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# Papers



## Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study

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### Abstract

**Objective** To examine whether adherence to the modified Mediterranean diet, in which unsaturates were substituted for monounsaturates, is associated with longer life expectancy among elderly Europeans.

**Design** Multicentre, prospective cohort study.

**Setting** Nine European countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden, United Kingdom).

**Participants** 74 607 men and women, aged 60 or more, without coronary heart disease, stroke, or cancer at enrolment and with complete information about dietary intake and potentially confounding variables.

**Main outcome measures** Extent of adherence to a modified Mediterranean diet using a scoring system on a 10 point scale, and death from any cause by time of occurrence, modelled through Cox regression.

**Results** An increase in the modified Mediterranean diet score was associated with lower overall mortality, a two unit increment corresponding to a statistically significant reduction of 8% (95% confidence interval 3% to 12%). No statistically significant evidence of heterogeneity was found among countries in the association of the score with overall mortality even though the association was stronger in Greece and Spain. When dietary exposures were calibrated across countries, the reduction in mortality was 7% (1% to 12%).

**Conclusion** The Mediterranean diet, modified so as to apply across Europe, was associated with increased survival among older people.


### Introduction

The association of diet with several diseases has attracted much attention.[1 2] Recently, interest has concentrated on dietary patterns, because they can accommodate the complex interplay of nutrients within a diet.[3 4] Dietary patterns have often been studied in relation to the mortality of elderly people,[5–9] because of interest in this important age group and because of methodological considerations—for example, the cumulative effects of diet over an extended period and the high frequency of deaths.

The Mediterranean diet has been used in many studies because several of its components have been related to common chronic diseases,[2 10] ecological evidence suggests that such a diet may be beneficial to health,[11] and variants of this diet have improved the prognosis of patients with coronary heart disease.[12 13] The Mediterranean diet is characterised by a high intake of vegetables, legumes, fruits, and cereals (in the past largely unrefined); a moderate to high intake of fish; a low intake of saturated lipids but high intake of unsaturated lipids, particularly olive oil; a low to moderate intake of dairy products, mostly cheese and yogurt; a low intake of meat; and a modest intake of ethanol, mostly as wine.[14] Adherence to a Mediterranean diet was operationalised through a 10 unit dietary score by Trichopoulou et al.[4 15] Several studies have used variants of this score and have reported inverse associations with overall mortality.[4 6 8 9 15] These studies, however, relied on small samples of mostly elderly participants or on the Greek population only.[15]

We calculated a score reflecting the Mediterranean diet.[15] To allow the score to be applied to non-Mediterranean populations, in which intake of monounsaturates from olive oil is minimal, we substituted monounsaturated lipids with the sum of monounsaturated and polyunsaturated lipids in the numerator of the lipid ratio. We investigated the relation of this modified score with overall mortality in a large sample of elderly Europeans participating in EPIC (the European prospective investigation into cancer and nutrition study).[16]

### Participants and methods

EPIC is a multicentre, prospective cohort study investigating the role of biological, dietary, lifestyle, and environmental factors in cancer and other chronic diseases, under the coordination of the International Agency for Research on Cancer.[16] Briefly, between 1992 and 2000, 519 978 apparently healthy volunteers were recruited in 23 centres from 10 European countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the United Kingdom). The criteria for sample selection and the methods are reported in detail elsewhere.[16]

Data for participants aged 60 or over at recruitment were included in the EPIC-elderly study. This study aims to identify dietary patterns among elderly Europeans and to investigate the associations of diet with survival.

### Dietary intakes

Usual dietary intakes were assessed through compatible instruments (food frequency questionnaires and, in some centres, records of intake over seven or 14 days) that had been developed and validated within each centre.[17–19] In addition, a computerised instrument for recall of dietary intake over 24 hours was developed to collect information from a stratified random sample of the aggregate cohort. The aim was to calibrate the measurements across countries.[17]

Nutrient intakes were calculated using food composition tables specific to the country.[20] In the present study, 14 food groups and nutrients were considered: potatoes, vegetables, legumes, fruits, dairy products, cereals, meat and meat products, fish and seafood, eggs, monounsaturated lipids, polyunsaturated lipids, saturated lipids, sugar and confectionery, and non-alcoholic beverages. For each participant, daily intake (grams) of each of the groups and total energy intake (megajoules) were estimated.

### Lifestyle, anthropometric, and medical variables

A precoded questionnaire was used to record data on lifestyle and health,[16] which included educational achievement, history of illnesses, history of smoking, and physical activity. For participants still in work, the physical demand of their job was recorded. For leisure, time spent on each of several activities was multiplied by an energy cost coefficient; the products were then summed to produce a score of daily physical activity.[21] Sex and centre specific thirds of the estimated physical activity score at leisure were used.

Anthropometric measurements were taken in all EPIC centres using similar, standardised procedures, except for France, Oxford (United Kingdom), and Norway. In these centres self reported values were recorded, but actual measurements were obtained for only a fraction of the participants.

### Mediterranean diet scale

A scale indicating the degree of adherence to the traditional Mediterranean diet has been constructed by Trichopoulou et al.[4 15] Values of zero or one were assigned to each of nine indicated components, using as cut-off values the sex specific medians among the participants. People whose consumption of presumed beneficial components (vegetables, legumes, fruits, cereals, fish) was below the median consumption were assigned a value of zero, and a value of one otherwise. People whose consumption of presumed detrimental components (meat and dairy products) was below the median consumption were assigned a value of one, and a value of zero otherwise. A value of one was given to men consuming from 10 g to less than 50 g of ethanol per day and to women consuming from 5 g to 25 g. For lipid intake, the ratio of the sum of monounsaturates and polyunsaturates to saturates was calculated. This modified Mediterranean diet score, as both monounsaturates and polyunsaturates are included in the numerator of the lipid ratio, can take a value from zero (minimal adherence) to nine (maximal adherence).

### Follow-up

Information on the vital status of participants was obtained from mortality registries and by active follow-up. Earliest and latest years of follow-up were 1999 (some participants in the Netherlands) and December 2003 (most centres). Participants were classified as alive at last follow-up, dead, emigrated, refused to participate further, and unknown.

Overall, 100 442 participants of the EPIC cohort were aged 60 years or more at recruitment and had acceptable records of energy intakes (those in the top and bottom 1% of the ratio of energy intake to estimated energy requirement were excluded).[22] Vital status has been ascertained for 100 309 (99.9%) of these participants; however, 15 362 were excluded from the EPIC-elderly study database because coronary heart disease, stroke, cancer, or a combination of these had been diagnosed at enrolment. Of the remaining 84 947 participants, 10 340 had missing information for one or more of the dietary, anthropometric, or lifestyle variables, or had died within the year after enrolment. Thus 74 607 individuals were included in the study.

### Statistical analysis

Analyses were carried out with Stata 7.0 and SAS 8.2. Descriptive presentation relied on cross tabulations. Survival data were modelled through Cox's proportional hazards regression,[23] with length of follow-up as the primary time variable. Adjustment was made for sex, age, self reported diabetes mellitus at enrolment, educational achievement, smoking status, physical activity, waist to hip ratio, body mass index, and total energy intake. In analyses that investigated the relation of the score with mortality, consumption of eggs, potatoes, and sugar and confectionery (which are not part of the score) were also controlled for continuously. Both fixed effects and random effects models were used. Separate proportional hazard models were used for all participants and for participants in each country. Models were stratified by country or by centre (for the country specific analyses).

Dietary exposures across centres were equilibrated using an additive calibration.[18] Briefly, the differences between the sex and centre specific means of the values from the food frequency questionnaire and the means of the 24 hour recall values were calculated and added to the questionnaire values. The calibrated score was computed and its association to mortality was investigated using similar models.

## Results

Table 1 shows the distribution of the participants in the EPIC-elderly study by country, sex, and age at enrolment. Participants from all countries involved in EPIC are included in the EPIC-elderly study database, except for Norway, which has a comparatively young cohort. These eligible participants were followed up for a median of 89 months (range 1 to 138 months) and contributed 541 872 person years. During follow-up, 4047 participants died. Most deaths occurred in the Swedish, Danish, and UK cohorts. These cohorts are larger than the other EPIC cohorts and have a higher mean age.

The patterns for deaths and accumulated person years by non-nutritional variables were generally as expected (table 2). Table 3 shows the cross classifications of broad categories of the score by non-nutritional variables. The score is higher among older people (≥ 70 years) and lower among current smokers.

Table 4 shows the associations of food groups and nutritional variables with overall mortality. Mortality ratios are adjusted for non-nutritional variables (see table 2) as well as for country, sex, and diabetes mellitus. They were not mutually adjusted, however, because underlying strong associations among food groups create technical problems—one of the reasons for opting for a nutrition score. Some of the associations are both plausible and statistically significant, notably the inverse associations of overall mortality with intake of vegetables, fruits, and cereals, ratio of

**Table 1** Distribution of 74 607 participants in EPIC-elderly cohort, by country, sex, and age at enrolment. Values are numbers (percentages)

| | Age of men | | | | Age of women | | | |
|---|---|---|---|---|---|---|---|---|
| **Country** | **60-64** | **65-69** | **≥70*** | **Total** | **60-64** | **65-69** | **≥70*** | **Total** |
| France† | NA | NA | NA | NA | 6070 (19.4) | 3403 (24.5) | 57 (1.2) | 9530 (19.1) |
| Italy | 1235 (7.7) | 195 (3.6) | 4 (0.2) | 1434 (5.8) | 3018 (9.7) | 740 (5.3) | 201 (4.1) | 3959 (7.9) |
| Spain | 1399 (8.8) | 187 (3.4) | 0 | 1586 (6.5) | 1949 (6.2) | 318 (2.3) | 0 | 2267 (4.5) |
| UK | 1457 (9.1) | 1472 (27.1) | 1445 (46.1) | 4374 (17.8) | 2294 (7.3) | 2086 (15.0) | 2000 (40.7) | 6380 (12.7) |
| Netherlands | 149 (0.9) | 24 (0.4) | 0 | 173 (0.7) | 2824 (9.0) | 2492 (17.9) | 111 (2.3) | 5427 (10.8) |
| Greece | 862 (5.4) | 1012 (18.6) | 889 (28.3) | 2763 (11.3) | 1653 (5.3) | 1682 (12.1) | 1281 (26.0) | 4616 (9.2) |
| Germany | 3132 (19.6) | 520 (9.6) | 0 | 3652 (14.9) | 3373 (10.8) | 530 (3.8) | 0 | 3903 (7.8) |
| Sweden | 3070 (19.2) | 1317 (24.2) | 799 (25.4) | 5186 (21.1) | 3746 (12.0) | 1656 (11.9) | 1266 (25.8) | 6668 (13.3) |
| Denmark | 4663 (29.2) | 714 (13.1) | 0 | 5377 (21.9) | 6323 (20.2) | 989 (7.1) | 0 | 7312 (14.6) |
| Total | 15 967 (100.0) | 5441 (100.0) | 3137 (100.0) | 24 545 (100.0) | 31 250 (100.0) | 13 896 (100.0) | 4916 (100.0) | 50 062 (100.0) |

EPIC=European prospective investigation into cancer and nutrition. NA=not applicable.
*In statistical models, ≥70 age group was categorised as 70-74 and ≥75.
†No men were included in French EPIC cohort.

unsaturated to saturated lipids, and the positive association of overall mortality with saturated lipids.

Table 5 shows the adjusted associations of non-calibrated and calibrated scores with overall mortality. The associations were

**Table 2** Number of deaths and accumulated person years among 74 607 participants in EPIC-elderly cohort by age, sex, sociodemographic, anthropometric, and lifestyle variables

| | Men | | | Women | | |
|---|---|---|---|---|---|---|
| **Variable** | **No of deaths** | **Accumulated person years** | **Age adjusted death rates* per 1000 person years** | **No of deaths** | **Accumulated person years** | **Age adjusted death rates* per 1000 person years** |
| Age: | | | | | | |
| 60-64 | 1000 | 112 685 | 8.87 | 1023 | 238 782 | 4.28 |
| 65-69 | 467 | 36 122 | 12.93 | 699 | 105 611 | 6.62 |
| 70-74 | 331 | 15 071 | 21.96 | 286 | 24 947 | 11.46 |
| ≥75 | 141 | 3567 | 39.53 | 100 | 5087 | 19.66 |
| Smoking status: | | | | | | |
| Never | 426 | 53 902 | 7.92 | 1060 | 241 400 | 4.40 |
| Former | 928 | 80 836 | 11.25 | 545 | 83 580 | 6.65 |
| Current | 585 | 32 707 | 17.70 | 503 | 49 447 | 10.19 |
| Educational achievement: | | | | | | |
| None or primary school | 1028 | 75 850 | 13.57 | 983 | 152 914 | 6.41 |
| Technical school | 429 | 38 049 | 11.10 | 486 | 74 912 | 6.54 |
| Secondary school | 156 | 17 009 | 8.37 | 385 | 88 109 | 4.45 |
| University degree | 326 | 36 537 | 8.93 | 254 | 58 492 | 4.33 |
| Body mass index (kg/m$^2$): | | | | | | |
| <25 | 656 | 52 034 | 12.05 | 906 | 171 848 | 5.38 |
| ≥25 | 1283 | 115 411 | 11.12 | 1202 | 202 579 | 5.92 |
| Waist to hip ratio†: | | | | | | |
| <0.90 | 369 | 35 453 | 9.76 | 1841 | 342 676 | 5.41 |
| ≥0.90 | 1570 | 131 992 | 11.94 | 267 | 31 751 | 8.23 |
| Energy intake (MJ): | | | | | | |
| <8.374 | 597 | 50 146 | 11.11 | 1267 | 221 517 | 5.80 |
| ≥8.374 | 1342 | 117 299 | 11.41 | 841 | 152 910 | 5.52 |
| Physical activity at work: | | | | | | |
| Retired or sedentary occupation | 1579 | 124 316 | 12.27 | 1821 | 311 057 | 5.94 |
| Standing occupation | 193 | 22 150 | 8.73 | 190 | 42 526 | 4.50 |
| Manual work | 134 | 16 437 | 8.17 | 84 | 17 662 | 4.57 |
| Heavy manual work | 33 | 4542 | 7.26 | 13 | 3182 | 3.70 |
| Physical activity at leisure‡: | | | | | | |
| First third (low) | 609 | 47 361 | 13.13 | 715 | 107 355 | 6.63 |
| Second third | 593 | 53 892 | 10.89 | 688 | 124 040 | 5.58 |
| Last third (high) | 737 | 66 192 | 10.74 | 705 | 143 032 | 5.02 |
| Alcohol intake (g): | | | | | | |
| Low§ | 1007 | 75 162 | 12.77 | 1273 | 212 362 | 6.12 |
| Moderate | 726 | 77 580 | 9.37 | 650 | 132 620 | 4.89 |
| High¶ | 206 | 14 703 | 13.94 | 185 | 29 445 | 6.24 |
| Total | 1939 | 167 445 | 11.39 | 2108 | 374 427 | 5.67 |

EPIC=European prospective investigation into cancer and nutrition.
*With direct adjustment, using study population (combined men and women) as standard, except for age.
†Values for some participants were imputed from a linear regression model, with weight and height as independent variables and waist to hip ratio as dependent variable.
‡Sex and centre specific thirds of scores for physical activity at leisure time.
§Men <10 g; women <5 g.
¶Men >50 g; women >25 g.

**Table 3** Baseline characteristics by categories of modified Mediterranean diet score among 74 607 participants in EPIC-elderly study and 4047 deaths

| | Men | | | | | | Women | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Diet score 0-3 | | Diet score 4-5 | | Diet score 6-9 | | Diet score 0-3 | | Diet score 4-5 | | Diet score 6-9 | |
| Characteristic | No (%) | No of deaths | No (%) | No of deaths | No (%) | No of deaths | No (%) | No of deaths | No (%) | No of deaths | No (%) | No of deaths |
| Age: | | | | | | | | | | | | |
| 60-64 | 5763 (36.1) | 443 | 6099 (38.2) | 388 | 4105 (25.7) | 169 | 11 580 (37.1) | 460 | 11 784 (37.7) | 361 | 7886 (25.2) | 202 |
| 65-69 | 1624 (29.9) | 183 | 1984 (36.5) | 183 | 1833 (33.7) | 101 | 4760 (34.3) | 312 | 5151 (37.1) | 265 | 3985 (28.7) | 122 |
| 70-74 | 701 (27.9) | 104 | 900 (35.8) | 136 | 912 (36.3) | 91 | 1249 (30.5) | 116 | 1550 (37.8) | 111 | 1303 (31.8) | 59 |
| ≥75 | 97 (15.5) | 32 | 217 (34.8) | 62 | 310 (49.7) | 47 | 166 (20.4) | 29 | 311 (38.2) | 36 | 337 (41.4) | 35 |
| Smoking status: | | | | | | | | | | | | |
| Never | 2516 (32.0) | 176 | 2920 (37.2) | 162 | 2417 (30.8) | 88 | 10 292 (31.4) | 386 | 12 239 (37.3) | 404 | 10 253 (31.3) | 270 |
| Former | 3657 (31.1) | 300 | 4653 (39.6) | 387 | 3449 (29.3) | 241 | 4097 (38.1) | 235 | 4359 (40.5) | 211 | 2305 (21.4) | 99 |
| Current | 2012 (40.8) | 286 | 1627 (33.0) | 220 | 1294 (26.2) | 79 | 3366 (51.7) | 296 | 2198 (33.7) | 58 | 953 (14.6) | 49 |
| Educational achievement: | | | | | | | | | | | | |
| None or primary school | 3828 (33.0) | 416 | 3857 (33.2) | 395 | 3922 (33.8) | 217 | 8073 (36.3) | 463 | 7785 (35.0) | 340 | 6367 (28.7) | 180 |
| Technical or professional school | 2008 (38.6) | 178 | 2177 (41.8) | 174 | 1023 (19.6) | 77 | 4835 (48.4) | 253 | 3835 (38.4) | 175 | 1327 (13.3) | 58 |
| Secondary school | 581 (23.5) | 46 | 944 (38.2) | 69 | 947 (38.3) | 41 | 2839 (26.9) | 130 | 4217 (40.0) | 145 | 3481 (33.0) | 110 |
| University degree | 1768 (33.6) | 122 | 2222 (42.3) | 131 | 1268 (24.1) | 73 | 2008 (27.5) | 71 | 2959 (40.5) | 13 | 2336 (32.0) | 70 |
| Body mass index ($kg/m^2$): | | | | | | | | | | | | |
| <25 | 2561 (34.7) | 265 | 2912 (39.5) | 262 | 1905 (25.8) | 129 | 7496 (35.1) | 402 | 8344 (39.0) | 318 | 5545 (25.9) | 186 |
| ≥25 | 5624 (32.8) | 497 | 6288 (36.6) | 507 | 5255 (30.6) | 279 | 10 259 (35.8) | 515 | 10 452 (36.5) | 455 | 7966 (27.8) | 232 |
| Waist to hip ratio*: | | | | | | | | | | | | |
| <0.90 | 1716 (34.5) | 154 | 1883 (37.9) | 144 | 1374 (27.6) | 71 | 16 203 (35.9) | 811 | 17 076 (37.9) | 666 | 11 840 (26.2) | 364 |
| ≥0.90 | 6469 (33.1) | 608 | 7317 (37.4) | 625 | 5786 (29.6) | 337 | 1552 (31.4) | 106 | 1720 (34.8) | 107 | 1671 (33.8) | 54 |
| Energy intake (MJ): | | | | | | | | | | | | |
| <8.374 | 2790 (36.6) | 238 | 2670 (35.0) | 231 | 2161 (28.4) | 128 | 12 196 (40.2) | 610 | 10 914 (36.0) | 49 | 7206 (23.8) | 208 |
| ≥8.374 | 5395 (31.9) | 524 | 6530 (38.6) | 538 | 4999 (29.5) | 280 | 5559 (28.2) | 307 | 7882 (39.9) | 324 | 6305 (31.9) | 210 |
| Physical activity at work: | | | | | | | | | | | | |
| Retired or sedentary occupation | 6157 (33.4) | 617 | 7051 (38.2) | 623 | 5231 (28.4) | 339 | 14 527 (35.0) | 776 | 15 612 (37.6) | 664 | 11 411 (27.5) | 381 |
| Standing occupation | 1017 (33.0) | 80 | 1111 (36.0) | 72 | 957 (31.0) | 41 | 1913 (33.1) | 79 | 2290 (39.6) | 81 | 1580 (27.3) | 30 |
| Manual work | 795 (33.0) | 52 | 797 (33.0) | 58 | 820 (34.0) | 24 | 1072 (45.7) | 52 | 788 (33.6) | 25 | 484 (20.7) | 7 |
| Heavy manual work | 216 (35.5) | 13 | 241 (39.6) | 16 | 152 (25.0) | 4 | 243 (63.1) | 10 | 106 (27.5) | 3 | 36 (9.4) | 0 |
| Physical activity at leisure†: | | | | | | | | | | | | |
| First third | 2470 (36.0) | 252 | 2493 (36.3) | 236 | 1901 (27.7) | 121 | 5482 (37.9) | 326 | 5266 (36.4) | 257 | 3732 (25.8) | 132 |
| Second third | 2643 (33.4) | 242 | 2973 (37.6) | 231 | 2300 (29.1) | 120 | 5828 (35.0) | 286 | 6289 (37.8) | 247 | 4520 (27.2) | 155 |
| Last third | 3072 (31.5) | 268 | 3734 (38.2) | 302 | 2959 (30.3) | 167 | 6445 (34.0) | 305 | 7241 (38.2) | 269 | 5259 (27.8) | 131 |
| Total | 8185 | 762 | 9200 | 769 | 7160 | 408 | 17 755 | 917 | 18 796 | 773 | 13 511 | 418 |

EPIC=European prospective investigation into cancer and nutrition.
*Values for some participants were imputed from a linear regression model, with weight and height as independent variables and waist to hip ratio as dependent variable.
†Sex and centre specific thirds of scores for physical activity at leisure time.

investigated by comparing mortality of participants with scores of 6 to 9 and 4 to 5 with those scoring 0 to 3, and by estimating the mortality ratio in relation to two unit increments of the score. Evidence shows that an increase in the score is associated with reduced overall mortality, a two unit increment corresponding to a statistically significant 8% reduction in both fixed effects and random effects models. No statistically significant evidence exists of heterogeneity among countries in the effect of score on overall mortality even though the effect is stronger in Greece and Spain and absent in the Netherlands and Germany (table 6). After excluding the Greek data, the reduction of overall mortality with an increase in the score remained statistically significant

**Table 4** Median and mean (standard deviation) daily intake of selected food groups and associated mortality ratio (95% confidence intervals) for chosen increment in EPIC-elderly study

| | Men | | Women | | | |
|---|---|---|---|---|---|---|
| **Food group intake (g/d)** | **Median** | **Mean (SD)** | **Median** | **Mean (SD)** | **Chosen increment*** | **Mortality ratio (95% CI)†** |
| Potatoes | 115.1 | 127.2 (90.9) | 75.4 | 87.8 (67.2) | 78 | 1.01 (0.98 to 1.05) |
| Vegetables | 156.8 | 198.5 (149.3) | 183.8 | 218.6 (141.9) | 145 | 0.94 (0.90 to 0.98) |
| Legumes | 3.3 | 12.2 (23.0) | 5.0 | 10.7 (16.8) | 19 | 1.02 (0.99 to 1.06) |
| Fruits | 176.7 | 232.5 (199.4) | 245.7 | 280.4 (188.4) | 193 | 0.96 (0.92 to 0.99) |
| Dairy products | 285.7 | 336.7 (251.9) | 301.1 | 341.4 (228.1) | 239 | 1.03 (0.99 to 1.07) |
| Cereals | 212.0 | 230.4 (115.4) | 168.4 | 185.1 (92.9) | 104 | 0.94 (0.91 to 0.98) |
| Meat | 111.6 | 119.4 (62.4) | 82.2 | 86.8 (46.7) | 55 | 1.03 (0.99 to 1.07) |
| Fish | 32.2 | 40.7 (35.0) | 26.9 | 33.5 (28.2) | 31 | 1.00 (0.97 to 1.04) |
| Eggs | 13.1 | 17.9 (17.9) | 12.6 | 16.6 (16.9) | 17 | 1.04 (1.01 to 1.07) |
| Confectionery | 33.9 | 43.2 (37.3) | 29.0 | 35.7 (30.3) | 33 | 0.99 (0.96 to 1.03) |
| Non-alcoholic beverages | 1030.5 | 1065.6 (722.7) | 1132.8 | 1157.8 (770.7) | 750 | 1.02 (0.98 to 1.07) |
| Monounsaturated lipids | 32.2 | 34.4 (13.7) | 25.6 | 27.6 (11.1) | 12 | 1.05 (0.99 to 1.11) |
| Saturated lipids‡ | 32.4 | 34.6 (14.2) | 27.0 | 28.5 (11.3) | 13 | 1.07 (1.02 to 1.12) |
| Polyunsaturated lipids | 13.8 | 15.2 (6.8) | 11.5 | 12.6 (5.8) | 6 | 0.99 (0.96 to 1.03) |
| Lipid ratios: | | | | | | |
| Monounsaturated to saturated lipids | 0.9 | 1.1 (0.4) | 0.9 | 1.0 (0.4) | 0.4 | 0.93 (0.88 to 0.99) |
| Unsaturated to saturated lipids | 1.4 | 1.5 (0.5) | 1.4 | 1.5 (0.5) | 0.5 | 0.95 (0.91 to 0.99) |
| Energy intake (MJ) | 9.609 | 9.820 (2.616) | 7.786 | 8.004 (2.162) | 2.492 | 1.01 (0.98 to 1.05) |

EPIC=European prospective investigation into cancer and nutrition.
*Arbitrary chosen number around average of within sex standard deviation.
†Stratified by country and adjusted for sex, age (60-64, 65-69, 70-74, and ≥75, categorically), diabetes mellitus at baseline (yes, no), waist to hip ratio (in ordered fifths), body mass index (in ordered fifths), educational achievement (none or primary school, technical school, secondary school, university degree, categorically), smoking status (never, former, and four categories of current smoker (cigarettes per day): 1-10, 11-20, 21-30, and >30, ordered), physical activity at occupation (retired or sedentary occupation, standing occupation, manual work, and heavy manual work, categorically), physical activity score at leisure (in centre and sex specific thirds, categorically), alcohol intake (low, moderate, high, categorically), and total energy intake (in ordered fifths) except for energy intake. Not mutually adjusted.
‡All sources.

(mortality ratio for a two unit score increase 0.93, 95% confidence interval 0.89 to 0.97). The results of the analysis over all countries changed little after calibration. A two unit increment of the score corresponds to a statistically significant 7% reduction in mortality in the fixed effects and random effects models.

## Discussion

A dietary score that assessed adherence to a modified Mediterranean diet relying on plant foods and unsaturated lipids was associated with a significantly longer life expectancy in apparently healthy elderly people living in nine European countries. This prospective trial, the EPIC-elderly study, relies on the largest available database for the investigation of the role of diet in the longevity of elderly people. The reduction in mortality in relation to a dietary score was more striking than expected from the associations of the score's components with mortality. It has been pointed out that a dietary score may be more discriminatory than each of its components because it captures the extremes of the nutritional exposures of interest and pre-empts nutritional confounding by incorporating possible confounders in the score.[3 15]

We slightly modified the definition of the score by including polyunsaturates in the numerator of the lipid ratio.[4 6 8 9 15] This was necessary because polyunsaturates are the principal unsaturated added lipids in diets in non-Mediterranean countries and have established beneficial effects on coronary heart disease.[12] Moreover, the definition of lipid ratio with monounsaturates alone in the numerator would strongly depend on meat consumption in northern European countries in which a principal source of monounsaturates is meat.

**Table 5** Mortality ratios (95% confidence intervals) for all countries (stratified by country) by category of modified Mediterranean diet score in 74 607 participants in EPIC-elderly study

| **Fully adjusted mortality ratio*** | **No of deaths** | **Mean score (95% CI)** | **Diet score 4-5†** | **P value for heterogeneity** | **Diet score 6-9†** | **P value for heterogeneity** | **2 unit increment** | **P value for heterogeneity** |
|---|---|---|---|---|---|---|---|---|
| Non-calibrated: | | | | | | | | |
| Fixed effects | 4047 | 4.33 (4.31 to 4.34) | 0.91 (0.85 to 0.98) | 0.075 | 0.83 (0.75 to 0.93) | 0.658 | 0.92 (0.88 to 0.96) | 0.328 |
| Random effects | | 4.33 (4.31 to 4.34) | 0.95 (0.85 to 1.07) | | 0.83 (0.75 to 0.93) | | 0.92 (0.88 to 0.97) | |
| Calibrated: | | | | | | | | |
| Fixed effects | 4047 | 4.45 (4.44 to 4.46) | 0.93 (0.87 to 1.01) | 0.742 | 0.91 (0.82 to 1.01) | 0.376 | 0.93 (0.89 to 0.98) | 0.091 |
| Random effects | | 4.45 (4.44 to 4.46) | 0.93 (0.87 to 1.01) | | 0.91 (0.82 to 1.02) | | 0.93 (0.88 to 0.99) | |

EPIC=European prospective investigation into cancer and nutrition.
*Adjusted for sex, age (60-64, 65-69, 70-74, and ≥75, categorically), diabetes mellitus at baseline (yes, no), waist to hip ratio (in ordered fifths), body mass index (in ordered fifths), educational achievement (none or primary school, technical school, secondary school, university degree, categorically), smoking status (never, former, and four categories of current smoker (cigarettes per day): 1-10, 11-20, 21-30, and >30, ordered), physical activity at work (retired or sedentary occupation, standing occupation, manual work, and heavy manual work, categorically), physical activity at leisure (in centre and sex specific thirds, categorically), consumption of potatoes (continuously), consumption of eggs (continuously), consumption of sugar and confectionery (continuously), and total energy intake (in ordered fifths).
†Reference category diet score 0-3.

**Table 6** Mortality ratios† (95% confidence intervals) by country (stratified by centre within country) by category of modified Mediterranean diet score in EPIC-elderly study

| Country | No in cohort/No of deaths | Mean score (95% CI) | Diet score 4-5* | Diet score 6-9* | 2 unit increment |
|---|---|---|---|---|---|
| France | 9530/302 | 5.01 (4.98 to 5.04) | 1.15 (0.84 to 1.57) | 0.93 (0.67 to 1.31) | 0.95 (0.82 to 1.10) |
| Italy | 5393/153 | 5.34 (5.30 to 5.38) | 0.89 (0.53 to 1.48) | 1.02 (0.60 to 1.72) | 0.99 (0.80 to 1.25) |
| Spain | 3853/136 | 5.61 (5.57 to 5.66) | 1.09 (0.51 to 2.32) | 0.92 (0.43 to 1.97) | 0.81 (0.63 to 1.05) |
| United Kingdom | 10 754/999 | 4.73 (4.70 to 4.76) | 0.82 (0.71 to 0.96) | 0.80 (0.68 to 0.96) | 0.92 (0.85 to 1.00) |
| Netherlands | 5600/284 | 2.92 (2.88 to 2.95) | 0.94 (0.71 to 1.23) | 1.29 (0.72 to 2.33) | 1.00 (0.84 to 1.19) |
| Greece | 7379/237 | 6.25 (6.22 to 6.27) | 1.16 (0.47 to 2.88) | 0.71 (0.29 to 1.75) | 0.70 (0.56 to 0.88) |
| Germany | 7555/253 | 3.34 (3.31 to 3.38) | 1.34 (1.03 to 1.73) | 1.09 (0.64 to 1.85) | 1.07 (0.89 to 1.28) |
| Sweden | 11 854/789 | 3.23 (3.20 to 3.25) | 0.92 (0.78 to 1.07) | 0.69 (0.49 to 0.97) | 0.92 (0.83 to 1.02) |
| Denmark | 12 689/894 | 3.75 (3.72 to 3.78) | 0.84 (0.73 to 0.97) | 0.79 (0.62 to 1.01) | 0.90 (0.82 to 0.98) |

EPIC=European prospective investigation into cancer and nutrition.
*Reference category diet score 0-3.
†Adjusted for sex, age (60-64, 65-69, 70-74, and ≥75, categorically), diabetes mellitus at baseline (yes, no), waist to hip ratio (in ordered fifths), body mass index (in ordered fifths), educational achievement (none or primary school, technical school, secondary school, university degree, categorically), smoking status (never, former, and four categories of current smoker (cigarettes per day): 1-10, 11-20, 21-30, and >30, ordered), physical activity at work (retired or sedentary occupation, standing occupation, manual work, and heavy manual work, categorically), physical activity at leisure (in centre and sex specific thirds, categorically), consumption of potatoes (continuously), consumption of eggs (continuously), consumption of sugar and confectionery (continuously), and total energy intake (in ordered fifths).

We focused on a variant of the Mediterranean diet with potentially wide applicability, because of the strong evidence that the traditional Mediterranean diet is beneficial to health. The principal characteristic of the modified Mediterranean diet score is that it relies on plant foods and unsaturated lipids. Reduction of total lipids, however, is not a prerequisite for a healthy diet provided the lipids are not saturated or trans and are not mainly derived from meat.[15 24] The question whether monounsaturates from olive oil, or specific categories of polyunsaturates, are particularly beneficial cannot be answered from this investigation, because the distributions of the intake of the particular lipids are so different in the participating countries as to introduce a strong ecological element into the study. The important point is that a diet that can be operationalised does have a relation with mortality, and that realistically achievable changes in diet—for example, 3 or 4 point increments—are associated with a reduction of total mortality by 11% or 14%, respectively.

The calibration used in this study deals with much of the concern about the comparability of results across different populations. No significant heterogeneity was found among the country specific results with or without calibration for dietary exposures. The results were generally more evident in Greece and Spain, probably because in these countries the modified Mediterranean diet is genuinely a Mediterranean diet (in Italy most of the deaths occurred in northern Italy, where the diet cannot be considered as Mediterranean). It is possible that the association of the score with mortality may vary among populations because of different distribution patterns for food and conceivably non-linear underlying relations of the components of the score with mortality. The parsimonious interpretation of the findings, however, supported by the non-significant heterogeneity in the analyses, is that the modified Mediterranean diet is beneficial to health across populations.

Advantages of this study include its prospective nature, its large size, its reliance on a European population sample, and the calibration of dietary exposures across countries. The study also exploited the availability of information on several non-dietary variables and was able to control for them as potential confounders. Socioeconomic status was controlled for by adjusting for educational achievement, the only factor that is both objectively ascertainable and internationally applicable. Control for physical activity took into account participants still working. Because the study is observational, it is possible for residual confounding from suboptimally measured factors. The association of the score with non-nutritional variables was, however, generally weak (see table 3), reducing the potential for such confounding. Exceptions were the clear associations of the score with sex, age, country, and tobacco consumption, but these variables were validly measured allowing little room for residual confounding.

In conclusion, adherence to a diet relying on plant foods and unsaturated lipids and that resembles the Mediterranean diet, may be particularly appropriate for elderly people, who represent a rapidly increasing group in Europe.

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## What is already known on this topic

Small cohort studies have shown that Mediterranean type diets increase longevity

No international study with assured comparability of dietary information through calibration has been undertaken

## What this study adds

Qualitative aspects of diet predict overall death rate and hence survival

A dietary pattern that resembles that of the Mediterranean is associated with a lower overall death rate

Polyunsaturated lipids are an acceptable substitute when monounsaturated lipids are not readily available

man Cancer Research Centre; German Federal Ministry of Education and Research; Associazione Italiana per la Ricerca contro il Cancro; Compagnia di San Paolo (Italy); Regione Sicilia, Provincia Regionale Sicilia, Comune di Ragusa, AIRE-ONLUS and AVIS-Ragusa (Italy); national cancer registry and comprehensive cancer centres east Amsterdam and Limburg (Netherlands); Dutch Ministry of Public Health, Welfare and Sports; health research fund (FIS) of the Spanish Ministry of Health (Spain); the Spanish Regional governments of Andalucia, Asturias, Basque country, Murcia, and Navarra (Spain); ISCIII Network RCESP (Spain); Swedish Cancer Society; Swedish Scientific Council, Malmö; regional government of Skåne (Sweden); Cancer Research UK; Medical Research Council (United Kingdom). The researchers were financed independently from the funding organisations.

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