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Dietary patterns and risk of asthma: results from three countries in European Community Respiratory Health Survey-II

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Dietary patterns offer an alternative to the analysis of individual foods or nutrients in nutritional epidemiological studies. The aim of the present study was to identify dietary patterns common to different European countries and examine their associations with asthma. In five study centres (two in Germany, two in the UK and one in Norway), 1174 adults aged 29–55 years completed a FFQ and respiratory symptoms questionnaire. A meta-analytic approach was used to identify the dietary patterns and analyse them in relation to current asthma, asthma symptoms and bronchial responsiveness (BHR). Two patterns emerged, generally correlating with the same foods at different centres: one associated with intake of meats and potatoes; the other with fish, fruits and vegetables. There was no evidence that the fish, fruits and vegetables pattern was associated with asthma (OR 1·11 (95 % CI 0·93, 1·33)), symptom score (ratio of means 1·07 (0·98, 1·17)) or BHR (regression coefficient −0·01 (−0·12, 0·10)), though these CI appeared to rule out large protective effects of consuming these foods. There was no overall evidence that the meat and potato pattern was associated with asthma (OR 1·02 (0·79, 1·31)), symptom score (ratio of means 1·07 (0·84, 1·36)) or BHR (regression coefficient −0·08 (−0·27, 0·10)), but there was heterogeneity between centres in the association with symptom score: a negative association at the two German centres; a positive association at the others. Heterogeneity in a multi-centre observational study of diet could suggest alternative explanations for apparent effects of diet, such as uncontrolled confounding.

Asthma: Bronchial responsiveness: Dietary patterns: Meta-analysis

There is accumulating evidence that diet affects the prevalence of asthma, for example via the protective effects of dietary antioxidants[1] and *n*-3 PUFA in oily fish[2]. Interpreting the evidence from observational nutritional studies is difficult, however, because of the wide potential for confounding and effect modification. The results of trials are often inconclusive or contradictory[3]. Statistical analysis can deal with questions of confounding and interaction of dietary exposures to some extent, but the sheer number of features of diet that can be measured will often defeat comprehensive investigation. An alternative approach is to extract a small number of dietary 'patterns' using data-analytic methods, such as principal components analysis (PCA)[4]. This approach is now routinely applied to FFQ data, though applications in respiratory epidemiology have so far been scarce. Prospective cohort studies of US men and women have found that a diet rich in refined grains, cured and red meats, desserts and French fries is positively associated with risk of chronic obstructive pulmonary disease, and a diet rich in fruits, vegetables and fish is negatively associated[5,6]. Dietary patterns were not associated with adult-onset asthma in these cohorts. A study of Chinese Singaporeans found that a diet rich in meats, Na and refined carbohydrates was positively associated with habitual cough and phlegm[7], while a study of Japanese female students found that a butter and rapeseed oil dietary pattern, and a fast-food, soft drink and juice dietary pattern were both positively associated with wheeze[8]. In France, a study of female teachers found that a pastry, processed meat and dessert pattern was positively associated with reporting frequent asthma attacks, and a nut and wine pattern was negatively associated[9]. One problem with the PCA approach is that it does not lend itself well to the synthesis of evidence from different studies. Indeed, there is no *a priori* guarantee that the same patterns will be seen in different countries with differing culinary traditions and sources for foods.

In the present study, we looked at dietary patterns in three countries participating in the European Community Respiratory Health Survey (ECRHS) and used these to investigate relationships between diet and asthma in adults.

Abbreviations: BHR, bronchial responsiveness; ECRHS, European Community Respiratory Health Survey; EPIC, European Prospective Investigation into Cancer and Nutrition; FEV_1, forced expiratory volume in 1 s; PCA, principal components analysis.

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We derived the dietary patterns using a meta-analytic approach to PCA which, to our knowledge, has not previously been used in the analysis of FFQ data.

Material and methods

Study design and population

The design of ECRHS has been described in detail elsewhere[10]. ECRHS-I ran from 1990 to 1995. At each centre, a random sample of at least 3000 adults aged 20–44 years was selected using a local sampling frame. From those who responded, a random sample of at least 600 adults was selected to undergo a detailed clinical examination. Eight to ten years later, these subjects were contacted to take part in a follow-up study (ECRHS-II) and invited to a local clinic for further assessments, including an interviewer-administered questionnaire. The sample size at each centre was sufficient for comparing changes in prevalence of wheezing, asthma and atopy between centres[10].

Dietary assessments were included in ECRHS-II at some centres, though the method and protocol differed between countries. In the present paper, we report results from five centres in three countries in ECRHS-II, where FFQ were administered: Hamburg and Erfurt in Germany; Ipswich and Norwich in the UK; Bergen in Norway. Three thousand three hundred and eighty-seven adults at these centres were contacted to take part in ECRHS-II.

Respiratory outcomes

Questions on asthma and respiratory symptoms were taken from the bronchial symptoms questions of the International Union against Tuberculosis and Lung Disease questionnaire[10]. Current asthma was defined as an attack of asthma or being woken by an attack of shortness of breath in the last 12 months or currently taking any medicines for asthma. Five questions on symptoms in the last 12 months (breathless when wheezing, woken with tightness in chest, shortness of breath while at rest, shortness of breath after exercise, woken by shortness of breath) were used to construct an asthma symptom score on a five-point scale[11].

Bronchial responsiveness (BHR) was assessed using a methacholine challenge. For safety reasons, the challenge was not carried out on participants whose forced expiratory volume in 1 s (FEV_1) was $<70\,\%$ of their predicted value or $<1{\cdot}5$ litres. The outcome referred to here as BHR ‘slope’ is $100/(\log \text{slope} + 10)$, where log slope is calculated by regressing percentage fall in FEV_1 on $\log_{10}$ dose[12]. A low ‘slope’ is indicative of high BHR. To help to assess the impact of having missing slope for low FEV_1 values, FEV_1 was also analysed as a separate outcome.

FFQ

The German FFQ was developed for use in the German part of the European Prospective Investigation into Cancer and Nutrition (EPIC-Heidelberg)[13]. It recorded a consumption of 158 different foods over the last 12 months as frequencies from never to five portions a day or more. Portion size was selected from a multiple choice, sometimes with reference photos. Supplementary questions covered aspects of diet, such as the preparation and fat content of foods. The FFQ was distributed after the clinical and questionnaire assessments, and the participants were asked to return the completed FFQ by mail.

The UK FFQ was adapted from one developed for EPIC-UK. It recorded a consumption of 198 different foods over the last 12 months as frequencies (from never to 7 d a week) and number of portions consumed on each of these days (portions being defined on the questionnaire). As on the German FFQ, there were also supplementary questions. The Norwegian FFQ was a translation of the UK FFQ, but contained six additional foods not appearing on the UK questionnaire. In Norway, the FFQ was administered at the same clinic visit as the other assessments in ECRHS-II; while in the UK, participants were invited to attend the clinic on a separate occasion to complete the FFQ. In each case, the FFQ was self-completed and checked in the clinic by one of the local research team to cut down on missing data.

Food frequencies were converted to intakes in g/d. In the UK and Norway, this used portion weights from the standard UK reference[14], while in Germany portion sizes were those used with the EPIC FFQ[13]. For a few foods, such as butter, intake was calculated both from the reported food frequency and the supplementary questions on food preparation and cooking.

Nutrient intakes

Nutrient intakes were calculated in each country from FFQ data and supplementary questions, using local food tables[15–17]. Because the Norwegian FFQ was originally translated from the UK FFQ, it contained a number of foods not commonly eaten in Norway, hence not included in the Norwegian food tables; UK references were used for these foods where they did occur.

Exclusions of dietary data

On the UK FFQ and Norwegian FFQ, respondents sometimes left individual items blank. This was assumed to denote zero intakes of these foods unless more than 20 % of items were blank, in which case the FFQ was considered incomplete, and the subject was excluded from analyses. Subjects in each country were also excluded if they had extreme values of total energy intake which might suggest an unrealistic response: we calculated expected BMR with given age, weight and sex[18], and excluded subjects with a ratio of energy intake to expected BMR below the 0·5th sample centile or above the 99·5th sample centile for their country[19].

Validity and repeatability of FFQ

Validity and repeatability of the German FFQ were assessed in 104 men and women aged 35–64 years as part of a pilot for the EPIC study[13]. The FFQ was administered on two occasions in the interval of 6 months. Twelve 24-h dietary recalls applied at monthly intervals served as the reference for the validity of the second FFQ assessment.

Repeatability of the UK FFQ was assessed in eighty-two adults (sixty-six from the sample described in the present

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Table 1. Energy and macronutrient intakes estimated from FFQ: estimates of repeatability and validity and observed distributions

(Median and interquartile range values)

	Results of validity and reliability studies*				Energy and macronutrient intakes among FFQ responders†					
	Germany		UK		Germany (*n* 388)		UK (*n* 239)		Norway (*n* 547)	
	Repeatability (FFQ_1 *v.* FFQ_2; *n* 104)	Validity‡ (FFQ_2 *v.* 24 h recall; *n* 104)	Repeatability (FFQ_1 *v.* FFQ_2; *n* 82)	Validity§ (FFQ_1 *v.* 24 h recall; *n* 263)	Median	Interquartile range	Median	Interquartile range	Median	Interquartile range
Total energy (MJ/d)	0·68	0·40	0·62	0·27	8·9	7·1–11·1	10·4	8·2–12·7	10·8	8·7–14·1
Protein (g/d)	0·68	0·44	0·51	0·25	78	61–97	88	73–111	105	82–134
Fat (g/d)	0·63	0·41	0·72	0·30	84	64–108	86	65–114	98	74–134
Carbohydrates (g/d)	0·69	0·42	0·57	0·30	227	182–292	315	244–390	288	230–365

FFQ_1, 1st FFQ; FFQ_2, 2nd FFQ.
* Figures are Pearson correlations, calculated from the logarithms of total energy and macronutrient intakes.
† Responders are those with complete clinical and questionnaire assessments who also completed the FFQ and had a realistic energy intake.
‡ Based on twelve 24-h dietary recalls. Multiple assessments mean that the estimate of validity can allow for within-person variation in 24-h dietary recall.
§ Based on a single 24-h dietary recall.

paper and sixteen others with asthma symptoms), using two assessments separated by an interval of 5–23 months. Validity of the UK FFQ was assessed in 263 adults (206 from the sample described in the present paper and 57 others with asthma symptoms), using a single 24-h dietary recall. The Norwegian FFQ was not assessed for repeatability or validity.

Validity and repeatability are summarised in Table 1.

Dietary patterns

Some aggregation of food items on each country's FFQ was necessary to allow intakes to be matched across questionnaires, for example, on the UK FFQ and Norwegian FFQ fried egg was aggregated with omelette or scrambled egg to allow comparison with the German FFQ, which simply recorded intake of fried egg, omelette or scrambled egg. We performed the minimum aggregation necessary to allow foods to be matched. This process led to a list of seventy-four foods or food groups whose intake in g/d was available in all three countries (see the Appendix). Aggregation of food items into broader, *a priori* groupings (often fewer than we have used) is commonplace in the analysis of FFQ[5,6,20].

In each centre, we evaluated the correlation matrix of foods on our list and pooled the correlations from different centres using the method of Rosenthal[21]. Specifically, each correlation coefficient was transformed using a Fisher transformation ($0{\cdot}5\log((1+r)/(1-r))$) to give it an approximately normal sampling distribution with variance $1/(n-3)$, where n is the sample size for that centre. A weighted average of these values was then calculated, in which each value was given a weight proportional to the inverse of its variance (analogous to pooling estimates of a mean, say, from subsamples of different sizes). An inverse Fisher transformation was then applied to give a pooled correlation coefficient. PCA was applied to the matrix of pooled correlation coefficients, giving us dietary patterns (linear combinations of standardised food intakes), which could be used in all the five centres. This meta-analytic approach to PCA has previously been applied in the field of psychiatry[22,23].

Data analysis

We looked at whether characteristics of participants influenced rates of responding to the FFQ using logistic regression, with responding as the outcome, adjusting for centre. Social class was based on occupation using International Standard Classification of Occupations-88 codes[24]. Subjects were categorised as never, ex- or current smokers based on questionnaire responses and were divided into four groups according to reported frequency of physical exercise ('How often do you usually exercise so much that you get out of breath or sweat?'): never; less than once a week; one to three times a week; or more than three times a week.

We used multivariable regression to investigate associations between the dietary patterns (in quintile groups) and respiratory outcomes at each centre. Logistic regression was used for asthma, negative binomial regression for symptom score and linear regression for BHR slope and FEV_1. Analyses were adjusted for age, sex, social class, smoking status, exercise, BMI and quintiles of total energy intake. The effects of the dietary patterns were also adjusted for each other, because although principal components are uncorrelated, rotations (even orthogonal ones) can introduce correlations between the dietary patterns.

Regression results were pooled across centres using random effects meta-analysis, with a test for heterogeneity of regression coefficients[25]. Heterogeneity was summarised using the I^2 statistic[26].

Statistical software

Some analyses of the German data were carried out locally using SAS (SAS Institute, Cary, NC, USA). All other analyses were done with Stata 10 (Stata Corporation, College Station, TX, USA).

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human participants were approved by the Bavarian General Medical Council in Germany, the Ipswich Hospital and Norfolk and Norwich Hospital ethics committees in the UK and the Regional Committee of Medical Research Ethics at the University of Bergen in Norway. Written informed consent was obtained from all the participants.

Results

Fig. 1 shows the numbers of people taking part, by centre. Clinical and questionnaire assessments were available for 1740 subjects. Complete FFQ data were provided by 1182 of these, but eight were excluded because they were at the extremes of the distribution of ratio of energy intake to expected BMR in their country (in Germany, there was one under-reporter (ratio $<0·59$) and one over-reporter ($>5·5$), in the UK one under-reporter ($<0·44$) and one over-reporter($>3·6$), and in Norway two under-reporter ($<0·50$) and two over-reporter ($>5·2$)). The 1174 people who responded to the FFQ with a realistic energy intake (35 % of those contacted) ranged in age from 29 to 55 years. Those in a higher social class were more likely to be responders ($P<0·001$), as were people who exercised more frequently ($P=0·012$). Current smokers were less likely than ex- or never-smokers to respond ($P=0·001$). There was no evidence that age, sex or BMI were associated with responding. Of the 1174 responders, reported asthma was available for 1173, asthma score for 1160 and BHR slope for 906. Table 1 summarises total energy and macro-nutrient intakes in responders.

Principal components analysis

The scree plot from the PCA showed a clear break in the curve after two components, with no natural choice of any larger but still parsimonious number of components to extract. These two dietary patterns explained 11·2 % of the variance in the FFQ data. Table 2 shows how individual foods were correlated with each of these patterns at the five centres. Although a pattern score is defined as the same weighted sum of standardised food intakes at each centre, correlations with individual foods may differ between the centres because of differences in local diets, and this table is a good way to judge the heterogeneity or homogeneity of dietary patterns. In our case, there was a close match between the centres in the foods which characterised each pattern. The first pattern was closely associated with sliced meat, beef, pork, bacon, sausage and fried egg/scrambled egg/omelette intake at all the centres and also with intake of potato or chips. Depending on the centre, it also correlated closely with bread, butter, biscuits and cakes. This pattern is referred to here, for conciseness, as the ‘meat and potato’ pattern. The second pattern was closely associated with intakes of several fruits at all the centres and less consistently with intakes of a number of vegetables and fish. This pattern is referred to here as the ‘fish, fruits and vegetables’ pattern.

Dietary patterns and respiratory outcomes

Fig. 2 shows the results of meta-analyses as forest plots. There was no overall evidence that the meat and potato pattern was associated with asthma ($P=0·90$), symptom score ($P=0·58$), BHR slope ($P=0·39$) or FEV_1 ($P=0·74$), and similarly no evidence that the fish, fruits and vegetables pattern was associated with asthma ($P=0·26$), symptom score ($P=0·16$), BHR slope ($P=0·89$) or FEV_1 ($P=0·19$).

There was no evidence of heterogeneity across the centres in any of these effects, except in the case of the association

	Hamburg (Germany)	Erfurt (Germany)	Ipswich (UK)	Norwich (UK)	Bergen (Norway)	Total
Contacted to take part in ECRHS II	900	731	448	473	835	3387
Clinical and questionnaire assessments	303	287	297	257	596	1740
Complete FFQ	202	188	144	97	551	1182
Realistic total energy intake	201	187	143	96	547	1174
Response rate (%; out of total contacted)	22	26	32	20	66	35

Fig. 1. Flow chart showing numbers of subjects in the study. ECRHS, European Community Respiratory Health Survey.

Table 2. How correlates of dietary patterns vary between centres*

	Centre									
	Meat and potato pattern					Fish, fruits and vegetables pattern				
Food	G1	G2	UK1	UK2	N	G1	G2	UK1	UK2	N
Bread and rolls	0·34			0·32	0·33					
Butter		0·33	0·31		0·30					
Jam and marmalade										
Honey						0·41	0·38			
Peanut butter										
Biscuits	0·36		0·38	0·38	0·35					
Cakes, puddings, desserts	0·31	0·37			0·36					
Donuts, pastries, tarts		0·30								
Yoghurt								0·47		
Ice cream			0·34		0·31					
Cream cheese										
Cottage cheese										
Hard cheeses			0·32	0·43						
Soft cheeses										
Boiled egg										
Fried/scrambled egg, omelette	0·34	0·37	0·45	0·31	0·51					
Quiche										
Sliced meat	0·36	0·45	0·59	0·56	0·45					
Beef steak	0·38	0·44	0·45	0·40	0·33					
Beef burger	0·64	0·42	0·37	0·39	0·30					
Meat-minced, meat stew, casserole	0·60	0·55	0·39	0·46	0·39					
Pork chops	0·59	0·55	0·53	0·46	0·48					
Bacon	0·44	0·40	0·42	0·69	0·55					
Poultry	0·57	0·41	0·34		0·44			0·30		
Maized beef and luncheon meat	0·42			0·36						
Sausages	0·40	0·50	0·53	0·55	0·49					
Liver		0·39	0·37	0·37						
Pate	0·36	0·33		0·31	0·36					
Fish fillets/cakes/fingers						0·32	0·34	0·43		0·31
Tinned fish	0·31									
Potato – boiled/mashed/baked	0·42	0·33	0·33		0·40				0·33	
Chips	0·30	0·33		0·34						
Rice and rice dishes					0·30	0·30	0·32		0·34	
Soya†, quorn, bulgur, polenta							0·44		0·40	
Vegetarian paste						0·30	0·32		0·34	
Pizza										
Soup		0·38						0·44		
Broccoli, cabbage, cauliflower	0·30					0·38	0·33	0·48	0·68	0·53
Carrots						0·51	0·36	0·54	0·47	0·45
Garlic							0·31	0·49	0·51	
Peas	0·36								0·34	
Peppers						0·63	0·37	0·47	0·41	0·31
Green beans								0·47	0·61	
Tomato						0·50	0·51	0·32	0·59	0·45
Bean sprouts							0·31	0·31		
Lentils, dahl, bean casserole								0·35	0·42	
Tomato ketchup			0·31		0·38					
Apple						0·45	0·42	0·40	0·53	0·48
Banana						0·35	0·38	0·51	0·53	0·43
Grapes						0·64	0·40		0·62	
Kiwi, mango, pineapple						0·63	0·53	0·45	0·64	0·49
Orange						0·55	0·53	0·49	0·48	0·44
Pear						0·41	0·39	0·50	0·55	0·47
Peach and nectarine						0·42	0·31	0·39	0·54	0·33
Raspberries, red/blackcurrants							0·33	0·35	0·47	0·35
Strawberries						0·46	0·43		0·40	0·41
Tinned/stewed fruit						0·30				
Breakfast cereals						0·48	0·41			
Chocolate bars and cereal bars										
Chocolate										
Nuts										0·37
Orange juice										
Other fruit juice										

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Table 2. *Continued*

	Centre									
	Meat and potato pattern					Fish, fruits and vegetables pattern				
Food	G1	G2	UK1	UK2	N	G1	G2	UK1	UK2	N
Fizzy drinks										
Tea – black/green						0·30				
Herbal tea									0·39	
Coffee (not decaffeinated)										
Decaffeinated coffee										
Milk and milky drinks					0·34					
Beer	0·30									
Cider and perry										
Wine										
Fortified wine										
Liqueurs and spirits		0·32		0·30	0·36					

G1, Hamburg, Germany; G2, Erfurt, Germany; UK1, Ipswich, UK; UK2, Norwich, UK; N, Bergen, Norway.
* Values are Pearson correlation coefficients. For clarity, only values > 0·30 or < −0·30 are shown.
† Foods made with soya protein: soya cheese; tofu; textured vegetable protein.

between meat and potato pattern score and symptom score ($I^2 = 75\,\%$; $P=0{\cdot}003$). In this case, it was evident from a visual inspection that the two German centres had qualitatively different results to the others; in fact, when countries were (meta-) analysed separately, increased meat and potato intake was associated with a decrease in symptoms in Germany (ratio of mean number of symptoms per quintile = 0·81; 95 % CI 0·68, 0·97; $P=0{\cdot}025$) but with an increase in symptoms in the UK (ratio per quintile = 1·34; 95 % CI 1·09, 1·67; $P=0{\cdot}007$) and Norway (ratio per quintile = 1·24; 95 % CI 1·00, 1·55; $P=0{\cdot}051$).

Discussion

We could not confirm any harmful or beneficial effects of fish, fruits and vegetable intake on asthma, though CI ruled out a reduction in the odds of current asthma of more than 7 % per quintile of fish, fruits and vegetable consumption or a reduction in the mean number of asthma symptoms of more than 2 % per quintile. Fish, fruits and vegetables are essential components of a Mediterranean diet, which other recent work has found to be associated with improved asthma control in adults[27], lower risk of current severe asthma in girls aged 6–7 years[28] and lower risk of allergic rhinitis in children aged 7–18 years[29]. Fish in the diet is a source of *n*-3 fatty acids, which may compete with the pro-inflammatory properties of *n*-6 fatty acids[30,31]. Recent results from the Respiratory Health in Northern Europe study indicated that infrequent fish intake was associated with increased asthma symptoms[32], but experimental support for this as a major influence on clinical disease is still weak[33]. Dietary antioxidants, of which fruits and vegetables should be a rich source, have also been hypothesised to be important in protecting against atopic disease[34]. Vitamin E, in particular, has been associated in some studies with a reduction in atopy[3], though a trial of vitamin E supplementation in asthma failed to show an effect[35].

The heterogeneous effect of the meat and potato pattern is not easy to explain. Patterns similar to this have often been labelled 'western' and are likely to represent a mixture of dietary components which may independently contribute to asthma risk[5,6]. Heterogeneity in multi-centre studies can also suggest alternative explanations for apparent effects of diet observed in single centres, such as uncontrolled confounding, and would make us cautious of progressing to a trial[36]. Our study was cross-sectional, and a further possibility is reverse causation, people with asthma may alter their diet in a systematic way at a given centre, for example, to be more 'healthy'.

Note that our analysis gives us common dietary patterns (weighted sums of standardised food intakes) that we can investigate at every centre. However, if a dietary pattern is acting as a proxy for individual foods associated with asthma, then some heterogeneity in its effect might be due to heterogeneity in its associations with these foods. The greatest variation in the correlations of individual foods with the meat and potato pattern was for beef burger (high in Hamburg, low in Bergen), bacon (high in Norwich, low in Erfurt) and poultry (high in Hamburg, low in Norwich).

FFQ are widely used in epidemiological studies to investigate dietary intake of individuals and its association with diseases. FFQ are cost-effective tools to assess the usual current and past patterns of food intake over an extended period of time[37]. Estimates of the validity of our FFQ data, for Germany at least, were good, being in the same range as those reviewed by Willett[38]. In the UK, validity was based on just a single 24-h dietary recall, but correlations were still notably high at 0·25–0·31, and we might reasonably expect that with multiple 24-h dietary recalls and adjustment for within-person variability, we would have observed correlations as good as those seen in Germany. 'True' validity may, in general, be worse than implied by studies using 24-h recall, because of correlated errors. This was the case for the EPIC-Norfolk FFQ, from which our FFQ was derived, for which estimates of Na and nitrogen intake correlated poorly with repeated 24-h urine measurements[39]. In Norway, we used a translation of the UK FFQ, but this included all the foods from the Norwegian EPIC FFQ[40,41], so we believe it is unlikely to have missed much in the Norwegian diet (we note that the total energy intake calculated from the FFQ in Norway was, if anything, higher than in the UK (Table 1)). Using a direct translation of the UK FFQ had

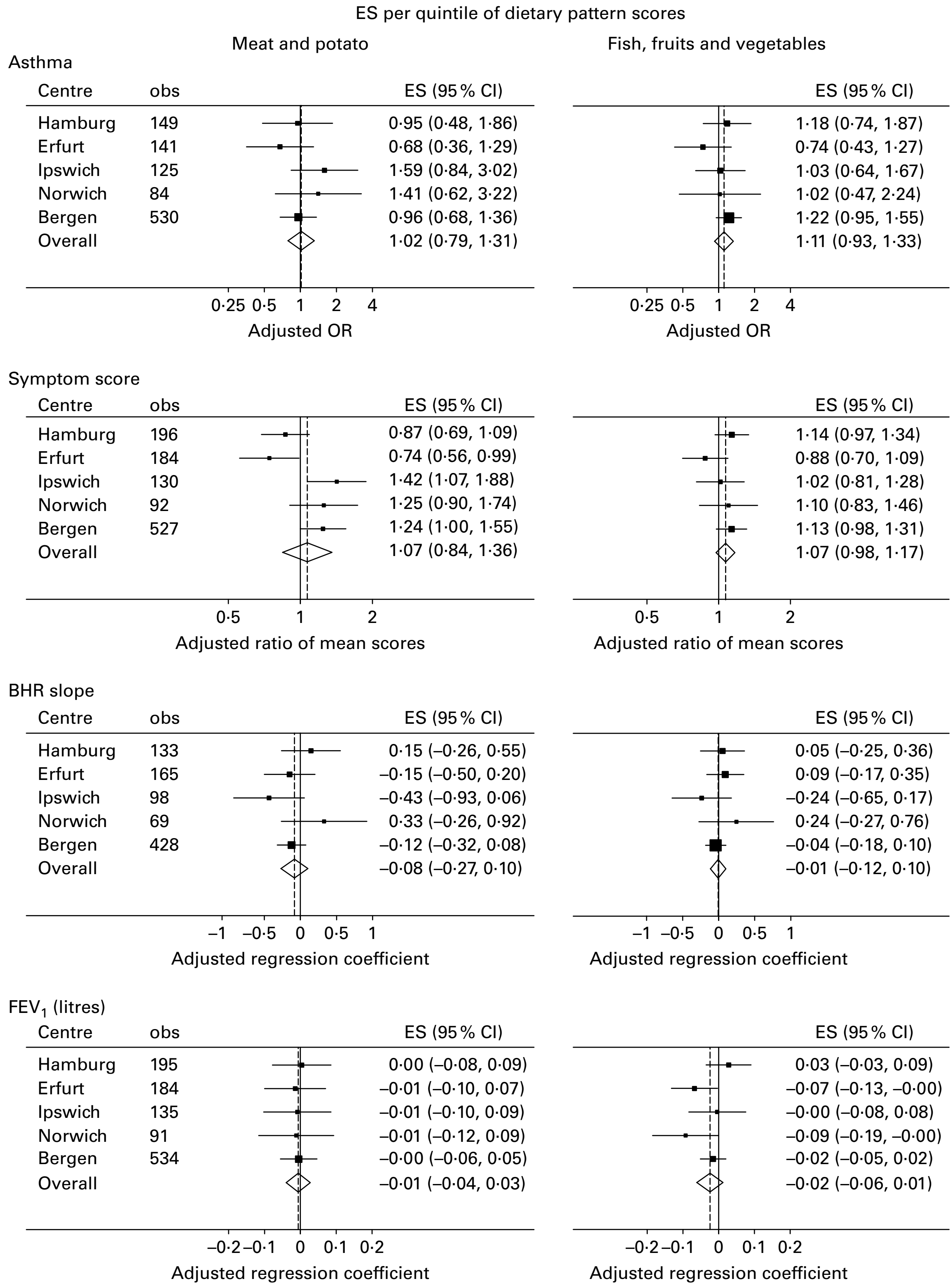

Fig. 2. Associations between the two dietary patterns and respiratory outcomes: results of meta-analyses. ES, effect size; BHR, bronchial responsiveness; FEV_1, forced expiratory volume in 1 s.

the great advantage of simplifying the pooling of data from Norway and the UK.

The poor response rates in our study were partly due to the time that had expired between the end of ECRHS-I and the recruitment of cohort members into ECRHS-II. Differences between response rates in different countries were also partly explained by differences in procedures. FFQ assessments in the UK were implemented much later than other

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assessments because the protocol had to be developed and approved separately, and the interval between the two clinic visits was up to 23 months (inter-quartile range 10–16 months) helping to explain the low rate of FFQ completion. In Norway, assessments were done in a single clinic visit. In Germany, participants were asked to complete the FFQ at home and return it by mail to reduce the burden placed on them in attending the clinic.

Methods for identifying dietary patterns, such as PCA, have proved a popular way to explore complex diet data in the last decade[4]. A meta-analytic approach to deriving dietary patterns across a number of centres has not, to our knowledge, been investigated before. This is, no doubt, partly because FFQ are often specific to a site, making it difficult to pool data. More work is needed to develop FFQ that allow directly comparable data to be collected in different countries. We have shown that the method can be successful in identifying common dietary patterns, as well as evidence for heterogeneity in the effects of those patterns. Heterogeneity in observational studies of diet can sometimes argue against progressing to trials.

In conclusion, we found no firm, consistent evidence for an association of diet with asthma, though CI appeared to rule out large beneficial effects of fish, fruits and vegetable consumption on current asthma or asthma symptoms. However, there are likely to be important, unmeasured confounders associated with dietary choices and observational studies of diet, particularly if they are cross-sectional, must be interpreted with caution.

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References

1. Shaheen SO, Sterne JAC, Thompson RL, *et al.* (2001) Dietary antioxidants and asthma in adults – population-based case–control study. *Am J Respir Crit Care Med* **164**, 1823–1828.
2. Hodge L, Salome CM, Peat JK, *et al.* (1996) Consumption of oily fish and childhood asthma risk. *Med J Aust* **164**, 137–140.
3. Devereux G & Seaton A (2005) Diet as a risk factor for atopy and asthma. *J Allergy Clin Immunol* **115**, 1109–1117.
4. Newby PK & Tucker KL (2004) Empirically derived eating patterns using factor or cluster analysis: a review. *Nutr Rev* **62**, 177–203.
5. Varraso R, Fung TT, Hu FB, *et al.* (2007) Prospective study of dietary patterns and chronic obstructive pulmonary disease among US men. *Thorax* **62**, 786–791.
6. Varraso R, Fung TT, Barr RG, *et al.* (2007) Prospective study of dietary patterns and chronic obstructive pulmonary disease among US women. *Am J Clin Nutr* **86**, 488–495.
7. Butler LM, Koh WP, Lee HP, *et al.* (2006) Prospective study of dietary patterns and persistent cough with phlegm among Chinese Singaporeans. *Am J Respir Crit Care Med* **173**, 264–270.
8. Takaoka M & Norback D (2008) Diet among Japanese female university students and asthmatic symptoms, infections, pollen and furry pet allergy. *Respir Med* **102**, 1045–1054.
9. Varraso R, Kauffmann F, Leynaert B, *et al.* (2009) Dietary patterns and asthma in the E3N study. *Eur Resp J* **33**, 33–41.
10. European Community Respiratory Health Survey II Steering Committee (2002) The European Community Respiratory Health Survey II. *Eur Respir J* **20**, 1071–1079.
11. Sunyer J, Pekkanen J, Garcia-Esteban R, *et al.* (2007) Asthma score: predictive ability and risk factors. *Allergy* **62**, 142–148.
12. Chinn S, Arossa WA, Jarvis DL, *et al.* (1997) Variation in nebulizer aerosol output and weight output from the Mefar dosimeter: implications for multicentre studies. *Eur Respir J* **10**, 452–456.
13. Bohlscheid-Thomas S, Hoting I, Boeing H, *et al.* (1997) Reproducibility and relative validity of energy and macro-nutrient intake of a food frequency questionnaire developed for the German part of the EPIC project (European Prospective Investigation into Cancer and Nutrition). *Int J Epidemiol* **26**, S71–S81.
14. Food Standards Agency (1993) *Food Portion Sizes*, 2nd ed. Norwich: HMSO.
15. Federal Institute for Health Protection of Consumers (BgVV) (1999) *Der Bundeslebensmittelschlussel (BLS II.3) (The Bundeslebensmittelschlussel (BLS II.3))/The German Food Code and Nutrient Database*. Berlin: BgVV.
16. Food Standards Agency (2002) *McCance and Widdowson's the Composition of Foods*, 6th ed. Cambridge: Royal Society of Chemistry.
17. Norwegian Food Safety Authority, Directorate for Health and Social Affairs, and University of Oslo (2006) http://matportalen.no/matvaretabellen
18. Department of Health (1991) *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom*. London: HMSO.
19. Welch AA, Luben R, Khaw KT, *et al.* (2005) The CAFE computer program for nutritional analysis of the EPIC-Norfolk food frequency questionnaire and identification of extreme nutrient values. *J Hum Nutr Diet* **18**, 99–116.
20. McCann SE, Marshall JR, Brasure JR, *et al.* (2001) Analysis of patterns of food intake in nutritional epidemiology: food classification in principal components analysis and the subsequent impact on estimates for endometrial cancer. *Public Health Nutr* **4**, 989–997.
21. Rosenthal R (1991) *Meta-analytic Procedures for Social Research*, revised ed., pp. 87. London: Sage.
22. Smith DA, Mar CM & Turoff BK (1998) The structure of schizophrenic symptoms: a meta-analytic confirmatory factor analysis. *Schizophr Res* **31**, 57–70.
23. Grube BS, Bilder RM & Goldman RS (1998) Meta-analysis of symptom factors in schizophrenia. *Schizophr Res* **31**, 113–120.

24. International Labour Office (1991) *International Standard Classification of Occupations (ISCO-88)*. Geneva: International Labour Organisation.
25. DerSimonian R & Laird N (1986) Meta-analysis in clinical trials. *Control Clin Trials* **7**, 177–188.
26. Higgins JPT, Thompson SG, Deeks J, *et al.* (2003) Measuring inconsistency in meta-analyses. *BMJ* **327**, 557–560.
27. Barros R, Moreira A, Fonseca J, *et al.* (2008) Adherence to the Mediterranean diet and fresh fruit intake are associated with improved asthma control. *Allergy* **63**, 917–923.
28. Garcia-Marcos L, Canflanca IM, Garrido JB, *et al.* (2007) Relationship of asthma and rhinoconjunctivitis with obesity, exercise and Mediterranean diet in Spanish schoolchildren. *Thorax* **62**, 503–508.
29. Chatzi L, Apostolaki G, Bibakis I, *et al.* (2007) Protective effect of fruits, vegetables and the Mediterranean diet on asthma and allergies among children in Crete. *Thorax* **62**, 677–683.
30. Black PN & Sharpe S (1997) Dietary fat and asthma: is there a connection? *Eur Respir J* **10**, 6–12.
31. Sausenthaler S, Koletzko B & Heinrich J (2006) Dietary fat intake and allergic diseases. *Curr Nutr Food Sci* **2**, 351–359.
32. Laerum BN, Wentzel-Larsen T, Gulsvik A, *et al.* (2007) Relationship of fish and cod oil intake with adult asthma. *Clin Exp Allergy* **37**, 1616–1623.
33. Thien FCK, Woods R & De Luca S, *et al.* (2002) Dietary marine fatty acids (fish oil) for asthma in adults and children *Cochrane Database of Systematic Reviews*, issue 2, CD001283. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001283/frame.html
34. Seaton A, Godden DJ & Brown K (1994) Increase in asthma – a more toxic environment or a more susceptible population? *Thorax* **49**, 171–174.
35. Pearson PJK, Lewis SA, Britton J, *et al.* (2004) Vitamin E supplements in asthma: a parallel group randomised placebo controlled trial. *Thorax* **59**, 652–656.
36. Burney P, Potts J, Makowska J, *et al.* (2008) A case–control study of the relation between plasma selenium and asthma in European populations: a GA^{2}LEN project. *Allergy* **63**, 865–871.
37. Cade JE, Burley VJ, Warm DL, *et al.* (2004) Food-frequency questionnaires: a review of their design, validation and utilisation. *Nutr Res Rev* **17**, 5–22.
38. Willett WC (1990) *Nutritional Epidemiology*. Oxford: Oxford University Press.
39. Day NE, McKeown N, Wong MY, *et al.* (2001) Epidemiological assessment of diet: a comparison of a 7-day diary with a food frequency questionnaire using urinary markers of nitrogen, potassium and sodium. *Int J Epidemiol* **30**, 309–317.
40. Engeset D, Alsaker E, Ciampi A, *et al.* (2005) Dietary patterns and lifestyle factors in the Norwegian EPIC cohort: the Norwegian Women and Cancer (NOWAC) study. *Eur J Clin Nutr* **59**, 675–684.
41. The Norwegian Women and Cancer Study (NOWAC), http://uit.no/kk/Questionnaire/ (accessed August 2009).

Appendix: Food items in each of the food groups analysed

	Food items on FFQ	
Food groups analysed	UK/Norway	Germany
Bread and rolls	Bread and toast Bread rolls, hamburger rolls, French bread, etc	Rye bread, rye-wheat bread White bread, wheat bread Wholemeal bread White rolls Brown and wholemeal rolls
Butter	Butter spread on bread, toast, rolls, crackers	Butter Butter, half-fat
Jam and marmalade	Jam, marmalade	Marmalade, jam and jelly
Honey	Honey	Honey
Peanut butter	Peanut butter Chocolate, chocolate and nut spreads	Chocolate and nut spread, chocolate spread, peanut butter
Biscuits	Chocolate biscuits Plain biscuits Sandwich or cream biscuits	Crackers, biscuits
Cakes, puddings and desserts	Cakes (sponge, gateau, chocolate, ginger, etc) Fruit cake Puddings and desserts (cheese cake, fruit pie, jelly, rice pudding, etc)	Fruit cake (e.g. apple cake, rhubarb cake) Pound cake, quick bread, ring-shaped cake Layer cake, cream cake, flan (including cheesecake) Yeast pastry (e.g. crumb cake, Stollen) Sweet casseroles (e.g. rice pudding, curd casserole) Pudding, fruit quark, sundae or other sweet food
Donuts, pastries and tarts	Donuts, custard tarts, and other pastries or tarts	Buns (e.g. apple turnover, cinnamon bun)
Yoghurt	Yoghurt, thick and creamy Yoghurt, low fat Yoghurt, low energy Yoghurt, Greek	Yoghurt
Ice cream	Ice cream	Ice cream
Cream cheese	Cream cheese, other cheese spread	Cream cheese
Cottage cheese	Cottage cheese	Quark, herb quark (but not fruit quark)

Appendix: *Continued*

Food groups analysed	Food items on FFQ: UK/Norway	Food items on FFQ: Germany
Hard cheeses	Cheddar cheese and other hard cheeses	Gouda, Emmental, Tilsiter and other hard cheese
Soft cheeses	Brie cheese and other soft cheeses	Soft cheese Camembert, brie, gorgonzola and other soft cheese
Boiled egg	Boiled or poached egg	Hard- and soft-boiled egg
Fried egg, scrambled egg and omelette	Omelette or scrambled egg Fried egg	Fried egg, scrambled egg, omelette
Quiche	Quiche and other savoury flans	Quiche, onion pancakes, bacon cakes
Sliced meat	Sliced meat (roast or boiled) – beef, lamb or pork Ham	Ham, cold smoked pork loin, cold roast meat Roast beef, boiled beef Roast pork
Beef steak	Beef steak	Beef steak, fillet, loin
Beef burger	Beef burger (with or without bun)	Beef burger, meatloaf
Minced meat, meat stew and casserole	Beef minced with gravy, chilli con carne, bolognese sauce, etc Meat stew, casserole, mince, curry	Minced meat in sauce, hash Stuffed roll of beef Beef stew, beef cut in pieces Pork stew, pork cut in pieces Boiled pork, knuckle of pork
Pork chops	Pork chops	Pork cutlet, chop, steak, fillet, loin Smoked pork loin, pork ribs
Bacon	Bacon	Pork belly
Poultry	Chicken, turkey, other poultry, roast Chicken, turkey, other poultry in sauce	Roast chicken Turkey strips, turkey in breadcrumbs, chicken fricassee, duck, goose, or other poultry
Corned beef and luncheon meat	Corned beef or luncheon meat	Salami, hard Mettwurst Bierschinken, Lyoner, Jagdwurst, Schinkenwurst, or other cold meats
Sausages	Sausages – beef, pork, other meat	Bratwurst Wienerle, Frankfurter, Bockwurst, Knackwurst, sausage loaf
Liver	Liver, kidney and other offal	Liver
Pâté	Pâté	Liverwurst Teewurst, soft Mettwurst, or other spreadable sausage
Fish fillets, fish cakes and fish fingers	White fish – not coated (cod, halibut, haddock, whiting, plaice, sole, etc) White fish – in batter or crumbs (cod, haddock, plaice, etc) Oily fish (herring, mackerel, salmon – not tinned, trout, kippers, etc) Fish cakes, fish fingers	Fish (e.g. natural or breaded fillet, fish fingers)
Tinned fish	Tinned fish (sardines, pilchards, tuna, salmon, etc)	Tinned fish, smoked fish (e.g. tuna, pickled herring, salmon, smoked trout)
Potato – boiled, mashed or baked	Potato, boiled or mashed Potato, baked in jacket	Boiled potatoes, jacket potato as side dish Mashed potato
Chips	Chips	Chips, potato croquettes
Rice and rice dishes	Plain rice Rice dishes (e.g. pilau, risotto, paella)	Rice (e.g. risotto, paella,... as a main course or as a side dish)
Foods made with soya protein, quorn, bulgur, polenta	Soya cheese Quorn dishes Textured vegetable protein, Sosmix, vegetable burger mix, soya sausage Bulgur wheat	Vegetarian foods (e.g. polenta, Getreidebratlinge, soya mince, tofu)
Vegetarian paste	Vegetable pâté Nut pâté	Vegetarian paste
Pizza	Pizza with meat Pizza with vegetables	Pizza
Soup	Packet soups Low energy soups Cream soups (tinned or fresh) Other soups (tinned or fresh)	Soup

Appendix: *Continued*

	Food items on FFQ	
Food groups analysed	UK/Norway	Germany
Broccoli, cabbage and cauliflower	Broccoli Savoy cabbage, spinach, spring greens, turnip tops, etc White cabbage Cauliflower	Cauliflower, red cabbage, white cabbage, kohlrabi, broccoli, and other varieties of cabbage Spinach
Carrots	Carrot (raw or cooked)	Raw carrots Cooked carrots
Garlic	Garlic	Garlic, fermented/roasted
Peas	Peas	Green peas
Peppers	Peppers (green, red, yellow, orange)	Raw pepper Cooked pepper
Green beans	Runner beans, green beans, mange tout, sugar snaps, other green beans	Green beans
Tomato	Tomato (raw, cooked, sauce)	Raw tomato in summer Raw tomato in winter Cooked tomato, tomato sauce
Bean sprouts	Bean sprouts	Bean sprouts
Lentils, dahl and mixed bean casserole	Lentils, dahl Mixed bean casserole	Lentil stew, pea stew, bean stew
Tomato ketchup	Tomato ketchup	Ketchup
Apple	Apple	Apple (summer/autumn) Apple (winter/spring)
Banana	Banana	Banana (summer/autumn) Banana (winter/spring)
Grapes	Grapes	Grapes
Kiwi, mango and pineapple	Kiwi Mango Pineapple	Kiwi, fresh pineapple, mango (summer/autumn) Kiwi, fresh pineapple, mango (winter/spring)
Orange	Orange	Orange, grapefruit Mandarin orange
Pear	Pear	Pear
Peach and nectarine	Nectarines peaches	Peach, nectarine
Raspberries, red currants and blackcurrants	Raspberries Red or black currants	Blackcurrants, raspberries, blackberries, or other berries
Strawberries	Strawberries	Strawberries
Tinned or stewed fruit	Canned or stewed fruit (not including dried fruit)	Stewed fruit, tinned fruit
Breakfast cereals	Breakfast cereals	Cereal flakes, grains, muesli Cornflakes etc
Chocolate bars and cereal bars	Chocolate bars (e.g. Mars, Twix) Cereal bars, flapjacks Fruit bar	Break-time snacks (e.g. Mars, cereal bar)
Chocolate	Milk chocolate bar Plain chocolate bar	Chocolate
Nuts	Peanuts Pistachios Cashews Almonds Walnuts, pecans Mixed nuts and raisins	Nuts (e.g. peanuts, walnuts, Brazil nuts)
Orange juice	Orange juice (pure fruit juice)	Orange juice, grapefruit juice
Other fruit juice	Other fruit juice (pure fruit juice)	Apple juice Grape juice, cherry juice, pineapple juice or other fruit juice Multivitamin juice
Fizzy drinks	Fizzy drinks (coke, lemonade, etc – not diet drinks) Low energy/diet drinks	Lemonade Cola
Tea – black and green	Tea, Indian Tea, Chinese (green tea)	Black tea, green tea
Herbal tea	Tea, herbal	Fruit tea, herb tea
Coffee (not decaffeinated)	Coffee, instant Coffee, fresh	Coffee with caffeine
Decaffeinated coffee	Coffee, decaffeinated	Decaffeinated coffee

Appendix: *Continued*

Food groups analysed	Food items on FFQ: UK/Norway	Food items on FFQ: Germany
Milk and milky drinks	Plain milk to drink Hot chocolate, cocoa Horlicks, Ovaltine, Bournvita, etc Low energy milky drinks	Milk, milky drink (e.g. cocoa, but not including milk with coffee)
Beer	Beer, lager	Beer
Cider and perry	Cider, perry	Alcohol made with fruit, e.g. cider, most
Wine	Red wine White wine Rosé wine	wine Sparkling wine
Fortified wine	Fortified wines (sherry, port, etc)	Aperitifs, dessert wine, fortified wine (e.g. sherry, port)
Liqueurs and spirits	Liqueurs Spirits (vodka, gin, whisky, brandy)	Spirits (e.g. brandy, whisky, schnapps)