100	–	–	–
Umeå	03/97–10/98	4349	100*	100	–	0	–	–	+	100	–	–	–
Norway	05/99–06/00	2993	100	–	–	1	–	+	–	–	100	–	–

*The subjects were contacted first by letter and then systematically approached by telephone to confirm the date and time of the interview.
†The subjects were all approached at the study centre when they came for the baseline examination. If it was not possible to fix an appointment immediately, the subjects were re-contacted by phone.
‡In Athens, the interviews were conducted in the co-ordinating and elderly centres. Elsewhere in the country, the interviews were conducted in public places and occasionally at home.

in the calibration study were then re-contacted either by letter (France, UK, Norway and Sweden) or by telephone (Spain, Italy (except Ragusa) and Greece). In contrast to recruitment at baseline, the subjects re-invited by letter or telephone were asked to return to provide further information but were not informed about the type of dietary method or time period to which it referred (i.e. the previous day). This precaution was taken in order to avoid changes in usual dietary habits and bias during the recalled dietary interview. According to what best suited the subjects and the local facilities available, the face-to-face 24-HDR interview was performed at the local research centre or at home, particularly if the people were living far from the research institute. In France, the overall study was co-ordinated from Paris and local authorities and cancer leagues made rooms available to conduct the dietary interviews (e.g. schools, town halls, local cancer leagues). In Greece, where it was particularly difficult to recruit local volunteers outside Athens, mobile units were used. In Norway, where the interviews were conducted by telephone, the subjects were all interviewed at home. According to the country and method of recruitment used, one to four reminders were sent when subjects did not reply.

Exclusions and inclusions of subjects from the 24-HDR dataset

The information reported in the following tables was calculated from the final 24-HDR dataset ($n = 35\,955$) obtained after further 24-HDR exclusions or inclusions from the original sample. We excluded 358 ($\sim 1\%$) interviews locally, mainly because of technical problems with the software during the interview or because subjects were not properly randomised or excluded from the EPIC cohort for other reasons (e.g. incomplete data). Subjects under 35 and over 74 years of age (who were present only in a few EPIC cohorts) were excluded from the dataset before statistical analyses. This represented a total of 945 subjects, mainly from Bilthoven (583 young people) and Greece (244, mainly elderly people).

In addition, 357 ($< 1\%$ of the total final sample) subjects not originally sampled were added to the calibration population (29 subjects from Naples, 130 from Potsdam, 46 from Cambridge, 152 from Oxford). These subjects were involved in other EPIC cross-sectional or validation studies on urinary or blood biological markers and diet and most of them were participants sampled from the calibration sub-populations. Apart from Oxford, all have an EPIC-SOFT 24-HDR measurement collected in previous EPIC pilot studies. In Oxford, the 152 subjects added, essentially vegans and vegetarians, were not part of the representative sample initially selected for the calibration study, had no EPIC-SOFT 24-hour dietary recall measurements and were difficult to re-contact because they were living throughout the UK. It was therefore decided to sample randomly one day from the 7-day records, collected at baseline in the UK, in addition to the EPIC food-frequency questionnaire, and enter them using EPIC-SOFT as a data-entry system (i.e. using the same rules as during a classic face-to-face interview).

Redefinition of the EPIC centres

With a view to the final statistical analyses, we decided to redefine the centres and geographical regions used to set up the field calibration studies in France, the UK and Norway and reported in Tables 1 and 2. In France, the seven geographical regions initially set up to facilitate the calibration field study were reduced, by clustering the 95 French 'départements', to four geographical regions more representative of the different dietary patterns existing across the country (i.e. North-east, North-west, South and South coast). The cohort of subjects recruited from the general population both in Cambridge and Oxford via general practitioners was grouped together ('general population group'). The UK 'health-conscious' group recruited by post was considered as a separate population group involving heterogeneous sub-populations of vegans, vegetarians, fish eaters and meat eaters. In Norway, it was decided to subdivide the study populations scattered all over the country into coastal (North & West) and inland (South & East) regions. The Dutch co-ordinating centre 'Bilthoven' covers three towns (Amsterdam, Doetinchem, Maastricht), where the subjects were recruited. In total, 27 centres were finally used for the analyses of the EPIC calibration dietary data and for presenting the results reported in Tables 3–9. These include administrative centres and geographical regions in France and Norway, but for convenience the term 'centre' is used for both.

Participation rates, general characteristics and representativeness of the EPIC calibration sub-populations

Participation rates in the EPIC calibration sub-studies

The participation rates in the calibration sub-studies obtained in the different EPIC administrative centres are reported in Table 2. These calculations were obtained before any of the exclusions or additions discussed previously. At the country level, they ranged from 91.6% (Germany) to 54.2% (Greece), and seven countries out of 10 had a participation rate of $\sim 75\%$ or more (Sweden, France, The Netherlands, Italy, Spain, Denmark, Germany). The response rate was about 60% for the general population in Norway and the UK, and lower in Greece (54.2%) and in the 'health-conscious' sub-cohort from Oxford (46.5%).

In Germany, Denmark and the general population in the UK, no differences were observed in the response rates across centres from the same country. In contrast, in France, a higher rate was observed in Ile-de-France, where

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Table 2 Participation rates obtained from the European Prospective Investigation into Cancer and Nutrition (EPIC) centres and countries*

Country and centre	Number of subjects selected to be approached	Number of subjects interviewed	Participation rate (%)	Non-response		
				Active (%)	Passive (%)	Total (%)
Greece	5406	2930	54.2	15.3	30.5	45.8
Spain	3741	3222	86.1	9.2	4.6	13.9
Granada	722	515	71.3	24.7	4.0	28.7
Murcia	591	548	84.1	3.4	3.9	7.3
Navarra	850	715	91.1	7.8	8.1	15.9
San Sebastian	806	734	86.1	5.2	3.7	8.9
Asturias	772	710	92.0	5.2	2.8	8.0
Italy	4418	3961	89.7	7.2	3.1	10.3
Ragusa	348	306	87.9	6.7	5.4	12.1
Naples	482	403	83.6	12.4	4.0	16.4
Florence	1155	1058	91.6	7.1	1.3	8.4
Turin	1172	1069	91.2	5.4	3.4	8.8
Varese	1261	1125	89.2	7.2	3.6	10.8
France	6456	4854	75.2	20.5	4.3	24.8
Languedoc/Roussillon	869	625	72.0	22.5	5.5	28.0
Aquitaine	578	443	76.6	19.2	4.2	23.4
Rhône-Alpes	1575	1018	64.6	33.3	6.3	39.6
Bretagne/Pays-de-Loire	803	635	79.1	15.2	4.6	19.8
Ile-de-France	1343	1201	89.4	9.2	1.7	10.9
Alsace-Lorraine	665	480	72.2	22.6	5.2	27.8
Nord-Pas-de-Calais	623	452	72.6	25.0	2.4	27.4
Germany	4693	4299	91.6	8.2	0.2	8.4
Heidelberg	2344	2126	90.7	8.9	0.4	9.3
Potsdam	2349	2173	92.5	7.5	–	7.5
The Netherlands	5642	4585	81.4	9.7	8.9	18.6
Bilthoven	3411	2708	79.4	10.7	9.9	20.6
Utrecht	2231	1877	84.1	8.1	7.8	15.6
United Kingdom	1900	1117	59.0	30.0	11.0	41.0
Cambridge	905	547	60.4	30.2	9.4	39.6
Oxford: general population	640	405	63.3	20.9	15.8	36.7
Oxford: 'health-conscious'	355	165	46.5	50.7	2.8	53.5
Denmark	4511	3919	86.9	13.1	–	13.1
Copenhagen	3268	2842	87.0	13.0	–	13.0
Aarhus	1243	1077	86.6	13.4	–	13.4
Sweden	8413	6195	73.6	20.4	5.9	26.3
Malmö	4064	3132	77.1	19.0	3.9	22.9
Umeå†	4349	3063	70.4	21.8	7.8	29.6
Norway	2993	1819	60.8	24.0	15.2	39.2

* Estimates obtained before any exclusion/addition of subjects.
† One hundred and forty-nine individuals were excluded due to a mix-up of food-frequency questionnaires.

the subjects were interviewed immediately after the baseline examination, than in other centres where study participants were re-invited for interviews sometimes more than 2 years afterwards. Within Italy and Spain, lower participation rates were reported in southern centres (Naples and Ragusa, Granada). In the UK, the rate was about 25% lower among the 'health-conscious' group (46.5%) compared with the general population group, both in Cambridge and Oxford (60.4% and 63.3%, respectively). One possible explanation is that the 'health-conscious' group's initial participation in EPIC was solely by post, so participation in the 24-HDR was their first visit to an EPIC examination centre that was, on average, a greater distance for them. In Greece, the low participation rate (54.2%) was largely due to logistic difficulties of approaching subjects living outside Athens.

Apart from The Netherlands and Greece, non-participation in the calibration sub-studies was due primarily to the subjects' failure or refusal to respond to the invitation or accept an appointment for the dietary interview ('active' non-response). This represents more than 20% of the total subjects approached in Sweden, France, Norway and the UK, with some variations across centres. In Spain for example, the active non-response rate ranged from 3.4% in Murcia to 24.7% in Granada. Overall, the active non-response was much lower when the subject was approached by surprise just after the main examination than when he/she was contacted afterwards. In Germany and Denmark the non-participation was exclusively active.

In contrast, in the Netherlands and Greece, 'passive' non-response (i.e. non-participation because it was impossible to get in touch with the subjects) was about the same as, or higher than, active non-response. In The Netherlands, this was because it was often impossible to contact subjects by phone and because staff at the baseline examination centre forgot to refer subjects to the dietitians. In Greece, the passive non-response rate was particularly

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high (30.5%), which explains the overall low participation rate (~54%). Mobile units visited the areas outside Athens for short periods only and passive non-response was unavoidably high because of time constraints for approaching and interviewing subjects. In Norway, 15% of the subjects approached could not be interviewed because of passive non-response.

General characteristics and representativeness of the EPIC calibration sub-populations

Tables 3–9 present a series of characteristics of the calibration sub-populations considered for analysis in this supplement. In addition, to estimate the representativeness of the calibration sub-populations, we compared these samples to the rest of the EPIC cohort according to certain variables known to influence dietary consumption. In order to take into account the differences in age distribution in the calibration samples, due to the age-stratified sampling strategy, all of the results are presented age-adjusted. We tested for significant differences in weight, height and body mass index (BMI) mean estimates between the calibration samples and the rest of the EPIC population. Differences in smoking status, level of education and physical activity at work (categorical variables) were tested using gender- and centre-specific logistic regressions. We modelled the different categorical variables separately as independent covariates, an indicator for distinguishing the calibration sample from the rest of the cohort as a binary outcome, and age as an adjusting variable. Significance was assessed using likelihood ratio statistics, at 95%, 99% and 99.9% levels. Analyses were performed using SAS software[21]. Since the main focus of this paper is the calibration sub-studies, the entire EPIC cohort, detailed elsewhere[17,22–24], will be described only for the purpose of comparing the two population groups.

Age and anthropometry

The calibration sample is composed of middle-aged populations, from 49.3 ± 4.3 years (Norway) to 58.6 ± 8.4 years (Sweden) in women, and from 50.0 ± 7.4 years (Bilthoven) to 61.1 ± 7.3 years (Sweden) in men (Tables 3a and 3b). Anthropometry varies considerably across countries. Height adjusted for age is about 9–10 cm higher for women in Norway than in Spain and for men in Sweden than in Spain. The same order of difference (~10 kg) is observed for weight among women in France and Greece, whereas a difference in weight of only 5.5 kg is observed in men between Italy and The Netherlands. Spain and Greece report both the lowest heights and the highest BMI in women and men, whereas Italy, The Netherlands, Germany, the UK general population, Sweden and Denmark report about the same BMI in women (25–26 kg m^{-2}) and men (26–27 kg m^{-2}). The lowest BMI (≤24 kg m^{-2}) is observed in the Norwegian female cohort and in highly selected study populations such as women teachers in France and 'health-conscious' people in the UK.

When compared with the rest of the EPIC cohort, the weight, height and BMI means of the calibration populations showed statistically significant differences in 20–30% of the sex-specific centres. However, in centres where there was a statistically significant difference, this was usually modest in absolute terms. In most cases, the mean BMI differed between the calibration population and the entire cohort for centres where a statistically significant difference was observed for weight and/or height.

Smoking status

In this calibration population, the number of never-smokers is about 1.2–2.7 times higher in women than men. For women in Greece, Spain, France and the UK 'health-conscious' group, never-smokers represent ≥65% of the population (Table 4) and about 35–60% elsewhere. In men, never-smokers represent 24–46%. The percentage of ex-smokers varies to a greater extent among women (7–33%) than among men (28–46%), as does the percentage of smokers, from less than 9% to ~25% for women and from 21% to 40% for men, except in the UK (~17%).

In about a quarter of the EPIC centres, the smoking status is not equally distributed between the calibration sub-sample and the entire EPIC cohort. Most of the imbalance is due, however, to differences of only a few percentage points (<5%) across classes. Apart from the Spanish centres, the number of current smokers is equal or lower in the calibration sample than in the entire cohort. In contrast, the number of ex-smokers is higher in the calibration population, except in Umeå and for men in Spain. The number of never-smokers is relatively lower in the calibration sample in women from southern centres (France North-west, Navarra and Greece) whereas it tends to be higher in central and Nordic centres. In men, never-smokers are always equal or over-sampled in the calibration group compared with the entire cohort.

Level of education

A common variable in five classes of level of education was used in EPIC (Tables 5a and 5b). In Malmö, however, where the cohort was recruited before joining EPIC, the education level of 7332 subjects (~25% of the total cohort) was defined differently and these subjects were therefore classified in the closest existing EPIC category (corresponding to 'technical school'). Large differences are observed in education level reflecting gender discrepancies and the diversity of origin of the cohorts (general population, blood donors, teachers and 'health-conscious' group)[17]. For example, the number of subjects who never completed primary school is high in Spain, particularly among women and in the south, and Greece, whereas it is

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Table 3a Comparison of mean age and anthropometry, adjusted for age, of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and the rest of the EPIC cohort: women

			Age (years)				Height (cm)					Weight (kg)					BMI (kg m^{-2})				
	n		Calibration		Cohort		Calibration		Cohort			Calibration		Cohort			Calibration		Cohort		
Country and centre	Calibration	Cohort	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*-value	Mean	SD	Mean	SD	*P*-value	Mean	SD	Mean	SD	*P*-value
Greece	1374	13 644	57.2	9.9	54.7	11.1	157.3	6.0	156.6	6.5	***	70.9	12.7	71.6	13.8	–	28.7	5.2	29.3	5.6	***
Spain	1443	24 088	52.9	8.3	48.4	8.3	156.7	5.7	156.1	6.2	–	69.2	11.2	70.2	12.2	–	28.3	4.5	28.9	4.9	–
Granada	300	5750	54.6	8.1	49.3	8.7	156.0	5.6	155.1	6.0	**	70.6	11.4	71.8	12.1		29.1	4.7	29.9	4.9	**
Murcia	304	5418	51.6	8.6	48.3	8.3	155.9	5.5	155.5	6.1		71.1	11.2	70.5	12.3		29.4	4.4	29.2	4.9	
Navarra	271	3900	53.6	7.8	48.4	8.0	157.2	5.5	156.7	6.0		67.5	10.7	69.4	11.7	**	27.4	4.3	28.3	4.7	***
San Sebastian	244	4009	51.8	8.2	48.1	8.1	158.5	5.7	157.8	6.3		68.0	11.0	68.4	12.2		27.1	4.3	27.5	4.8	
Asturias	324	5011	52.9	8.4	47.7	8.1	156.2	5.5	156.1	6.3		68.4	11.0	69.9	12.5	*	28.1	4.4	28.7	5.0	*
Italy	2512	29 757	54.7	7.3	50.6	8.0	158.7	6.1	158.3	6.2	–	64.8	11.0	64.9	11.3	–	25.8	4.3	25.9	4.4	–
Ragusa	138	3115	50.6	8.3	46.2	7.7	155.7	5.7	156.5	7.2		65.3	11.0	66.4	13.9		26.9	4.4	27.1	5.5	
Naples	403	4582	54.2	6.7	50.4	7.5	157.2	5.7	156.3	5.9	**	67.0	11.1	66.6	11.6		27.1	4.3	27.3	4.5	
Florence	785	9212	55.3	7.0	51.9	7.6	160.2	6.1	159.9	6.3		64.8	10.8	64.6	11.1		25.3	4.0	25.3	4.1	
Turin	392	4147	54.2	6.9	50.6	7.5	159.2	6.1	158.8	6.3		64.5	11.0	64.3	11.3		25.5	4.2	25.5	4.3	
Varese	794	8701	55.3	7.6	50.9	8.4	158.3	5.9	157.9	6.0		63.7	11.1	64.1	11.3		25.5	4.3	25.7	4.4	
France	4639	68 357	57.0	6.9	52.8	6.7	161.5	5.7	161.4	6.0	–	60.8	9.8	60.7	10.3	–	23.3	3.5	23.3	3.7	–
South coast	612	9283	57.6	6.8	53.7	6.6	161.4	5.7	161.2	6.2		59.9	9.3	60.0	10.1		23.0	3.4	23.1	3.7	
South	1396	17 035	56.6	7.0	53.0	6.6	161.4	5.7	161.3	6.0		59.9	9.4	60.0	10.0		23.0	3.4	23.1	3.6	
North-west	622	11 041	56.9	6.7	52.8	6.7	160.9	5.6	160.9	5.9		60.2	9.8	60.4	10.4		23.2	3.6	23.3	3.8	
North-east	2009	30 998	57.1	7.0	52.5	6.6	161.8	5.8	161.7	6.1		61.9	10.1	61.3	10.6	*	23.7	3.6	23.5	3.8	*
Germany	2150	27 961	51.6	8.7	49.2	9.0	163.0	6.1	162.8	6.5	–	69.1	12.5	69.0	13.3	–	26.1	4.6	26.0	4.8	–
Heidelberg	1087	12 530	50.3	8.5	49.4	8.6	163.6	6.1	163.3	6.4		68.9	12.5	68.8	13.1		25.8	4.6	25.8	4.8	
Potsdam	1063	15 431	53.0	8.6	49.1	9.2	162.3	6.0	162.4	6.5		69.4	12.6	69.2	13.6		26.3	4.5	26.3	4.9	
The Netherlands	2960	23 264	55.1	8.3	54.3	7.9	164.9	6.2	164.5	6.5	–	70.1	11.7	69.8	12.3	–	25.8	4.2	25.8	4.4	–
Bilthoven	1086	7781	48.9	7.5	48.0	7.5	164.5	6.7	163.9	8.2	**	70.9	12.3	70.5	15.1		26.2	4.4	26.3	5.4	
Utrecht	1874	15 483	58.7	6.3	57.5	6.0	164.9	6.1	164.4	7.3	**	70.2	11.7	70.0	13.8		25.9	4.1	25.9	4.9	
United Kingdom	768	45 184	55.6	8.9	52.7	10.0	162.5	6.4	162.7	6.7	–	66.2	11.7	66.1	12.1	–	25.1	4.3	25.0	4.4	–
General population	571	19 978	56.1	9.0	56.0	8.5	162.2	6.1	161.8	6.3		67.6	12.4	68.1	12.7		25.7	4.6	26.0	4.7	
'Health-conscious'	197	25 206	54.1	8.7	50.0	10.2	163.1	6.6	163.6	7.2		62.5	10.9	64.4	11.9	*	23.5	3.9	24.1	4.2	*
Denmark	1995	27 880	56.8	4.4	56.8	4.4	164.1	6.0	163.9	6.0	–	68.9	12.2	68.8	12.4	–	25.6	4.4	25.6	4.4	–
Copenhagen	1485	19 669	57.1	4.4	56.9	4.4	164.3	6.0	164.0	6.1		69.2	12.2	68.9	12.4		25.6	4.4	25.6	4.4	
Aarhus	510	8211	55.9	4.4	56.4	4.4	163.7	5.8	163.7	5.9		68.0	12.1	68.6	12.4		25.4	4.4	25.6	4.4	
Sweden	3285	24 728	58.6	8.4	54.1	8.9	164.4	6.0	164.1	6.0	–	67.9	12.0	68.1	12.0	–	25.1	4.3	25.3	4.3	–
Malmö	1711	15 324	61.4	7.8	57.2	7.9	164.3	6.0	164.0	6.2	*	68.1	11.9	67.9	12.2		25.2	4.3	25.3	4.4	
Umeå	1574	9404	55.6	8.0	49.0	7.9	164.0	6.1	163.7	6.2	*	67.9	12.4	68.9	12.5	**	25.3	4.4	25.7	4.4	***
Norway	1798	35 428	49.3	4.3	48.2	4.3	166.8	5.7	166.5	7.5	–	67.6	12.1	68.2	15.9	–	24.3	4.1	24.6	5.4	–
South & East	1136	19 576	49.5	4.3	48.2	4.3	167.1	5.7	166.8	7.5		67.2	12.1	68.2	16.0	**	24.1	4.1	24.5	5.5	**
North & West	662	15 852	49.0	4.3	48.1	4.3	166.3	5.6	166.1	7.4		68.1	12.0	68.3	15.8		24.6	4.1	24.7	5.4	

SD – standard deviation.
*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

Table 3b Comparison of mean age and anthropometry, adjusted for age, of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and the rest of the EPIC cohort: men

			Age (years)				Height (cm)					Weight (kg)					BMI (kg m^{-2})				
	n		Calibration		Cohort		Calibration		Cohort			Calibration		Cohort			Calibration		Cohort		
Country and centre	Calibration	Cohort	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*-value	Mean	SD	Mean	SD	*P*-value	Mean	SD	Mean	SD	*P*-value
Greece	1312	9350	60.5	9.8	53.1	11.4	170.5	6.6	169.8	7.0	***	82.5	12.8	81.9	13.5		28.4	4.0	28.4	4.2	
Spain	1777	13 847	55.1	7.4	50.5	7.2	169.0	6.2	168.7	6.4	–	81.1	10.9	81.2	11.2	–	28.4	3.4	28.5	3.5	–
Granada	214	1581	58.1	6.7	51.1	8.1	169.4	6.5	167.6	6.5	***	83.4	11.4	81.4	11.3	*	29.1	3.7	29.0	3.7	
Murcia	243	2440	55.6	7.5	50.2	7.4	167.4	6.1	167.7	6.3		79.4	11.4	80.3	11.8		28.3	3.7	28.5	3.8	
Navarra	444	3462	56.3	6.8	50.2	6.8	168.6	6.1	168.7	6.3		80.8	10.4	82.4	10.8	**	28.4	3.3	29.0	3.4	**
San Sebastian	490	3667	51.5	6.8	51.2	7.0	170.4	6.3	169.9	6.3		80.9	10.8	81.0	11.0		27.8	3.2	28.0	3.3	
Asturias	386	2697	56.2	7.5	49.9	7.0	168.8	6.2	168.4	6.5		82.0	11.1	80.8	11.6		28.7	3.4	28.5	3.5	
Italy	1444	13 655	55.2	7.0	49.9	7.5	171.9	6.7	171.3	7.0	–	78.2	11.0	78.4	11.5	–	26.5	3.4	26.7	3.5	–
Ragusa	168	2883	53.5	6.8	48.4	7.0	169.2	6.1	168.3	7.0		78.2	11.0	78.5	12.7		27.3	3.4	27.7	3.9	
Florence	271	3211	54.4	7.3	50.5	7.3	173.1	6.4	173.0	6.6		78.9	11.1	79.0	11.4		26.3	3.3	26.4	3.4	
Turin	677	5332	55.0	7.0	49.3	7.7	172.0	6.7	171.8	7.1		78.2	11.0	78.3	11.6		26.4	3.2	26.5	3.4	
Varese	328	2229	57.1	6.2	52.7	7.1	172.1	6.7	171.4	6.5		77.6	11.2	77.9	10.9		26.2	3.4	26.5	3.4	
Germany	2268	20 549	54.6	7.3	52.3	7.5	175.5	6.5	175.4	6.5	–	83.5	12.3	83.0	12.3	–	27.1	3.6	27.0	3.6	–
Heidelberg	1033	10 896	53.7	7.0	52.5	7.1	175.9	6.5	175.9	6.5		84.0	12.2	83.3	12.2		27.1	3.6	26.9	3.6	
Potsdam	1235	9653	55.4	7.4	52.2	8.0	175.2	6.5	174.8	6.5	*	83.3	12.4	82.7	12.4		27.1	3.7	27.1	3.7	
The Netherlands	1024	6635	50.0	7.4	48.1	7.4	177.2	7.2	176.6	8.8	–	83.8	12.7	82.7	15.5	–	26.7	3.6	26.5	4.4	–
Bilthoven	1024	6635	50.0	7.4	48.1	7.4	177.2	7.2	176.6	8.8	**	83.8	12.7	82.7	15.5	**	26.7	3.6	26.5	4.4	
United Kingdom	518	21 514	57.5	8.9	55.1	9.9	176.4	6.9	175.9	7.1	–	79.7	11.8	79.5	12.2	–	25.7	3.5	25.7	3.6	–
General population	404	13 831	58.1	9.1	57.5	8.5	175.9	6.7	175.0	7.1	*	81.6	11.7	81.0	12.4		26.4	3.4	26.4	3.6	
'Health-conscious'	114	7683	55.4	7.7	50.9	10.9	177.8	6.9	177.4	7.6		73.5	11.4	76.8	12.7	**	23.3	3.3	24.4	3.7	***
Denmark	1923	25 256	56.7	4.3	56.6	4.4	176.7	6.5	176.5	6.6	–	83.1	12.4	82.9	12.6	–	26.6	3.6	26.6	3.7	–
Copenhagen	1356	17 390	57.0	4.4	56.7	4.4	176.8	6.5	176.7	6.6		83.2	12.5	83.0	12.7		26.6	3.7	26.6	3.7	
Aarhus	567	7866	56.0	4.2	56.4	4.4	176.4	6.3	176.1	6.5		82.7	12.1	82.6	12.4		26.6	3.5	26.6	3.6	
Sweden	2765	18 444	61.1	7.3	54.0	9.0	177.8	6.9	177.2	6.7	–	82.2	12.8	82.1	12.4	–	26.0	3.7	26.1	3.6	–
Malmö	1421	9642	64.2	6.2	58.9	7.1	177.5	7.0	176.9	7.3	**	82.2	13.0	82.0	13.6		26.1	3.7	26.2	3.9	
Umeå	1344	8802	57.8	6.9	48.7	7.8	177.6	7.0	177.0	6.9	**	82.1	12.9	82.0	12.8		26.0	3.7	26.2	3.7	

SD – standard deviation.
*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

Table 4 Comparison of smoking status, adjusted for age, of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and the rest of the EPIC cohort

	Smoking status																
	Women									Men							
	Calibration				Cohort					Calibration				Cohort			
Country and centre	Never smoker (%)	Ex-smoker (%)	Smoker (%)	Missing (%)	Never smoker (%)	Ex-smoker (%)	Smoker (%)	Missing (%)	*P*-value	Never smoker (%)	Ex-smoker (%)	Smoker (%)	Missing (%)	Never smoker (%)	Ex-smoker (%)	Smoker (%)	Missing (%)	*P*-value
Greece	70.9	6.5	18.0	4.6	74.1	5.3	15.4	5.3	***	26.2	33.5	34.0	6.3	23.2	30.2	38.4	8.2	***
Spain	69.3	11.2	19.5	0.1	72.0	9.6	18.4	0.1	–	32.5	27.5	39.9	0.1	28.7	30.9	40.3	0.1	–
Granada	80.6	6.2	13.2	0.0	77.6	7.5	14.9	0.0		31.1	39.4	29.4	0.0	27.4	39.4	33.1	0.1	
Murcia	72.0	9.2	18.5	0.3	73.7	8.2	18.1	0.0		28.2	28.0	43.8	0.0	24.3	38.0	37.7	0.1	**
Navarra	60.7	15.1	24.2	0.0	68.4	10.0	21.4	0.1	**	31.0	18.4	50.6	0.0	31.2	24.5	44.3	0.0	*
San Sebastian	65.2	16.8	18.0	0.0	69.3	13.3	17.4	0.1		32.0	26.3	41.6	0.0	30.4	26.6	42.9	0.1	
Asturias	66.8	9.4	23.8	0.0	68.5	10.4	21.1	0.1		32.6	32.4	34.7	0.3	28.3	33.5	38.2	0.1	
Italy	54.1	21.7	24.2	0.0	52.9	19.8	25.8	1.4	–	28.5	42.6	26.5	2.4	25.6	39.4	29.0	5.9	–
Ragusa	51.6	19.4	28.9	0.0	53.8	18.1	25.5	2.7		23.5	44.3	31.7	0.6	22.0	37.4	34.9	5.7	
Naples	46.4	21.2	32.4	0.0	41.5	18.3	40.2	0.0		–	–	–	–	–	–	–	–	–
Florence	46.5	25.2	28.1	0.1	47.6	24.0	27.8	0.6		27.0	44.7	25.4	3.0	25.0	42.9	27.8	4.3	
Turin	57.3	24.0	18.7	0.0	53.2	20.6	19.8	6.4		27.5	42.5	26.9	3.1	26.9	37.2	27.1	8.7	
Varese	64.6	17.2	18.2	0.0	64.2	16.4	19.1	0.2		34.9	39.8	23.7	1.5	27.9	42.3	28.1	1.7	
France	67.5	20.1	7.1	5.3	66.4	18.3	8.6	6.8	–	–	–	–	–	–	–	–	–	–
South coast	71.6	15.4	8.4	4.6	66.4	17.2	9.4	7.0		–	–	–	–	–	–	–	–	–
South	66.2	21.0	7.2	5.7	67.1	18.0	8.2	6.6		–	–	–	–	–	–	–	–	–
North-west	65.3	22.0	8.5	4.2	67.7	17.9	7.8	6.7	*	–	–	–	–	–	–	–	–	–
North-east	68.7	18.3	7.4	5.6	65.5	18.8	8.9	6.8		–	–	–	–	–	–	–	–	–
Germany	52.3	28.9	18.8	0.0	53.7	27.8	18.5	0.0	–	30.3	46.2	23.4	0.0	30.1	45.1	24.7	0.0	–
Heidelberg	47.9	31.3	20.9	0.0	48.3	30.6	21.1	0.0		32.7	44.4	23.0	0.0	29.7	44.3	26.0	0.0	
Potsdam	57.3	26.6	16.0	0.1	58.0	25.5	16.5	0.1		28.4	47.8	23.8	0.0	30.5	46.1	23.3	0.1	
The Netherlands	41.7	33.1	24.8	0.4	39.6	33.1	26.6	0.6	–	24.3	38.0	37.1	0.6	25.1	36.2	38.5	0.2	–
Bilthoven	33.7	31.9	33.8	0.6	34.4	30.5	34.9	0.1		24.3	38.0	37.1	0.6	25.1	36.2	38.5	0.2	
Utrecht	46.0	33.8	19.9	0.3	42.3	34.4	22.5	0.8	**	–	–	–	–	–	–	–	–	–
United Kingdom	61.4	28.4	8.8	1.4	56.3	30.3	10.4	3.0	–	39.4	41.9	17.2	1.5	38.5	41.4	15.2	4.9	–
General population	59.9	28.5	9.8	1.8	52.7	28.0	12.8	6.5	*	38.1	42.7	17.2	2.0	31.9	43.3	17.3	7.5	
'Health-conscious'	64.6	28.3	6.5	0.5	59.2	32.1	8.5	0.3		40.5	36.0	23.6	0.0	50.7	37.6	11.3	0.3	
Denmark	47.9	26.7	24.9	0.4	43.0	24.5	31.9	0.6	–	29.0	37.9	32.3	0.7	25.2	36.6	37.4	0.8	–
Copenhagen	49.0	26.4	24.2	0.3	42.2	24.3	32.8	0.7	***	29.5	38.4	31.6	0.5	25.1	36.0	38.0	0.9	***
Aarhus	44.2	27.9	27.3	0.6	45.2	24.9	29.5	0.4		28.5	36.9	33.4	1.2	25.6	38.0	36.0	0.4	
Sweden	53.7	24.7	20.8	0.8	49.2	24.0	26.1	0.6	–	45.7	32.5	20.7	1.1	38.7	35.5	24.6	1.1	–
Malmö	46.2	30.0	23.7	0.0	44.1	27.6	28.3	0.1		30.0	43.0	27.0	0.0	27.8	43.3	28.7	0.1	
Umeå	60.0	16.9	21.5	1.6	57.8	18.1	22.5	1.5	**	57.0	24.9	15.8	2.3	51.6	26.3	19.8	2.2	**
Norway	34.9	33.4	26.5	5.2	33.5	29.1	31.8	5.7		–	–	–	–	–	–	–	–	–
South & East	35.9	34.2	24.9	5.0	33.7	29.1	31.5	5.7	***	–	–	–	–	–	–	–	–	–
North & West	33.4	32.1	29.0	5.4	33.2	29.0	32.1	5.6		–	–	–	–	–	–	–	–	–

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

Table 5a Comparison of education level, adjusted for age, of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and the rest of the EPIC cohort: women

	Education level												
	Calibration						Cohort						
Country and centre	Incomplete primary school (%)	Primary school (%)	Technical school (%)	Secondary school (%)	University (%)	Missing (%)	Incomplete primary school (%)	Primary school (%)	Technical school (%)	Secondary school (%)	University (%)	Missing (%)	*P*-value
Greece	20.9	32.2	7.5	22.6	16.2	0.7	27.9	37.9	5.6	16.8	10.4	1.3	***
Spain	28.6	41.8	6.9	7.4	10.0	5.3	35.9	39.0	5.2	5.2	9.1	5.7	–
Granada	38.7	33.2	4.7	5.5	6.2	11.7	47.1	25.6	3.7	4.1	8.9	10.6	**
Murcia	40.9	22.4	4.9	6.2	16.0	9.5	45.8	26.0	3.4	3.8	11.3	9.6	**
Navarra	15.7	62.3	7.5	4.1	9.7	0.7	29.3	50.7	5.7	5.2	7.4	1.8	***
San Sebastian	20.7	47.7	12.2	10.8	7.5	1.2	22.9	53.2	9.4	5.4	7.7	1.4	*
Asturias	24.0	47.1	6.2	10.1	10.2	2.5	28.0	47.6	5.1	8.0	9.1	2.1	
Italy	0.9	24.0	10.9	49.4	14.5	0.2	1.8	28.1	10.9	44.7	13.0	1.6	–
Ragusa	0.6	28.9	5.7	49.7	15.1	0.0	3.7	21.6	4.4	50.2	17.2	2.9	
Naples	1.6	18.8	9.3	51.9	18.3	0.0	2.8	24.4	6.8	49.5	16.5	0.0	
Florence	1.0	20.8	10.2	49.5	18.0	0.5	1.1	26.1	12.1	42.8	17.0	0.8	***
Turin	1.0	18.3	13.2	55.8	11.7	0.0	1.5	20.7	13.7	47.6	10.1	6.4	
Varese	0.6	32.3	12.7	44.2	10.1	0.1	1.4	37.8	12.7	40.9	6.9	0.4	**
France	0.4	9.5	0.0	46.5	39.8	3.8	0.4	10.9	0.0	49.1	35.5	4.1	–
South coast	0.4	10.4	0.0	47.1	38.2	3.9	0.4	10.7	0.0	48.3	36.3	4.3	
South	0.4	8.0	0.0	47.9	38.9	4.8	0.3	10.7	0.0	50.1	34.9	4.0	**
North-west	0.2	14.5	0.0	52.2	30.7	2.4	0.5	11.9	0.0	52.6	30.5	4.4	
North-east	0.5	10.4	0.0	45.2	40.3	3.6	0.4	10.8	0.0	47.4	37.3	4.0	**
Germany	0.6	23.5	41.6	8.5	25.6	0.2	0.6	23.4	41.5	7.9	26.5	0.1	–
Heidelberg	0.3	25.1	41.5	9.0	23.8	0.2	0.6	26.8	39.8	8.4	24.2	0.1	
Potsdam	0.7	20.5	44.0	7.2	27.4	0.2	0.6	20.8	42.8	7.4	28.3	0.1	
The Netherlands	0.0	19.6	33.1	29.5	17.6	0.2	0.0	20.2	31.8	29.9	17.2	1.0	–
Bilthoven	0.0	13.2	34.9	28.5	22.9	0.5	0.0	16.7	34.6	28.6	19.1	1.0	**
Utrecht	0.0	22.6	31.8	30.4	15.1	0.1	0.0	22.1	30.3	30.4	16.2	0.9	
United Kingdom	0.0	12.8	31.0	9.8	26.2	20.2	0.0	14.4	27.3	10.0	26.4	22.0	–
General population	0.0	17.9	34.9	8.4	17.4	21.4	0.0	29.8	30.5	6.7	12.6	20.4	***
'Health-conscious'	0.0	0.0	17.6	14.5	51.1	16.8	0.0	0.0	25.0	12.8	39.0	23.2	**
Denmark	0.0	27.2	47.8	13.5	11.4	0.0	0.0	31.8	46.2	11.6	10.1	0.2	–
Copenhagen	0.0	26.0	47.8	13.8	12.5	0.0	0.0	29.1	47.4	11.9	11.3	0.3	*
Aarhus	0.0	31.3	47.4	12.8	8.4	0.0	0.0	38.2	43.4	10.9	7.5	0.1	*
Sweden	0.5	27.9	29.2	13.0	29.0	0.3	0.5	37.1	27.5	12.1	22.4	0.4	–
Malmö†	0.9	33.3	32.3	6.6	26.7	0.2	0.8	39.1	30.0	7.0	22.8	0.3	***
Umeå	0.0	18.8	24.2	24.0	32.6	0.4	0.0	34.0	23.4	20.2	21.7	0.7	***
Norway	0.8	17.4	32.9	34.6	14.3	0.0	1.5	22.0	36.0	28.2	12.2	0.0	–
South & East	0.6	16.0	33.0	35.6	14.9	0.0	1.4	19.1	36.3	30.1	13.1	0.0	***
North & West	1.1	20.1	32.7	32.6	13.4	0.0	1.6	25.6	35.6	26.0	11.2	0.0	***

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

† For the Malmö cohort, which existed before EPIC, 7332 subjects were defined differently from the EPIC variables and were classified in the closest EPIC category corresponding to 'technical school'.

Table 5b Comparison of education level, adjusted for age, of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and the rest of the EPIC cohort: men

	Education level												
	Calibration						Cohort						
Country and centre	Incomplete primary school (%)	Primary school (%)	Technical school (%)	Secondary school (%)	University (%)	Missing (%)	Incomplete primary school (%)	Primary school (%)	Technical school (%)	Secondary school (%)	University (%)	Missing (%)	*P*-value
Greece	12.0	30.3	17.4	15.5	24.3	0.5	14.5	38.0	17.1	13.2	13.7	3.5	***
Spain	19.7	38.6	15.5	9.0	14.2	2.9	24.8	37.1	12.4	7.7	14.7	3.4	–
Granada	21.4	22.8	6.4	9.9	33.0	6.5	30.8	25.0	4.9	8.8	19.8	10.8	***
Murcia	33.3	26.2	6.1	5.6	19.8	9.1	29.4	27.1	6.8	7.9	22.1	6.6	
Navarra	17.5	46.2	15.6	10.9	8.9	0.9	25.7	42.1	11.1	8.2	11.7	1.2	***
San Sebastian	17.5	42.5	21.6	8.0	9.0	1.4	20.1	43.4	19.0	6.0	9.8	1.7	
Asturias	18.0	39.4	15.3	9.7	16.3	1.3	22.3	37.9	14.7	8.5	15.3	1.4	
Italy	0.4	15.0	18.6	53.1	12.6	0.3	0.5	16.3	14.0	51.6	14.1	3.5	–
Ragusa	1.8	19.6	9.8	49.5	18.7	0.6	1.1	19.0	8.1	50.2	17.1	4.4	
Florence	0.2	13.3	17.2	50.8	17.7	0.7	0.2	17.3	11.2	55.2	14.1	2.0	*
Turin	0.3	11.8	21.5	55.0	11.3	0.1	0.3	12.1	17.1	50.3	14.8	5.4	**
Varese	0.0	21.7	19.4	52.8	5.8	0.3	0.4	20.9	18.3	51.4	8.8	0.3	
Germany	0.5	24.3	28.7	4.7	41.7	0.1	0.6	24.4	27.5	5.2	42.2	0.1	–
Heidelberg	0.5	31.7	29.9	5.3	32.3	0.3	0.6	30.8	26.7	5.5	36.4	0.1	
Potsdam	0.5	17.4	28.3	4.1	49.7	0.0	0.6	17.2	28.4	4.9	48.8	0.1	
The Netherlands	0.0	12.5	41.3	17.6	28.3	0.3	0.0	14.0	40.0	18.2	27.1	0.7	–
Bilthoven	0.0	12.5	41.3	17.6	28.3	0.3	0.0	14.0	40.0	18.2	27.1	0.7	
United Kingdom	0.0	8.5	31.4	10.5	30.5	19.1	0.0	16.6	29.3	9.7	28.3	16.0	–
General population	0.0	12.1	36.0	10.8	23.8	17.3	0.0	25.1	36.5	8.8	15.8	13.9	***
'Health-conscious'	0.0	0.0	17.5	7.1	50.0	25.4	0.0	0.0	16.4	11.5	52.3	19.8	
Denmark	0.0	30.4	30.2	9.3	30.1	0.1	0.0	35.1	29.1	7.6	27.9	0.3	–
Copenhagen	0.0	29.0	30.0	9.3	31.7	0.1	0.0	33.0	29.3	8.0	29.4	0.4	**
Aarhus	0.0	34.0	30.5	9.1	26.4	0.0	0.0	39.8	28.8	6.8	24.5	0.1	*
Sweden	0.1	33.2	26.1	16.5	23.8	0.3	0.5	40.7	22.6	15.9	19.8	0.5	–
Malmö†	0.1	43.2	20.6	12.0	23.9	0.2	0.9	45.5	19.5	11.7	22.2	0.3	*
Umeå	0.0	24.8	27.0	23.7	24.1	0.3	0.0	35.5	26.4	20.5	16.9	0.7	***

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

† For the Malmö cohort, which existed before EPIC, 7332 subjects were defined differently from the EPIC variables and were classified in the closest EPIC category corresponding to 'technical school'.

Table 6a Comparison of work-based physical activity, adjusted for age, of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and the rest of the EPIC cohort: women

	Work-based physical activity												
	Calibration						Cohort						
Country and centre	Non-worker (%)	Sedentary occupation (%)	Standing occupation (%)	Manual work (%)	Heavy manual work (%)	Missing (%)	Non-worker (%)	Sedentary occupation (%)	Standing occupation (%)	Manual work (%)	Heavy manual work (%)	Missing (%)	*P*-value
Greece	58.5	19.1	16.8	5.1	0.0	0.5	61.0	14.4	13.3	8.8	0.1	2.5	***
Spain†	–	15.0	80.2	1.7	0.2	0.0	2.7	12.7	82.6	1.9	0.1	2.8	–
Granada	–	8.3	87.8	0.7	0.0	0.0	1.0	11.9	85.9	1.2	0.1	3.2	
Murcia	–	17.9	78.1	2.0	1.1	0.0	1.9	14.0	82.0	1.8	0.3	1.0	
Navarra	–	13.4	81.5	2.1	0.0	0.0	3.6	10.5	84.2	1.6	0.1	2.9	
San Sebastian	–	19.7	76.3	3.0	0.0	0.0	0.5	15.7	81.3	2.5	0.0	1.0	
Asturias	–	14.7	78.6	1.2	0.3	0.0	6.8	11.3	79.1	2.8	0.1	5.3	
Italy	48.6	29.4	13.1	6.1	2.2	0.6	51.1	27.4	12.5	5.3	1.9	1.7	–
Ragusa	41.6	33.1	19.8	2.3	3.2	0.0	43.2	31.5	17.1	3.2	2.1	2.9	
Naples	52.2	32.6	7.1	5.9	2.2	0.0	59.0	27.2	5.0	6.4	2.4	0.0	
Florence	46.6	31.9	14.5	4.8	1.6	0.6	46.0	31.9	14.3	5.2	1.5	1.1	
Turin	51.5	23.0	15.2	7.0	3.2	0.0	49.7	25.2	11.7	4.0	2.5	6.8	
Varese	49.6	27.3	12.0	8.0	1.9	1.1	55.9	22.4	13.2	6.3	1.8	0.5	***
France	27.4	17.4	48.6	1.8	0.0	4.9	31.7	16.4	44.8	2.0	0.0	5.1	–
South coast	33.6	14.5	47.5	1.2	0.0	3.3	35.9	15.2	41.5	2.0	0.0	5.4	***
South	28.8	16.3	48.3	1.7	0.0	4.9	32.8	15.4	44.9	2.1	0.0	4.7	***
North-west	30.2	14.8	47.4	2.1	0.0	5.5	34.0	13.7	45.5	2.2	0.0	4.6	***
North-east	25.5	19.1	48.1	2.2	0.0	5.1	29.0	18.2	45.5	2.0	0.0	5.3	***
Germany	34.8	37.4	24.7	2.4	0.1	0.6	32.5	40.1	23.9	2.9	0.1	0.5	–
Heidelberg	34.3	35.1	26.2	3.2	0.2	1.0	33.8	36.1	25.7	3.3	0.1	1.0	
Potsdam	34.2	40.9	23.3	1.3	0.2	0.1	31.4	43.3	22.5	2.5	0.1	0.2	**
The Netherlands	49.5	17.5	16.0	9.3	4.9	2.9	48.0	17.7	14.3	8.3	4.9	6.8	–
Bilthoven	45.4	19.5	16.1	8.0	3.2	7.9	47.8	15.9	10.0	5.0	2.6	18.7	***
Utrecht	50.9	16.7	16.2	10.3	5.9	0.1	48.5	18.1	16.4	10.0	6.1	0.9	
United Kingdom	37.9	32.0	20.9	7.3	0.0	2.0	39.8	25.8	20.2	6.1	0.2	7.9	–
General population	41.9	29.0	19.2	7.6	0.0	2.3	44.1	16.7	15.9	8.0	0.1	15.2	***
'Health-conscious'	38.2	32.3	24.6	4.0	0.0	1.0	35.9	33.3	23.8	4.6	0.3	2.0	
Denmark	30.8	33.4	16.7	17.9	1.2	0.1	27.2	32.3	17.6	20.6	1.6	0.7	–
Copenhagen	30.5	35.3	15.4	17.3	1.5	0.1	25.2	35.3	16.8	20.2	1.6	1.0	***
Aarhus	32.6	27.7	20.1	19.4	0.2	0.0	31.9	25.4	19.6	21.5	1.6	0.1	
Sweden	24.8	27.6	32.6	12.3	2.1	0.6	33.4	23.3	28.0	12.6	2.1	0.6	–
Malmö	34.5	31.1	28.3	5.7	0.1	0.4	40.9	27.2	26.3	5.0	0.2	0.4	***
Umeå	13.0	20.4	42.7	19.1	4.0	0.9	20.3	17.2	31.2	25.3	5.1	0.9	***
Norway	–	–	–	–	–	–	–	–	–	–	–	–	–
South & East	m	m	m	m	m	m	m	m	m	m	m	m	m
North & West	m	m	m	m	m	m	m	m	m	m	m	m	m

m – missing.
*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.
† In Spain, all participants were classified in one of the categories of work activity independently from employment status.

Table 6b Comparison of work-based physical activity, adjusted for age, of the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations and the rest of the EPIC cohort: men

	Work-based physical activity												
	Calibration						Cohort						
Country and centre	Non-worker (%)	Sedentary occupation (%)	Standing occupation (%)	Manual work (%)	Heavy manual work (%)	Missing (%)	Non-worker (%)	Sedentary occupation (%)	Standing occupation (%)	Manual work (%)	Heavy manual work (%)	Missing (%)	*P*-value
Greece	26.2	27.5	20.8	20.1	1.7	3.7	27.1	26.3	17.0	22.2	2.0	5.5	***
Spain†	–	33.7	31.0	25.1	5.9	0.0	4.8	34.5	34.1	21.1	5.5	4.3	–
Granada	–	40.3	32.1	17.6	6.5	0.0	4.3	36.4	37.3	14.3	7.7	3.5	
Murcia	–	33.6	37.4	13.4	10.5	0.0	6.2	38.8	33.7	13.0	8.4	5.1	
Navarra	–	31.6	32.7	28.8	4.0	0.0	3.9	33.9	33.6	24.1	4.5	2.9	
San Sebastian	–	34.1	26.6	35.4	3.2	0.0	1.2	32.6	31.0	31.3	3.8	0.8	
Asturias	–	32.4	34.2	16.4	8.8	0.0	10.1	32.3	37.2	15.3	5.0	8.3	
Italy	19.4	40.8	21.1	12.5	5.1	1.0	19.6	36.8	21.4	12.8	5.1	4.3	–
Ragusa	8.8	41.5	25.0	10.5	12.9	1.2	11.3	35.1	27.0	11.8	9.7	5.1	
Florence	15.3	45.9	19.5	13.7	4.6	1.1	18.4	41.1	19.8	13.2	5.5	2.0	
Turin	21.6	39.9	22.2	11.0	3.9	1.3	21.2	38.0	19.4	11.9	2.9	6.6	
Varese	27.6	36.3	17.3	15.3	3.2	0.3	28.5	30.3	21.3	15.3	3.9	0.7	
Germany	28.4	43.3	22.0	5.6	0.7	0.0	25.3	45.0	21.8	7.1	0.7	0.1	–
Heidelberg	23.5	47.4	22.8	5.4	0.9	0.0	21.4	48.5	22.2	6.9	0.9	0.1	
Potsdam	32.7	39.8	21.2	5.8	0.5	0.0	29.8	41.0	21.3	7.3	0.5	0.1	
The Netherlands	20.0	37.1	16.5	9.0	8.4	8.9	20.7	27.7	11.4	8.2	6.0	26.0	–
Bilthoven	20.0	37.1	16.5	9.0	8.4	8.9	20.7	27.7	11.4	8.2	6.0	26.0	***
United Kingdom	35.0	30.7	13.2	14.6	3.4	3.1	35.0	28.8	12.6	12.8	3.6	7.2	–
General population	37.6	27.3	14.1	14.0	3.8	3.2	37.2	21.9	10.7	15.4	4.6	10.2	
'Health-conscious'	29.9	41.8	6.9	18.3	0.4	2.6	30.5	41.6	16.1	8.2	1.8	1.7	*
Denmark	16.6	42.1	16.8	18.2	6.3	0.0	15.3	39.1	16.8	20.1	8.1	0.6	–
Copenhagen	16.3	43.3	16.4	17.7	6.2	0.0	14.8	40.7	15.9	19.8	8.0	0.8	*
Aarhus	17.9	38.9	17.8	19.3	6.1	0.0	16.3	35.6	18.8	20.9	8.4	0.0	
Sweden	29.0	23.4	27.2	17.3	2.4	0.6	33.3	23.5	25.6	14.0	3.0	0.6	–
Malmö	43.8	29.9	16.7	7.8	1.7	0.1	42.6	27.6	20.2	6.8	2.3	0.4	**
Umeå	18.8	20.6	33.7	22.4	3.3	1.1	22.1	18.7	32.1	22.6	3.8	0.7	***

*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.
† In Spain, all participants were classified in one of the categories of work activity independently from employment status.

Table 7 Number, percentage and type of special diets reported in the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-populations

	Women						Men					
	Reported special diet		Type of special diet reported				Reported special diet		Type of special diet reported			
Country and centre	*n*	%	Obesity (%)	Vegetarian* (%)	Diseases (%)	Other (%)	*n*	%	Obesity (%)	Vegetarian* (%)	Diseases (%)	Other (%)
Greece	424	29.3	4.1	0.4	20.2	4.6	382	27.8	1.2	0.3	21.0	5.3
Spain	306	20.5	5.6	0.1	12.1	2.7	300	16.4	1.5	0.1	12.2	2.7
Granada	75	23.4	3.8	0.0	15.0	4.7	60	26.4	2.6	0.4	18.5	4.9
Murcia	49	15.5	5.7	0.3	7.3	2.2	24	9.8	1.2	0.0	6.5	2.0
Navarra	52	19.0	5.5	0.0	11.7	1.8	95	21.0	1.1	0.0	18.4	1.6
San Sebastian	24	9.8	2.9	0.0	4.5	2.5	30	6.1	0.8	0.0	2.4	2.8
Asturias	106	31.0	9.1	0.0	19.6	2.3	91	22.2	2.4	0.0	16.9	2.9
Italy	434	16.9	6.3	0.2	7.5	3.0	134	9.2	1.7	0.3	5.8	1.4
Ragusa	11	8.0	4.4	0.0	0.7	2.9	7	4.1	1.2	0.0	1.8	1.2
Naples	96	23.4	11.7	0.5	8.5	2.7	–	–	–	–	–	–
Florence	136	16.9	6.3	0.4	8.7	1.5	32	11.6	1.5	0.7	8.3	1.1
Turin	45	11.4	4.8	0.0	4.3	2.3	54	7.9	2.2	0.4	4.3	1.0
Varese	146	18.0	4.6	0.0	8.4	5.1	41	12.5	1.2	0.0	8.8	2.4
France	1129	23.8	5.7	0.4	14.4	3.3	–	–	–	–	–	–
South coast	176	28.0	7.6	0.2	17.0	3.2	–	–	–	–	–	–
South	251	17.8	3.1	0.4	10.8	3.5	–	–	–	–	–	–
North-west	213	32.6	3.8	0.3	22.6	5.8	–	–	–	–	–	–
North-east	489	23.8	7.6	0.6	13.3	2.3	–	–	–	–	–	–
Germany	432	19.7	3.0	2.1	13.5	1.1	528	22.4	2.2	1.0	18.2	1.0
Heidelberg	245	22.1	2.8	3.6	15.3	0.4	240	22.5	2.1	2.1	18.2	0.2
Potsdam	187	17.2	3.1	0.6	11.7	1.8	288	22.2	2.2	0.2	18.2	1.6
The Netherlands	680	22.4	5.9	0.5	11.1	4.9	72	7.0	1.2	0.0	3.8	2.0
Bilthoven	129	11.7	3.2	0.5	5.0	3.1	72	7.0	1.2	0.0	3.8	2.0
Utrecht	551	28.4	7.4	0.5	14.5	6.0	–	–	–	–	–	–
United Kingdom	318	39.4	2.6	17.2	12.4	7.2	158	29.7	0.9	18.2	7.7	2.8
General population	155	26.3	2.7	1.5	13.2	8.8	56	13.6	0.7	2.0	8.3	2.7
'Health-conscious'	163	75.1	2.3	59.9	10.1	2.8	102	84.3	1.7	73.6	5.8	3.3
Denmark	242	12.0	2.1	0.2	8.8	1.0	146	7.6	0.9	0.0	6.3	0.3
Copenhagen	200	13.3	1.5	0.2	10.4	1.3	123	9.0	0.8	0.0	7.8	0.4
Aarhus	42	8.2	4.1	0.0	3.9	0.2	23	4.1	1.2	0.0	2.8	0.0
Sweden	1073	31.2	0.8	0.8	22.4	7.2	729	25.5	0.7	0.2	19.0	5.5
Malmö	382	22.0	0.1	0.6	11.8	9.5	242	16.9	0.4	0.4	8.5	7.6
Umeå	691	40.6	1.5	1.0	33.3	4.9	487	34.1	1.1	0.1	29.6	3.4
Norway	359	19.2	1.5	0.8	13.5	3.4	–	–	–	–	–	–
South & East	233	19.7	1.7	1.1	13.3	3.6	–	–	–	–	–	–
North & West	126	18.4	1.2	0.3	13.7	3.2	–	–	–	–	–	–

*'Vegetarian' includes vegans, ovo-lacto vegetarians and fish eaters (no meat eaters).

zero in the other countries and centres. In contrast, in Italy and France about half of the population, and a third in The Netherlands (women), have a secondary school diploma, and 40–50% of the UK 'health-conscious' group, French women teachers and men in Germany have a university degree.

In more than half of the centres, the distribution according to level of education is not strictly comparable between the calibration and the entire EPIC cohort populations. In certain centres, this difference is due to a few percentage-point differences in distribution across six classes. However, a quite consistent systematic tendency to under-represent the lowest education level classes (i.e. incomplete primary school and primary school) and to over-represent secondary and particularly university is observed.

Work-based physical activity

The subjects were asked to report their professional physical activities using a variable in four categories (sedentary, standing, manual work and heavy manual work)[23,25]. In Malmö, subjects were asked about their physical activity at work as typical professional activity without referring to current occupational status, and a different physical activity questionnaire was used in Norway that was therefore not included in the analysis. In Spain, all participants were classified in one of the categories of work activity independently of employment status, so these variables are not directly comparable with the professional activities reported elsewhere[23]. These differences should not, however, affect the comparison of the calibration sub-sample with the entire cohort because the statistical analysis was stratified by centre.

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Table 8 Characteristics of the 24-hour dietary recall measurements

Country and centre	*n*	Time interval between dietary measurements (months)*		Time period recalled (hours)†		Interview duration (minutes)		Number of food items reported‡	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Greece	2686	23.7	13.7	24.1	0.8	27	16	15.3	5.3
Spain	3220	24.9	10.4	24.1	1.2	31	10	26.2	7.2
Granada	514	27.0	12.9	24.0	0.8	31	11	27.2	6.9
Murcia	547	21.3	8.7	24.0	1.1	26	8	26.5	7.3
Navarra	715	31.1	7.1	24.1	1.3	34	9	25.3	6.2
San Sebastian	734	19.5	9.1	24.1	1.4	30	10	28.5	7.1
Asturias	710	25.6	9.9	24.1	1.1	34	10	23.7	7.4
Italy	3956	20.1	12.4	24.1	0.9	29	11	25.0	6.9
Ragusa	306	21.3	10.0	24.0	0.9	22	7	22.2	6.0
Naples	403	34.2	11.7	24.0	0.9	27	10	21.3	5.9
Florence	1056	16.9	15.7	24.0	0.9	28	10	24.6	6.1
Turin	1069	19.4	9.2	24.1	1.1	33	10	28.7	7.5
Varese	1122	18.6	8.5	24.1	0.9	30	13	23.9	6.2
France	4639	31.7	9.3	24.1	0.9	29	11	27.2	6.7
South coast	612	32.1	8.1	24.1	0.8	33	13	27.5	7.1
South	1396	27.5	8.9	24.1	0.9	26	8	26.2	6.3
North-west	622	33.2	8.9	24.1	0.9	32	9	28.5	6.8
North-east	2009	34.1	8.9	24.1	0.9	30	11	27.3	6.7
Germany	4418	0.5	1.8	24.0	1.1	35	17	23.2	6.3
Heidelberg	2120	1.0	2.1	24.0	1.2	35	15	23.4	6.6
Potsdam	2298	−0.1	1.2	24.1	1.1	36	18	23.0	6.1
The Netherlands	3984	0.5	1.5	24.1	1.2	33	12	27.7	7.7
Bilthoven	2110	0.2	0.5	24.0	1.3	31	13	26.7	7.7
Utrecht	1874	0.9	2.1	24.2	1.0	35	10	28.9	7.6
United Kingdom	1286	12.4	11.0	24.1	0.8	39	20	30.4	8.3
General population	975	11.9	10.8	24.2	0.8	37	17	30.8	8.1
'Health-conscious'	311	13.9	11.5	24.0	0.5	43	28	28.8	8.7
Denmark	3918	0.1	0.5	24.0	1.2	27	11	24.1	7.0
Copenhagen	2841	0.1	0.5	24.0	1.2	27	11	23.5	6.9
Aarhus	1077	0.1	0.4	24.0	1.2	25	11	25.5	7.0
Sweden	6050	34.1	16.0	24.1	1.2	33	13	25.3	7.1
Malmö	3132	30.0	14.9	24.0	1.1	31	12	24.9	7.2
Umeå	2918	38.5	15.9	24.1	1.3	35	14	25.7	7.0
Norway	1798	12.8	3.5	24.0	1.6	30	12	23.3	6.4
South & East	1136	12.8	3.5	24.0	1.6	31	13	23.5	6.6
North & West	662	12.9	3.5	24.0	1.6	30	11	22.9	6.1

SD – standard deviation.
* Time interval between baseline dietary assessment and 24-hour diet recall measurements.
† Mean time period covered from wake-up on the recalled day to wake-up on the following day.
‡ Food + recipe items.

Except Denmark, Italy and The Netherlands (≤20%) in men only, all countries report a relatively high proportion of subjects with no professional physical activity, particularly women (Tables 6a and 6b). EPIC cohorts have overall moderate professional physical activities, with predominantly sedentary or standing occupations, but a higher proportion of men with manual or heavy manual jobs and a lower number of non-workers compared with women is consistently observed in all EPIC cohorts.

The distribution of professional activities shows statistical differences between the calibration group and the entire EPIC cohorts for about 40% of the sex-specific centres. We consistently observed a tendency to under-sample non-workers in most centres and both genders and to over-sample people with a sedentary and/or standing occupation. A more comparable distribution is, however, observed between the study groups when sedentary plus standing and manual plus heavy manual activities are grouped together. In Bilthoven and the UK 'health-conscious' group, the discrepancies observed are mainly due to a higher completeness of the calibration (i.e. lower number of missing values) compared with the entire-cohort data.

Special diet

The number of study subjects who reported having a special diet during the 24-HDR interview was higher among women (12–39.4%) than among men (7–29.7%) (Table 7). Apart from the UK 'health-conscious' group, long-term health problems related to diet (e.g. hyperlipidaemia, hypertension, diabetes, stomach or intestinal problems) were the main reason given to explain their usual dietary habits, particularly in Umeå and, to a lesser

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Table 9 Day-to-day and seasonal distribution obtained in the European Prospective Investigation into Cancer and Nutrition (EPIC) calibration sub-studies

	Day of the week							Season			
Country and centre	Monday (%)	Tuesday (%)	Wednesday (%)	Thursday (%)	Friday (%)	Saturday (%)	Sunday (%)	Spring (%)	Summer (%)	Autumn (%)	Winter (%)
Greece	14.4	14.5	15.4	15.0	12.6	13.1	15.0	36.1	6.5	25.9	31.5
Spain	16.4	15.8	16.0	12.5	12.4	13.2	13.6	28.5	26.5	20.6	24.5
Granada	21.6	20.4	18.9	15.6	4.5	6.6	12.5	28.2	38.9	13.2	19.7
Murcia	14.4	15.0	14.4	14.1	14.1	14.6	13.4	28.3	21.6	25.1	25.1
Navarra	17.5	15.4	14.8	11.1	13.7	14.7	12.9	29.9	22.0	22.5	25.6
San Sebastian	14.6	14.2	15.8	12.5	13.8	14.4	14.7	25.6	32.6	16.8	25.1
Asturias	15.1	15.4	16.5	10.3	14.2	14.2	14.4	30.1	19.6	24.4	25.9
Italy	16.0	16.5	16.4	15.6	11.2	10.2	14.3	30.5	18.1	25.4	26.0
Ragusa	13.7	23.5	22.6	17.0	7.2	3.6	12.4	46.7	12.1	28.8	12.4
Naples	18.4	13.9	20.6	17.1	6.0	7.9	16.1	22.3	8.9	15.9	52.9
Florence	14.9	14.7	14.5	14.5	14.0	12.6	14.9	31.6	17.1	29.9	21.4
Turin	15.4	16.0	15.3	16.8	12.3	9.3	14.9	32.5	22.4	19.5	25.7
Varese	17.2	17.7	15.9	14.4	10.4	11.3	13.1	25.9	20.0	29.4	24.7
France	18.6	18.3	17.1	15.5	8.3	11.2	11.1	34.5	13.0	22.7	29.8
South coast	17.3	19.3	16.3	14.2	10.6	10.6	11.6	33.3	4.6	25.8	36.3
South	17.8	17.5	16.9	16.8	8.0	11.7	11.5	37.7	16.3	22.3	23.8
North-west	17.7	15.9	16.4	17.2	9.7	11.4	11.7	29.1	7.2	18.2	45.5
North-east	19.8	19.2	17.7	14.4	7.4	10.9	10.6	34.3	15.2	23.5	27.1
Germany	20.2	21.6	17.6	13.2	4.8	11.1	11.6	29.7	33.1	16.1	21.1
Heidelberg	22.2	21.4	17.3	14.5	1.2	11.0	12.4	22.0	39.3	17.6	21.1
Potsdam	18.3	21.8	17.8	12.1	8.1	11.1	10.8	36.9	27.4	14.7	21.1
The Netherlands	15.2	15.3	14.7	13.6	13.0	13.8	14.5	24.6	30.6	22.8	22.0
Bilthoven	15.9	16.5	14.7	13.3	11.4	13.7	14.6	26.3	28.9	24.3	20.6
Utrecht	14.4	13.9	14.8	13.9	14.8	13.9	14.3	22.8	32.6	21.1	23.5
United Kingdom	17.0	15.0	16.5	14.7	11.3	11.8	13.7	31.7	21.4	24.5	22.4
General population	15.3	13.3	15.7	15.3	12.9	12.4	15.1	31.4	21.9	25.1	21.6
'Health-conscious'	22.5	20.3	19.0	12.9	6.1	10.0	9.3	32.8	19.9	22.5	24.8
Denmark	19.5	21.4	16.6	14.9	8.3	8.7	10.8	22.8	12.7	24.6	40.0
Copenhagen	18.5	23.2	16.7	15.2	8.2	7.7	10.4	25.8	12.9	21.2	40.1
Aarhus	22.0	16.5	16.3	14.0	8.5	11.1	11.7	14.9	12.0	33.4	39.7
Sweden	15.1	15.2	14.7	14.6	12.1	14.1	14.3	26.3	24.2	19.4	30.2
Malmö	15.8	15.5	14.8	14.4	10.5	14.1	14.9	24.2	18.7	25.2	31.8
Umeå	14.3	14.8	14.5	14.8	13.9	14.0	13.7	28.5	30.1	13.1	28.3
Norway	16.9	17.2	17.0	12.3	7.7	11.4	17.5	25.8	13.5	30.3	30.5
South & East	17.3	17.5	17.5	13.4	6.9	10.3	17.2	25.1	13.3	30.6	31.1
North & West	16.3	16.6	16.2	10.4	9.2	13.1	18.1	26.9	13.8	29.8	29.6

extent, Greece. Except in Sweden, the number of subjects who reported restricting their dietary intake because of overweight or obesity was in all centres 1.4–5 times higher in women than in men. In the UK, 60% of the women and 74% of the men from the 'health-conscious' sample are vegans, ovo-lacto vegetarians or fish eaters who do not consume meat. The number of vegetarians in the other EPIC cohorts is 3.6% or lower.

Logistics and methodological issues of the 24-hour dietary recall method

Some of the characteristics of the reference dietary calibration method used are reported in Table 8.

Time interval between baseline dietary assessment and 24-HDR measurements

The time interval between dietary measurements varies from 1 day (or a few days) to several years. In The Netherlands, Germany and Denmark, most of the interviews were conducted at the same time as the baseline examination or shortly afterwards. In the UK, Italy, Greece and Spain, the interval between the two dietary measurements was between 12.4 and 25 months whereas in France, for logistic reasons, and Sweden, where the cohort existed before joining EPIC, the interval was as high as between 31.7 and 34.1 months.

Duration of the recalled day

The period to be covered during the recalled dietary interview was defined as the individual's time between waking up on the recalled day to waking up on the following day (interview day). This procedure was chosen instead of the time period from midnight to midnight to facilitate memory retrieval during the interview. Whatever the centre or country, the mean time interval was always about 24 hours.

Interview duration

The average duration of the 24-HDR interviews was 31.1 ± 13.3 min, and ranged from 27 ± 11 min in Denmark to 39 ± 20 min in the UK. The variations observed across

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centres may be explained by differences in dietary habits, total number of food items reported and the proportion of mixed recipes, which usually require more time to process than single food items. In the UK, the average duration was almost twice as high as the mean shortest interview time (22 ± 7 min in Ragusa), particularly among the 'health-conscious' study population (43 ± 28 min).

Number of food items

The mean number of items reported per interview varied twofold across countries, from 15.3 ± 5.3 (Greece) to 30.4 ± 8.3 (UK). However, when these two countries are disregarded, the total number of food items reported varied much less, 23.2 ± 6.3 in Germany to 27.2 ± 6.7 in France (women only). The variation between centres from the same country was small except for Turin (Italy) and Asturias (Spain) where the number of food items reported was, respectively, higher (28.7 ± 7.5) and lower (23.7 ± 7.4) than in the other local centres.

Coverage of days of the week and seasons

The optimal coverage of days of the week, particularly Fridays and Saturdays, was restricted both by a low participation rate for interviews performed during week-ends and by the logistic problems of approaching and interviewing the subjects during non-working days. Table 9 shows that Fridays were highly under-represented in Germany (4.8%), Norway (7.7%), Denmark (8.3%) and France (8.3%), and far below the expected 14.3% corresponding to an equal distribution of the seven days of the week. For Saturdays, the under-sampling was much lower than for Fridays, except in Denmark (Copenhagen mainly) where it was below 9%. This is probably because data concerning Saturdays were mostly collected on Mondays (i.e. during a working day) with a 48-hour time interval. In contrast, the interviews covering Fridays were always obtained during a weekend, Saturdays (24-hour interval) or Sundays (48-hour interval), which decreased the participation rate because of the logistic problems of interviewing subjects during non-working days. In the other countries, the same tendency to under-sample Fridays (and Saturdays) is observed, although to a lesser extent.

In certain countries, the interviews collected according to seasons tend to be under-sampled in summer and, to a lesser extent, autumn (Table 9). The 24-HDRs collected in summer were under-sampled by about 45–50% (Denmark, France and Norway) and up to 70% in Greece. In the other countries, both under-sampling and over-sampling were observed but to a lesser degree. However, when the four seasons are grouped into two classes (spring/summer and autumn/winter), the coverage of seasons is much better balanced, except for Germany, where spring/-summer tended to be over-sampled, whereas in Norway and Denmark it tended to be under-sampled by about 20–25%.

Discussion

The EPIC calibration sub-studies were set up in order to improve the comparability of dietary data across the participating centres. The calibration concept imposes a number of requirements, which include the following:

1. Calibration sub-populations must be representative of the EPIC cohorts.
2. The common reference method for dietary intake assessment must provide correct estimates of mean population intakes.
3. Random errors in the reference measurements, i.e. variations not structurally related to subjects' true intake levels, must be statistically independent of (i.e. not correlated with) random errors in the dietary questionnaire assessments used for the full cohort.

For the above requirements to be met, much depends on practical, logistic and methodological issues. In order to obtain the necessary representative population, a high participation rate must be achieved from the individuals invited to take part in the calibration sub-study. In our studies, about 70% of the study centres reported a participation rate above 75%. This response rate was consistently better when the subjects were recruited immediately after baseline examination than in centres where the subjects had to be re-invited at a later date. Important logistic constraints to re-approaching the subjects, as suggested by a high passive non-response rate, were observed in Greece and, to a lesser extent, in The Netherlands. It can be expected, however, that a passive non-response is random with regard to relevant subject characteristics.

Apart from study logistics, variations in the participation rates across study centres may also be partially explained by differences in social attitude and culture. In particular, the comparatively low response rates from representative samples of general populations (UK general population and Norway) or from an atypical population group (the 'health-conscious' group from Oxford) suggest that a number of other uncontrolled factors may determine the subjects' participation rate, as observed in the SENECA (Survey in Europe on Nutrition and the Elderly: a Concerted Action) study[26].

The sampling procedures for the calibration sub-studies were stratified by age group and gender, and the sample size requirement was weighted by the expected numbers of cases of cancer in age–gender categories over 10 years of follow-up. This relative weighting will increase the precision of the statistical calibration procedure when it is used to correct relative risk estimates for biases induced by errors in the baseline dietary questionnaire assessments[7,9]. Within strata of age and gender, however, the aim was to obtain the participation of a random, fully representative sample of cohort members in the calibration studies.

In most centres, after adjustment for age, no significant

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differences in height, weight, BMI and smoking status were observed between the calibration sample and the rest of the individual cohort for either men or women. Greater differences were observed for level of education and physical activity. The large and heterogeneous study populations involved in the analysis may explain the higher likelihood of detecting statistically significant differences. Indeed, the actual differences observed were modest in most centres. However, we observed a slight tendency to under-represent current and never-smokers compared with ex-smokers and subjects with a low education level in the calibration sample, compared with the rest of the cohort. Non-workers were also under-represented compared with sedentary and/or standing professional occupations in the calibration, compared with the cohort, in both genders. A higher completeness (i.e. a lower number of missing values) of the calibration compared with the entire cohort dataset also explains some differences between distributions, particularly for work-based physical activity in Bilthoven and the UK general population. Although most of the discrepancies in the distributions of these categorical variables were due to differences of only a few percentage points across classes, this might also suggest a possible selection/sampling bias that should not be completely disregarded, particularly in certain study centres.

In order to investigate further whether the observed differences in subjects' characteristics influence dietary estimates from the calibration sub-samples as representative of the entire cohort, we compared the centre mean dietary intakes obtained from the baseline dietary methods between the calibration and the rest of the cohort. Dietary intakes estimated from baseline assessment methods were used in this analysis because they were the only dietary measurements available from *all* of the EPIC study subjects (24-HDRs were collected from only 5–12% of the EPIC cohorts). The statistical analysis was stratified by centre in order to control for differences in baseline dietary methods used across EPIC and the dietary comparison was made for 16 main food groups, using the same EPIC-SOFT classification system across centres. Overall, 89% of the centre–sex–food group combinations considered show a mean difference of less than ±10% (69% had a difference within ±5%). However, 59% of the differences above ±10% were observed in only four centres (UK 'health-conscious' group, Ragusa, Granada and Umeå) out of the 24 centres involved in this analysis. The UK 'health-conscious' sub-group alone represented about a quarter of these values, probably because of the low participation rate, the small size of the calibration sample and the lack of representativeness of the different sub-components of this group (i.e. vegans, vegetarians and fish eaters) compared with the rest of the 'health-conscious' cohort. For Granada and Umeå, the relatively low response rate (~70%) and statistically significant difference in distribution between the calibration and the rest of the cohort for anthropometric measurements (women in both centres), smoking status and physical activity at work (Umeå) suggest that they may not be strictly representative of the entire cohort, but further investigations are required. For Ragusa, no explanation was found to explain the systematic differences in mean estimates observed in about one-third of the combinations.

This analysis will be presented in greater detail elsewhere and further explanatory statistical analyses will consider the impact of imperfect representativeness of the calibration sub-samples observed in certain centres, particularly the 'health-conscious' group, when calibrating individual dietary questionnaire measurements.

Logistic constraints in performing interviews during weekends were reported in several EPIC countries. They were partially overcome by conducting interviews for Saturdays on Mondays, allowing a 48-hour time interval. However, this made it impossible to distinguish whether observed variations in average food intakes between Saturdays and other days of the week reflected the true differences or whether they were the result of bias because of the increased time elapsed (48 hours instead of 24), which may have affected the subjects' memory and capacity to report their diet. Fridays, for which interviews could only be performed during the weekend, were frequently under-sampled compared with the other days of the week. Collecting dietary interviews by telephone, using an adapted version of the EPIC-SOFT program as successfully experimented in Norway, may be a promising alternative to improve the coverage of all days of the week and seasons in future[27]. However, the practical difficulty of obtaining an equal distribution of 24-HDR according to days of the week and seasons, and the confirmation that a high day-to-day variation for different food groups such as meat, fish and alcohol exists[28–30], suggests that adjustments for imperfect distributions of season and particularly day of the week are needed in statistical analyses on diet and when applying the calibration.

In most situations, the 24-HDRs were collected either at the time of baseline examination or after re-contacting the subjects. In several centres, cohorts existed before they joined the EPIC network. In other centres, where baseline recruitment had started relatively early, the calibration studies were initiated several years later because the EPIC-SOFT program had not yet been finalised. In these centres, subjects were re-contacted up to three years after their baseline examination and dietary questionnaire assessment. A somewhat longer time interval between the baseline dietary questionnaire assessment and 24-HDR for the calibration studies may have the advantage of reducing correlations between random errors of the two measurements, to the extent that such correlations depend on whether measurements were collected over a short interval of time. A disadvantage, however, is that over longer time intervals more subjects may have changed their diet because of age, development of disease, or other

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changes in life status. The calibration studies were set up to correct for between-centre differences in the effects of errors in the baseline dietary questionnaire assessments. This correction will have to rely on the assumption that changes in true mean intake level over time did not substantially affect the validity of the 24-HDR measurements for inferences about between-centre differences in subjects' true habitual intake level at the time of recruitment.

The time needed to perform the interviews with the EPIC-SOFT program (~30 min) was quite comparable across centres and compatible with the cost and logistic constraints of large nutritional studies. This includes both the time needed to perform the dietary interview and the automatic data entry. However, more time – varying across centres – was needed to update incomplete 24-hour dietary recalls after the interview. The degree of standardisation of 24-HDR measurements for use in calibration sub-studies has been reported elsewhere[19]. Overall, 24-HDR measurements were reasonably well standardised across the interviewers involved in the calibration studies, although within certain centres an interviewer or gender effect was observed. The extent of systematic underreporting associated with 24-HDR measurements and its main determinants, discussed elsewhere in this supplement, will give further insights into the relative validity of mean 24-HDR measurements[31].

This was the first time that calibration sub-studies had been set up in a large multi-centre European study. These studies showed that, despite some inherent methodological and logistic constraints, such a study design works relatively well in practice and can provide valuable additional measurements for better interpreting results from multi-centre epidemiological studies on diet and risk of chronic disease. In addition, the overall results suggest that, after adjustment for age, the calibration samples are fairly representative of the entire group of cohorts and that dietary intakes estimated from these sub-samples should reasonably be interpreted as representative of the main cohorts in most of the EPIC centres.

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