

Dietary patterns and survival of older Europeans: The EPIC-Elderly Study (European Prospective Investigation into Cancer and Nutrition)

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Abstract

Objective: To investigate the association of *a posteriori* dietary patterns with overall survival of older Europeans.

Design and setting: This is a multi-centre cohort study. Cox regression analysis was used to investigate the association of the prevailing, *a posteriori*-derived, plant-based dietary pattern with all-cause mortality in a population of subjects who were 60 years

or older at recruitment to the European Prospective Investigation into Cancer and Nutrition (EPIC-Elderly cohort). Analyses controlled for all known potential risk factors.

Subjects: In total, 74 607 men and women, 60 years or older at enrolment and without previous coronary heart disease, stroke or cancer, with complete information about dietary intakes and potentially confounding variables, and with known survival status as of December 2003, were included in the analysis.

Results: An increase in the score which measures the adherence to the plant-based diet was associated with a lower overall mortality, a one standard deviation increment corresponding to a statistically significant reduction of 14% (95% confidence interval 5–23%). In country-specific analyses the apparent association was stronger in Greece, Spain, Denmark and The Netherlands, and absent in the UK and Germany.

Conclusions: Greater adherence to the plant-based diet that was defined *a posteriori* in this population of European elders is associated with lower all-cause mortality. This dietary score is moderately positively correlated with the Modified Mediterranean Diet Score that has been constructed *a priori* and was also shown to be beneficial for the survival of the same EPIC-Elderly cohort.

Keywords
Dietary patterns
Elderly
Cohort study
Survival

Dietary patterns have attracted considerable interest in nutritional epidemiology for assessing the impact of dietary intakes on the risk of several diseases and mortality^{1,2}. Assessing diet by dietary patterns rather than by selected nutrients or foods has the advantage of capturing the high inter-correlation of nutrients and foods within a diet, as well as integrating complex interactive effects of many dietary exposures^{3,4}. In this context, dietary patterns and their association with longevity have been studied for the elderly, an age group that is gradually increasing in most developed countries^{5–13}.

Two general approaches have been used to define dietary patterns. The '*a priori*' approach' focuses on the construction of patterns that reflect hypothesis-oriented combinations of foods and nutrients¹⁴. These patterns are operationalised through the calculation of a graded score which identifies groups with 'better' or 'worse' nutritional intakes. *A priori* scores that have been used in the literature are based either on dietary recommendations^{6,15–18} or on previous knowledge concerning the favourable or adverse health effects of various dietary constituents^{5,12,13,19–21}.

The second approach builds on exploratory statistical methods – usually principal components and factor analyses – and uses the observed dietary data in order to extract dietary patterns *a posteriori*. The '*a posteriori*' approach' has been used in nutritional studies either of a descriptive nature^{22–28} or in relation to a particular health outcome^{8,20,29–37}. The *a posteriori* approach is considered a useful tool for identifying the prevailing dietary habits of a particular study population⁴. Although this procedure is promising in summarising diet or certain combinations of foods, its utility in investigating associations of diet and disease is debatable because the extracted dietary patterns may have little relation to disease or mortality if, for example, nutrients or foods relevant to the aetiology of specific diseases are not incorporated in their definition²⁰. In addition, *a posteriori* patterns identified in one study

population may not be reproduced in other study populations^{4,38}.

We have previously evaluated the effect of an *a priori* dietary pattern on survival in a large, multi-centre cohort of elders living in nine different European countries – The EPIC-Elderly Study (European Prospective Investigation into Cancer and Nutrition)¹³. In the present paper we investigate the association with survival of an *a posteriori* dietary pattern, extracted from this multi-centre population as reported previously²⁷.

Methods

Recruitment

The EPIC-Elderly project aimed to identify the prevailing dietary patterns across European elders and examine their association with overall mortality. The cohort includes individuals who were 60 years or older at recruitment and participated in the EPIC study. EPIC is a multi-centre cohort study examining the role of diet on the aetiology of cancer and other chronic diseases, under the coordination of the International Agency for Research on Cancer (IARC). Details on the design, sample selection and methodology of the EPIC study have been described in detail elsewhere^{39,40}. In brief, between 1992 and 2000, 519 978 apparently healthy volunteers were recruited in EPIC from 23 centres in 10 European countries (Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden and the UK). Centre-specific cohorts consisted, in general, of subjects who agreed to participate and were recruited from populations living in various regions. In France, Norway, Utrecht (The Netherlands) and Naples (Italy) only females were enrolled. The study protocol has been approved by ethical committees at both IARC and the participating centres. All participants signed an informed consent form before enrolment. All procedures have been in line with the Helsinki Declaration on Human Rights.

Data for 100 442 participants from all countries are included in the EPIC-Elderly database with the exception of Norway, where the cohort is relatively young (all of the Norwegians in the EPIC cohort were younger than 60 years at enrolment).

Dietary intakes

Information on foods and beverages consumed during the year preceding enrolment was collected with the use of instruments that had been developed and validated within each centre⁴¹. The dietary questionnaires were, in general, food-frequency questionnaires (FFQs) that were developed in a common way with deviations aiming at capturing the unique characteristics of diets followed in each participating centre/country.

The results presented in this paper are based on overall dietary intakes (in g day^{-1}) obtained from the FFQs and calculated taking into account standard recipes and edible fractions. Alcohol consumption was expressed in $\text{g ethanol day}^{-1}$. Total energy intake (in kJ day^{-1}) for each participant was also estimated.

The *a posteriori* dietary pattern

Principal component analysis (PCA) using the correlation matrix was performed on residuals from linear regressions of each of 22 food groups (vegetables, fruits, potatoes, legumes, pasta/rice/other grains, bread, other cereals, cakes, sugar & confectionery, vegetable oils, margarine, butter, dairy products, meat & products, eggs, fish & shellfish, non-alcoholic beverages, wine, other alcoholic beverages, condiments & sauces, soups and soy) on total energy intake, in order to control for the role of energy intake on the reported individual food intakes⁴². The retained *a posteriori* dietary patterns were labelled on the basis of food groups, the consumption of which produced high positive scores in the respective principal component. A detailed list of the food groups and the food items contained in them, as well as results from this work, has been reported elsewhere²⁷.

The most important *a posteriori* dietary pattern, which was labelled 'plant-based', was defined by the first principal component and explained 14.6% of the total variation. This procedure-derived pattern was expressed through a score, estimated as a weighted linear combination of intakes of vegetables (positive coefficient), vegetable oils (positive coefficient), fruit (positive coefficient), pasta/rice/other grains (positive coefficient), legumes (positive coefficient), potatoes (negative coefficient), margarine (negative coefficient) and non-alcoholic beverages (negative coefficient). Hence, high plant-based dietary scores denote a diet rich in plant foods such as vegetables and vegetable oils, fruit, pasta/rice/other grains and legumes, but poor in potatoes, margarine and non-alcoholic beverages. Naturally, low scores imply the opposite pattern of consumption. The plant-based dietary

pattern was used as the *a posteriori* dietary exposure in the present study.

Lifestyle, anthropometric and medical variables

Data on a number of lifestyle and health variables were recorded with the use of a core lifestyle questionnaire, which contained a common set of questions and possible answers, for all participating centres. The lifestyle questionnaire included questions on educational achievement, history of previous illnesses, history of smoking, and physical activity at recruitment (at occupation and during leisure). For leisure, time spent on each of a number of activities (in hours per week) was multiplied by an energy cost coefficient to convert hours per week into kJ^{43} ; all products were then summed to produce a score of daily physical activity at leisure expressed in gender- and centre-specific tertiles.

Anthropometric measurements (height, weight, waist and hip circumferences) were taken in all EPIC centres using similar standardised procedures, except for France, Oxford and Norway. In the latter centres self-reported values were recorded instead, with actual measurements being obtained for a fraction of the participants. Body mass index (BMI) was calculated as the ratio of weight in kilograms divided by the square of height in metres; for participants with self-reported weight and height, these values were used in the respective calculations.

Follow-up

Information on vital status of EPIC participants was obtained by population mortality registries (at the national or regional level), as well as by active follow-up.

As of December 2003, vital status had been ascertained for 100 309 of the 100 442 participants with acceptable reports of dietary energy intakes (i.e. excluding over- and underreporters with intakes within the top and bottom 1% of the ratio of energy intake to estimated energy requirement). A further 15 362 subjects were excluded because at enrolment they had been diagnosed with coronary heart disease, stroke or cancer. In addition, 10 340 subjects had missing information for one or more of the dietary anthropometric or lifestyle variables, or had died within the first year after enrolment. Thus, 74 607 individuals were included in this study.

Statistical analysis

Analyses were carried out with Stata 8.0 (StataCorp). Descriptive presentation relied on cross-tabulations using overall tertiles of the plant-based dietary score. Survival data were modelled through Cox proportional hazards regression models, which assessed the association between the plant-based dietary pattern and overall mortality. The associations were investigated by estimating the adjusted mortality rate ratio by tertile of the plant-based dietary score, as well as in relation to an increment of one standard deviation (1SD) (1.84 units). For analyses

by country, country-specific tertiles of the plant-based dietary score were used. In all models, ethanol intake – which did not contribute to the derivation of the principal component under consideration – was also included as a categorical variable (<10 g day⁻¹, 10–20 g day⁻¹, >20 g day⁻¹) in order to take into account the reported U-shaped association of alcohol with mortality from coronary heart disease^{44,45}.

Adjustment was performed for sex, age, self-reported diabetes mellitus at enrolment, educational achievement, smoking status, physical activity at recruitment (occupation and leisure-time), waist-to-hip ratio (WHR), BMI and total energy intake. The proportionality assumption was checked with the log–log plots. No time-dependent variables were included in the Cox models. Both fixed- and random-effects models were calculated, the latter in order to accommodate between-country variation in the estimated effects.

In all models, subjects who were alive as of the date of last follow-up or had emigrated to another region or country or were lost from follow-up were considered as censored as of the date of last contact, whereas the focal event was death from any cause. Separate proportional hazard models were performed for all 74 607 subjects as well as for participants in each country. Proportional hazard models were stratified by country (for analysis of the total EPIC-Elderly cohort) or by centre (for the country-specific analyses) to account for different methods of follow-up and questionnaires used for data collection. In all analyses a 5% statistical level of significance was used.

Results

The distribution of the 74 607 study participants by country, sex and age at enrolment has been reported elsewhere¹³. There were, in general, more women than men in the cohort and distributions by age varied by country. Calculated mean energy intake ranged from

8157 kJ day⁻¹ in Umeå (Sweden) to 11 188 kJ day⁻¹ in San Sebastian (Spain) for males, and from 5958 to 9450 kJ day⁻¹ for females of the Umeå (Sweden) and Naples (Italy) centres, respectively.

Table 1 shows the distribution of 74 607 participants and 4047 deaths in the EPIC-Elderly cohort, by country and overall tertile of the plant-based diet. The percentages of individuals falling into the different tertiles of this dietary pattern vary markedly across countries. Subjects in Greece, Italy, Spain, and to a lesser extent France, are highly in favour of this dietary pattern since their scores belong generally to the third tertile of the score. In contrast, most people in Sweden and Denmark have low scores, indicating that their diets consist of potatoes, margarine and non-alcoholic beverages rather than vegetables, vegetable oils, legumes, fruit and pasta/rice/other grains. In the UK, Germany and The Netherlands, the highest proportion of individuals belong to the second tertile, i.e. they do not consume many of the above-indicated food groups that contribute to this pattern with either positive or negative scoring coefficients. Regarding number of deaths, there was a negative trend, both overall and within most countries, in the proportion of deaths with increasing tertile of the score.

Table 2 shows the mean intakes of food groups by tertile of the plant-based dietary pattern. The food groups shown in this table are the food groups that were originally used to extract dietary patterns in the EPIC-Elderly cohort²⁷. As expected, there is a clear, positive trend across tertiles of this pattern in the mean intakes of food groups which had positive scoring coefficients (vegetables, legumes, fruit, pasta/rice/other grains and vegetable oils) and a negative trend regarding consumption of potatoes, margarine and non-alcoholic beverages (food groups with negative scoring coefficients). Regarding the consumption of food groups not included in the principal component score, only that of wine is steadily increasing from the first to the third tertile. The consumption of bread, fish & shellfish and eggs does not vary greatly whereas there is an inverse

Table 1 Distribution of 74 607 participants and 4047 deaths of the EPIC-Elderly cohort, by country and tertile of the plant-based dietary score. The EPIC-Elderly Study (European Prospective Investigation into Cancer and Nutrition)

Country	Plant-based dietary pattern											
	Distribution of participants						Distribution of deaths					
	1st tertile		2nd tertile		3rd tertile		1st tertile		2nd tertile		3rd tertile	
<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Denmark	6462	51	5828	46	399	3	524	8.1	349	6.0	21	5.3
France	122	1	3349	35	6059	64	6	4.9	110	3.9	186	3.1
Germany	3221	43	4165	55	169	2	116	3.6	130	3.1	7	4.1
Greece	0	0	16	0	7363	100	0	0	1	6.3	236	3.2
Italy	3	0	135	3	5255	97	0	0	6	4.4	147	2.8
Netherlands	1892	34	3484	62	224	4	121	6.4	155	4.5	8	3.6
Spain	0	0	126	3	3727	97	0	0	7	5.6	129	3.5
Sweden	9121	77	2612	22	121	1	640	7.0	144	5.5	5	4.1
UK	4048	38	5154	48	1552	14	463	11.4	431	8.4	105	6.8
Total	24 869	33.3	24 869	33.3	24 869	33.3	1870	7.5	1333	5.4	844	3.4

Table 2 Mean daily intakes of selected food groups and associated standard deviations (SD) by tertile of the plant-based dietary score. The EPIC-Elderly Study (European Prospective Investigation into Cancer and Nutrition)

Food group	Plant-based dietary score					
	1st tertile		2nd tertile		3rd tertile	
	Mean (g)	SD (g)	Mean (g)	SD (g)	Mean (g)	SD (g)
Vegetables	134.62	80.21	194.46	105.26	307.00	173.16
Legumes	4.05	8.56	7.53	11.83	22.01	26.38
Fruit	159.83	102.03	234.73	139.11	399.39	229.00
Pasta/rice/other grains	20.75	21.30	36.41	31.53	86.65	66.75
Bread	123.18	64.61	120.85	67.11	129.95	79.26
Other cereal	44.80	80.26	25.90	44.90	11.56	26.28
Vegetable oils	1.61	2.68	2.96	3.62	25.09	19.53
Fish & shellfish	37.04	30.63	34.58	29.52	35.98	32.06
Dairy products	416.78	269.21	342.24	222.63	260.45	182.01
Meat & products	109.29	56.32	95.65	54.15	87.74	50.97
Potatoes	149.96	91.88	97.21	57.36	55.17	45.15
Margarine	20.31	22.14	8.60	11.64	2.52	5.70
Butter	3.71	9.74	4.43	8.33	2.30	5.56
Cakes	54.86	52.68	39.84	39.08	27.57	31.75
Sugar & confectionery	50.65	39.70	36.18	27.84	27.65	25.33
Condiments & sauces	24.24	24.74	18.80	17.15	16.48	15.35
Non-alcoholic beverages	1488.51	707.77	1342.19	598.38	551.70	591.48
Wine	32.56	58.67	70.67	110.36	98.31	165.25
Other alcoholic beverages	167.63	325.40	91.47	185.48	31.84	102.18
Eggs	17.69	17.87	16.69	17.06	16.81	16.80
Total energy intake (kJ day ⁻¹)	9070.38	2538.79	8142.20	2303.78	8569.14	2476.25

trend in the consumption of other cereals, meat & products, dairy products, butter, cakes, sugar & confectionery, condiments & sauces and alcoholic beverages (except wine) across tertiles of the plant-based dietary score. With respect to energy intake, subjects in the second tertile seem to have a lower energy intake than subjects who either follow (third tertile) or do not follow (first tertile) the plant-based diet.

Table 3 shows the association of the plant-based diet with overall mortality, after adjustment for potential confounders, overall (using global tertiles) and by country (using country-specific tertiles). There is evidence that an increase in the plant-based dietary score is associated with reduced overall mortality, with a 1SD increment corresponding to a statistically significant 14% reduction in all-cause mortality (random-effects model). Subjects whose scores belong to the second (mean plant-based dietary score -0.5 , SD 0.4) or third (mean plant-based dietary score 2.2 , SD 1.4) tertile of this pattern have a 10% and 11% reduced mortality rate, respectively, compared with those who belong to the first tertile (mean plant-based dietary score -1.7 , SD 0.6). Results in this table indicate that subjects with greater consumption of a diet rich in plant foods and vegetable oils and poor in potatoes, margarine and non-alcoholic beverages have substantially reduced mortality compared with those who follow the opposite pattern of consumption.

There was some evidence of heterogeneity in the apparent effect among countries, the association being stronger in Greece, Spain, Denmark and The Netherlands,

and absent in the UK and Germany. Nevertheless, this heterogeneity is accommodated through the random-effects model. It should be noted that the mortality ratios for the second and third country-specific tertiles of the plant-based dietary score are not comparable between countries since the referent category (first tertile) varies across countries.

Discussion

In the present prospective study of apparently healthy elderly Europeans, we found that an *a posteriori* dietary pattern, predominantly reflecting high intakes of vegetables, vegetable oils, fruit, legumes and pasta/rice/other grains and low intakes of potatoes, margarine and non-alcoholic beverages, may be associated with a longer life expectancy, after adjusting for relevant confounders. The chosen plant-based dietary pattern has been identified as prevailing in a previous descriptive analysis in the EPIC-Elderly cohort²⁷ by means of PCA. The dietary characteristic of this pattern is that it relies on plant foods and vegetable oils for which inverse associations with the risk of disease and/or death have been reported^{42,46}. In addition, increasing plant-based dietary scores were accompanied with a reduction in the intakes of food groups of which high consumption may be considered non-beneficial, such as meat and dairy products^{31,47,48}. In this context, the protective effect of an increasing score in the evaluated principal component is compatible with the

Table 3 Fully adjusted* mortality ratio (95% confidence interval) by category and one standard deviation (1SD) increment of the plant-based dietary score. The EPIC-Elderly Study (European Prospective Investigation into Cancer and Nutrition)

	Plant-based dietary score		
	2nd tertile	3rd tertile	1SD increment (overall)
<i>Over all countries†</i>			
Fixed effects	0.93 (0.86–1.00)	0.92 (0.79–1.06)	0.90 (0.85–0.96)
Random effects	0.90 (0.84–0.98)	0.89 (0.79–0.99)	0.86 (0.77–0.95)
<i>P</i> -value for heterogeneity	0.502	0.124	0.06
<i>Analyses by country‡¶</i>			
Denmark	0.92 (0.78–1.07)	0.85 (0.72–1.01)	0.85 (0.72–1.01)
France	0.89 (0.67–1.17)	0.95 (0.71–1.28)	0.89 (0.68–1.16)
Germany	0.97 (0.71–1.32)	1.08 (0.79–1.48)	1.25 (0.85–1.82)
Greece	0.72 (0.52–0.99)	0.55 (0.36–0.85)	0.67 (0.50–0.89)
Italy	1.01 (0.67–1.52)	0.93 (0.56–1.55)	0.83 (0.61–1.15)
Netherlands	0.81 (0.61–1.07)	0.70 (0.52–0.96)	0.55 (0.37–0.82)
Spain	0.67 (0.42–1.07)	0.71 (0.43–1.18)	0.83 (0.61–1.12)
Sweden	1.04 (0.87–1.24)	0.95 (0.78–1.15)	0.91 (0.76–1.08)
UK	0.88 (0.75–1.02)	1.03 (0.86–1.22)	0.97 (0.86–1.10)

*Adjusted for sex (men, women), age (60–64 years, 65–69 years, 70–74 years, >75 years), diagnosis of diabetes mellitus at baseline (yes, no), waist-to-hip ratio (in ordered quintiles), body mass index (in ordered quintiles), educational achievement (none/primary school, technical school, secondary school, university degree), smoking status (never, former and four categories of current smoker: 1–10 cigarettes day⁻¹, 11–20 cigarettes day⁻¹, 21–30 cigarettes day⁻¹, >31 cigarettes day⁻¹, considered as an ordered variable), physical activity at current work (retired or sedentary occupation, standing occupation, manual work, heavy manual work), physical activity score at leisure time (in centre- and sex-specific tertiles, categorically), ethanol intake (<10 g day⁻¹, 10–20 g day⁻¹, >20 g day⁻¹) and total energy intake (in ordered quintiles).

† Stratified by country.

‡ Country-specific tertiles of the plant-based diet score were used in the country-specific analyses.

¶ Stratified by centre within country.

empirical evidence concerning the foods and the loading factors contributing to this component.

The EPIC-Elderly study comprises data from the largest existing database set up to investigate the role of diet on the longevity of older people. Previous analysis of data from this study has resulted in recommending an *a priori* dietary pattern, the Modified Mediterranean Diet Score (MMDS), as conducive to survival¹³. The effect of MMDS on survival of the EPIC-Elderly cohort was comparable to that of the extracted main principal component. Nevertheless, the overall correlation between MMDS and the plant-based dietary score was only 0.621, indicating that the MMDS and the main principal component extracted from the foods consumed by the study participants capture partially (but not fully) overlapping beneficial aspects of diet.

Recently *a priori* scores have gained popularity in the scientific community^{12,19,49,50}, possibly because they identify a desirable pattern, adherence to which could maximise health benefits. *A posteriori* scores, on the other hand, frequently assessed in conjunction with cluster analysis, point to patterns that are spontaneously developed in particular populations on the basis of inter-correlations among food groups. In a sense *a posteriori* scores trace existing patterns whereas *a priori* scores target nutritional objectives variously defined. In any case both *a priori* and *a posteriori* scores should be studied, and the convergence of the inferences drawn from their relationships to health indicators can circumscribe the space where an optimal diet may be identified.

The *a posteriori* plant-based dietary score was a strong indicator of the participating countries in the population of EPIC elders – all countries in the Mediterranean region belong generally to its third tertile whilst elders in Central and Northern Europe belong to the first and second tertiles of the respective score. Whilst this may raise concern about the effect of the plant-based diet on survival being largely ecological, this cannot be the case when country-specific analyses were performed, since country-specific tertiles were used. Our results also suggest that although intakes of the various food groups within country-specific tertiles may differ substantially between countries, a consumption pattern with stronger resemblance to the plant-based pattern is beneficial, regardless of the exact levels of intake.

Results from our study are in agreement with those from previous studies of the elderly which have identified *a posteriori* dietary patterns and investigated their association with biomarkers, morbidity and mortality. Kumagai and colleagues⁸ found an inverse association between a plant-food pattern score and overall mortality of elderly Japanese. In The Netherlands, Huijbregts and colleagues⁵¹ used cluster analysis and identified a 'healthful' cluster with lower cardiovascular risk factors. Studies in the USA also showed a benefit from healthy eating patterns derived by cluster analyses on bone mineral density⁵² and cardiovascular events⁵³.

Although *a posteriori*-derived dietary patterns have great intuitive appeal in nutritional epidemiology because they can summarise dietary habits of a population, their

use in examining diet–disease relationships remains controversial mainly because the identification of these patterns depends strongly on the statistical methodology that is used⁴². Specifically, PCA aims at maximising the fraction of variance explained by a weighted linear combination of original variables; this, however, does not necessarily increase the ability to discriminate between deceased and not deceased subjects. In addition, *a posteriori* dietary patterns have interpretability problems since their definition is not based on previous evidence or dietary recommendations. Our plant-based dietary pattern was relatively easy to interpret and its elements turned out to be part of ‘healthy’ or ‘prudent’ dietary patterns in several studies among the elderly^{8,28,51–53} as well as among other populations^{22,30,32,52}.

Advantages of this study include its prospective nature, its large size and its reliance on a European population of subjects aged 60 years or older. This study allowed control for several non-dietary confounders such as education and physical activity, as well as anthropometry such as BMI and WHR. However, residual confounding cannot be entirely ruled out because of the observational study design. It has been argued that observed dietary patterns are part of specific lifestyles³⁸. Whilst this may strengthen the usefulness of the *a posteriori* approach to describe diet, it may also mean that it is difficult to separate the effects of the extracted pattern from the effects of other lifestyle characteristics⁵⁴.

In conclusion, our study suggests that greater adherence to a diet, defined *a posteriori* in the overall population of European elders and relying on intakes of plant foods and avoidance of margarine, non-alcoholic beverages and potatoes, is associated with lower all-cause mortality. This dietary pattern is moderately positively correlated with the MMDS that has been constructed *a priori* and was also shown to be beneficial for the survival of the same EPIC-Elderly cohort¹³.

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