

Nutrition and mortality in the elderly over 10 years of follow-up: the Three-City study

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Nutrition and mortality in the elderly over 10 years of follow-up, the 3-city study

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2 **Nutrition and mortality in the elderly over 10 years of follow-up, the 3-city study**

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22 **Short title:** Nutrition and mortality in the elderly23 **Key Words:** mortality, dietary habits, fruits and vegetables, olive oil, regular fish consumption.

24

25 **Abstract**

26 In the last 20 years, many prospective cohort studies assessed the relationships between food
27 consumption and mortality. Result interpretation is mainly hindered by the limited adjustment for
28 confounders and, to a lesser extent, the small sample sizes. The aim of this study was to investigate
29 the association between dietary habits and all-cause mortality in a multicentre prospective cohort
30 that included non-institutionalized community-based elderly individuals (3-City Study). A brief
31 Food Frequency Questionnaire was administered at baseline. Hazard ratios (HRs) and 95%
32 confidence intervals (95% CIs) for all-cause mortality were estimated relative to the consumption
33 frequency of several food groups, using Cox proportional hazards models adjusted for sex, centre,
34 socio-demographic characteristics and health status indicators. Among the 8937 participants (mean
35 age: 74.2 y, 60.7% women), 2016 deaths were recorded during an average follow-up of nine years.
36 The risk of death was significantly lower among subjects with the highest fruit and vegetable
37 consumption (HR=0.90, 95%CI=0.82-0.99, p=0.03) and with regular fish consumption (HR=0.89,
38 95%CI=0.81-0.97, p=0.01). The benefit of olive oil use was found only in women (moderate olive
39 oil use: HR=0.80, 95%CI=0.68-0.94, p=0.007; intensive use: HR=0.72, 95%CI=0.60-0.85,
40 p=0.0002). Conversely, daily meat consumption increased the mortality risk (HR=1.12,
41 95%CI=1.01-1.24, p=0.03). No association was found between risk of death and diet diversity, use
42 of various fats. These findings suggest that fruits/vegetables, olive oil and regular fish consumption
43 have a beneficial effect on the risk of death, independently of the sociodemographic features and the
44 number of medical conditions.

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47 **Nutrition and mortality in the elderly over 10 years of follow-up, the 3-city study**48 **Introduction**

49 The number of elderly people is progressively increasing. Besides medical progress, the life
50 expectancy increase could be linked also to environmental and behavioural factors, some of which
51 can be modified to achieve beneficial effects for health, particularly dietary habits ⁽¹⁾. The
52 importance of diet has led public health policy-makers to develop specific prevention programmes.
53 Moreover, large observational studies have examined the relationship between diet and all-cause
54 mortality in elderly subjects using various food habit classifications that focus, for example, on
55 specific foods or food consumption groups, or dietary patterns that combine multiple features. They
56 showed that some dietary patterns (eating habits, including several food groups), such as the
57 Mediterranean diet ^(2; 3; 4; 5; 6; 7; 8; 9; 10; 11; 12; 13), or “healthy” dietary groups defined by high
58 consumption of fruits and vegetables and fish ^(14; 15; 16; 17), or greater consumption of olive oil with
59 raw vegetables ⁽¹⁸⁾, have a protective effect. Similarly, some studies on consumption frequency
60 found that high intake of fruits and/or vegetables ^(19; 20; 21), fish ^(20; 22) or coffee ^(23; 24; 25) has a
61 beneficial effect on survival. However, few of these studies have considered the most relevant
62 adjustment factors. Indeed, dietary habits and mortality are both influenced by many factors not
63 only at the individual level (age, sex, health status, socio-economic, cultural and genetic factors),
64 but also at the population level (for instance, food availability and accessibility in terms of cost).

65 Another way to assess the effect of diet on health is to consider the concept of food
66 diversity. The advantage of studying the diversity of diets and of used fats compared with
67 monotonous diets is that this allows evaluating the consumption of the most essential micronutrients
68 and of different types of fatty acids (FA). This concept is part of the French National Health and
69 Nutrition Programme ⁽²⁶⁾. Indeed, a varied diet, defined by the daily consumption of at least one unit
70 of each essential food group, has been associated with a lower mortality risk ^(27; 28). However, few
71 studies have focused on this approach.

72 Therefore, our main objective was to examine the associations between dietary habits and
73 mortality in an elderly population. The data collected by the 10-year follow-up study of the large
74 French population-based Three-City (3C) cohort allowed investigating whether some dietary habits
75 (consumption of fruits, vegetables, olive oil, fish and caffeine, diet diversity and diversity of used

76 fats) are associated with reduced all-cause mortality in people aged >65 years, independently of
77 previously identified major confounders.

78

79 **Methods**

80 Data were extracted from the database of the 3C study, a prospective cohort study of
81 vascular risk factors of dementia⁽²⁹⁾. The present study was conducted according to the Declaration
82 of Helsinki guidelines. The 3C study protocol was approved by the Consultative Committee for the
83 Protection of Persons participating in Biomedical Research of the Kremlin-Bicêtre University
84 Hospital (Paris, France). All participants signed a written informed consent.

85 *Participants*

86 A sample of community dwellers aged 65 years and older was selected in 1999–2000 from the
87 electoral rolls of Bordeaux (South-West of France), Montpellier (South-East of France) and Dijon
88 (North-East of France). To be eligible for recruitment into the study⁽²⁹⁾, persons had to be (1) living
89 in these cities or their suburbs and registered on the electoral rolls, (2) aged 65 years and over, and
90 (3) not institutionalized. The cohort size by center was set at 2,500 in Bordeaux, 5,000 in Dijon and
91 2,500 in Montpellier. A personal letter was sent to each potential subject inviting them to participate
92 and including a brief description of the study protocol and an acceptance/refusal form. The
93 spouse/partner was also invited to participate in the study if he/she met eligibility criteria. As
94 electoral rolls are occasionally inaccurate (persons who have moved may still be registered at their
95 previous address), no further correspondence was sent to persons who did not respond to the first
96 letter, but an attempt was made to contact them by telephone. Twenty-four percent of the eligible
97 persons selected on the electoral rolls (n = 34,922) could not be reached; among those contacted, the
98 acceptance rate was 37%. A total of 9,693 persons were included; 7 persons aged less than 65 years were
99 subsequently excluded. Participants who had subsequently refused to participate in the baseline medical
100 interview (n = 392) were excluded from all analyses leading to an original sample of 9294 community
101 dwellers.

102 The participants were administered standardized questionnaires and underwent clinical
103 examinations at baseline and after 2, 4, 8 and 10 years. Baseline data were collected by standardized
104 face-to-face interview. They included information on sociodemographic features, lifestyle
105 (including a brief Food Frequency Questionnaire), current symptoms and complaints, medical

106 history, blood pressure, past and present consumption of tobacco, alcohol and drug use,
107 anthropometric data, neuropsychological testing and blood sampling.

108 For the current study, the following participants were excluded: 132 (1.4%) subjects with missing
109 data for at least one dietary variable, 214 (2.3%) people with a diagnosis of dementia at baseline,
110 and 11 (0.12%) individuals with no available vital statistics data. The analysis was thus carried out
111 using a sample of 8,937 participants with a mean follow-up of 8.85 years.

112 *Baseline dietary assessment*

113 The brief Food Frequency Questionnaire (FFQ) was administered at baseline to assess the
114 participants' dietary habits concerning nine broad food categories: (1) meat and poultry, (2) fish
115 (including seafood), (3) eggs, (4) milk and dairy products, (5) cereals (including bread and
116 starches), (6) raw fruits, (7) raw vegetables, (8) cooked fruits or vegetables, and (9) pulses.
117 Consumption frequency was classified as follows: never, less than once per week, once per week,
118 2–3 times per week, 4–6 times per week and daily. The dietary habits of the whole sample have
119 been described previously⁽³⁰⁾. Participants were also invited to indicate the dietary fats used at least
120 once per week for dressing, cooking, or spreading among those included in the following list:
121 butter, margarine, maize oil, peanut oil, sunflower or grapeseed oil, olive oil, blended oil, duck or
122 goose fat, lard, 'Vegetaline'© (mainly saturated fat), colza oil, walnut oil, soybean oil. Caffeine
123 consumption was calculated by multiplying the number of tea and coffee cups drunk per day by
124 their estimated caffeine content (about 50mg/cup for tea and 100mg/cup for coffee, respectively)
125⁽³¹⁾.

126 Fruits/vegetables, fish, meat and olive oil were the four main food consumption groups of
127 interest that were studied as categorical variables. Their consumption thresholds were based on the
128 French National Nutrition and Health Programme guidelines, when applicable to the available data
129⁽²⁶⁾. Cooked fruits and vegetables, olive oil and caffeine consumption were investigated using
130 previously defined categories^(31; 32; 33). Dietary habits included the intake of fish/seafood (less than
131 twice per week versus more than twice a week), fruits and vegetables (less than one fruit and one
132 vegetable, cooked or raw, per day versus at least one fruit and one vegetable, cooked or raw, per
133 day, and less versus more than 4–6 servings of cooked fruits or vegetables per week), meat (less
134 versus more than once per day), caffeine (<250mg/day, 250–375mg/day, >375mg/day). Three
135 categories of olive oil consumption were defined: 'no use', 'moderate use' (for cooking or dressing
136 alone), or 'intensive use' (for cooking and for dressing)^(32; 34). To calculate the Diet Diversity Score
137 (DDS) (from 0 to 5), one point was assigned for each of the following food categories consumed at

138 least once per day: dairy products, meat, cereals, fruits and vegetables. Low diversity was defined
139 by a DDS <3 and high diversity by a DDS ≥ 4 ⁽³⁵⁾. Fat diversity was evaluated as ≤ 3 different fats
140 versus >3 fats. The threshold of three different fats corresponds to the median value of various fats
141 used by the population included in the 3C cohort.

142 *Baseline covariates*

143 Socio-demographic information recorded at baseline included age, sex, centre, educational
144 level (no or primary/middle/high school/university), occupation (white collar, employee, blue
145 collar, housewife) and monthly income level ($<1,500$, $>1,500$ euros). Health behaviours were
146 assessed based on smoking status (no, 0-10, 10-30 or >30 packets per year), intake of alcoholic
147 beverages (0-24g/day, >24 g/day for women; 0-36g/day, >36 g/day for men).

148 Blood pressure and anthropometric data were measured in standardized conditions. Health-
149 related variables included body mass index (BMI: <27 and ≥ 27 kg/m²) ⁽³⁶⁾, hypertension (defined as
150 a systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, or use of
151 antihypertensive drugs) ⁽³⁷⁾, diabetes (fasting blood glucose ≥ 7.0 mmol/l, or taking an anti-diabetic
152 treatment), hypercholesterolemia (yes/no, self-reported) and the number of drugs (0, 1-4, ≥ 5).
153 History of cardiovascular diseases (yes/no) and other chronic diseases (chronic respiratory disease,
154 cancer, Parkinson's disease or hypothyroidism) were reported. Disability was estimated using the
155 Instrumental Activities of Daily Living scale (IADL; yes (score >0 /no,). Depressive mood was
156 assessed using the Center for Epidemiological Studies-Depression scale (CES-D) and was defined
157 by a score <17 for men and <23 for women. Self-rated health was grouped in three categories (poor,
158 average, fair) and self-assessment of correct diet in two classes (no /yes).

159 Physical activity was assessed differently in the three centres (self-reported or not and with
160 different accuracy levels). Therefore, a common binary variable was considered for the three
161 centres (none or low/regular). Regular physical activity was defined as doing some sport regularly
162 or having at least one hour of leisure or household activity per day ⁽³⁸⁾. Given the important amount
163 of missing data for this variable (1115 missing data for the Bordeaux centre, 11% of the whole
164 sample), it was used only in sensitivity analyses.

165 *Vital status*

166 Mortality was ascertained from the civil registry by systematic request for all subjects not included
167 in follow-up visits. The date of death was defined as the date of event and the date of the last
168 follow-up or phone contact for the 10-year follow-up as the date of censoring. Follow-up included

169 the precise assessment of all causes of death that were coded according to the tenth revision of the
170 International Classification of Diseases (ICD-10)⁽³⁹⁾. Mortality from cardiovascular disease (CVD)
171 (ICD-10: I) and cancer (ICD-10: C), the two leading causes of death in aged populations, were
172 considered for the analyses⁽³⁹⁾.

173 *Statistical Analyses*

174 Survival analysis was carried out using the Kaplan Meier method. Comparisons of baseline
175 characteristics and dietary habits were performed with the log-rank test.

176 The associations between dietary habits, diet diversity and mortality risk were determined by
177 using Cox proportional hazards regression with delayed entry, with age (in years) used as the time
178 axis and left truncation at the age of study entry. The results of the survival analysis were expressed
179 as hazard ratios (HRs) with 95% confidence intervals (CI).

180 In these analyses, the adjustments for covariates were performed in three steps. Univariate
181 analysis was the basic model to test associations between dietary features and mortality (crude
182 model). The second model (model 1) was adjusted for sex and study centre, educational level,
183 occupation and income. Health behaviours and health factors, chosen based on literature data, were
184 then added in the third model (model 2). Interactions between the different dietary habits and
185 covariates included in model 2 were tested and stratified analyses were carried out accordingly.

186 For missing data, multiple imputations were used by generating five copies of the original
187 dataset in which the missing values for the covariates considered in the analysis were replaced by
188 values generated according to the Markov Chain Monte Carlo (MCMC) method and using the
189 PROC MI procedure. Each imputed dataset was analysed as if it were complete to calculate the
190 mean HRs and CI with the PROC MIANALYZE procedure⁽⁴⁰⁾. Imputation were performed for
191 covariates included in analyses: education (missing data 0.17%), income (6.13%), occupation
192 (0.29%), smoking (1.63%), alcohol (1.51%), history of cardiovascular disease (0.08%), , depression
193 (1.28%), diabetes (5.65%), hypertension (0.06%), hypercholesterolemia (1.1%), dependence (
194 0.69%)self-rated health (0.57%), number of chronic diseases (0.09%), self rated diet quality
195 (2.38%).

196

197 Analyses were carried out using the SAS software (version 9.2).

198

199 **Results**

200 The baseline characteristics and dietary habits of the participants (n=8937) according to their
201 vital status (dead/alive) at the end of the 10-year follow-up are reported in Table 1 and Table 2,
202 respectively. Participants who died (n=2016) were significantly older at baseline than those still
203 alive (mean age: 77 vs 73, respectively) and more often men, heavy smoker or alcohol consumers.
204 They also had more often a history of cardiovascular or chronic diseases, more vascular risk factors
205 and poor self-rated health. In these crude comparisons, mortality risk was higher among individuals
206 with low income and blue collar workers. Conversely, survival was not influenced by the education
207 level in this highly educated population. Daily consumption of fruits and vegetables, regular
208 consumption of cooked vegetables/fruits, intensive olive oil use, wide fat diversity and bi-weekly
209 fish consumption were more frequently reported by subjects still alive at the end of the 10-year
210 follow-up. Caffeine consumption and DDS were not associated with survival.

211 Then, the associations between the 10-year mortality risk and dietary habits or diet diversity
212 (at baseline) were assessed after multiple imputations for missing data (Table 3 and Table 4,
213 respectively). In crude analyses, various well-known healthy food habits were significantly
214 associated with better survival: eating at least one fruit and one vegetable (raw or cooked) per day,
215 consumption of at least four cooked fruit/vegetable servings per week, fish at least twice per week,
216 meat less than once per day, greater diet diversity and diversity in fat use.

217 In the partly (only sociodemographic covariates) and fully (sociodemographic and health-
218 related covariates) adjusted models, consuming at least one fruit and vegetable per day and
219 consuming more than four cooked fruit/vegetable servings per week remained significantly
220 associated with a better survival compared with lower levels of consumption (HR=0.90, 95%
221 CI=0.82-0.99, p=0.03 and HR=0.80, 95% CI=0.70-0.90, p=0.0005, respectively, in the fully
222 adjusted models). Fish intake at least twice per week was also significantly associated with better
223 survival (HR=0.89, 95% CI=0.81-0.97, p=0.01), while consuming meat more than once per day had
224 a deleterious effect on survival in the fully adjusted models (HR=1.12, 95% CI=1.01-1.24, p=0.03)
225 (Table 3).

226 For the two indicators of diet diversity (DDS and diversity in fats used), the significant
227 associations observed in crude and partly adjusted analyses were no longer significant after
228 adjustment also for health-related variables (Table 4).

229 As the interaction between sex and consumption of olive oil was significant, analyses were
230 stratified by sex (Supplementary Table 1). The use of olive oil was inversely correlated with the
231 mortality risk after adjustment for all covariates, but only in women (moderate olive oil use:
232 HR=0.80, 95%CI=0.68-0.94, p=0.007; intensive use: HR=0.72, 95%CI=0.60-0.85, p=0.0002).

233 Furthermore, sensitivity analyses were performed on the 5322 individuals with available
234 data on physical activity. In this sub-sample, the consumption of at least 4-6 servings of cooked
235 fruits or vegetables per week was again associated with a lower mortality risk at the end of the 10-
236 year follow-up, independently of physical activity (HR=0.75, 95% CI=0.62-0.90, p=0.002). No
237 association was observed between mortality risk and meat, fish or olive oil consumption
238 (Supplementary Table 2) or diet diversity (Supplementary Table 3).

239 Finally, there was no significant association between dietary habits/diversity and the main
240 causes of death (389 due to CVD and 542 to cancer) after controlling for sex, centre, educational
241 level, income and occupation (data not shown).

242

243 **Discussion**

244 The present study based on the 10-year follow-up of a French cohort of people aged 65 or
245 older suggests that healthy dietary habits, such as daily consumption of fruits and vegetables, eating
246 fish twice per week and regular use of olive oil (this only in women), are linked to better survival,
247 independently of sociodemographic, health-related and lifestyle variables. Overall, higher diet
248 diversity also is significantly associated with lower mortality risk.

249 A major difficulty when assessing food habits concerns the heterogeneity of the collected
250 data. Indeed, each country has its consumption standards, tailored to cultural habits and the local
251 availability of food resources. Moreover, the methods used to collect such data also are not
252 homogeneous and consequently results are difficult to compare and generalize from one country to
253 another. Nevertheless, the various eating habits can be standardized in dietary patterns (such as
254 composite scores or consumption patterns of some preferred foods) or by quantitative
255 measurements of food types. Studies on diet quality or adherence to a particular diet are used to
256 determine the most beneficial approach; however, in the case of composite scores, the proper role of
257 each score component cannot be identified. In the present study where food habits were evaluated
258 with a short FFQ, we examined food groups that have been found to be associated with longer
259 lifespan in previous studies using these different approaches. Our results are in agreement with the
260 French National Nutrition and Health Programme guidelines that include the promotion of daily
261 consumption of fruit and vegetables ⁽²⁶⁾.

262 We observed a significant association between high consumption of fruits and vegetables
263 and survival after adjusting for major confounders. This result is consistent with earlier studies ^{(19;}
264 ^{20; 21)}. In the EPIC study, a better adherence to a plant-based diet was associated with a reduced
265 mortality risk in Southern Europe, but not in the UK nor in Germany, after controlling for all known
266 risk factors ⁽¹⁵⁾. Similarly, the “Olive oil and salad” pattern was associated with longevity in an
267 Italian elderly cohort ⁽¹⁸⁾.

268 Fruits and vegetables, which were not separate entities in our FFQ, are the main source of
269 antioxidants that are the basis of the free radical theory of ageing ⁽⁴¹⁾. According to this theory, a
270 balance between free radicals and antioxidants increases life expectancy. Some authors hypothesize
271 that plant foods promote the activation of immune functions or have protective properties ^(16; 17). A
272 recent literature review highlighted the effect of high concentration of polyphenols, carotenoids,
273 folic acid and vitamin C on mortality ⁽¹³⁾. High consumption of flavonoids, found mainly in fruits,
274 could be associated with reduced mortality risk ⁽⁴²⁾. The beneficial effects of fruits and vegetables

275 could be also explained by their fibre content that modulates LDL cholesterol level, insulin
276 sensitivity and blood pressure ⁽⁴³⁾, all conditions associated with increased mortality risk. This
277 hypothesis is supported by the PREDIMED study that demonstrated a significant association
278 between lower risk of death and baseline higher fibre intake and fruit consumption ⁽⁴⁴⁾.

279 Our results are in agreement with the few studies that investigated fish consumption and risk
280 of death ^(20; 22). A Japanese study found that high consumption of vegetables and fish in subjects
281 older than 75 years is associated with better survival ⁽¹⁷⁾. Most of the published results on the
282 positive association between fish and lower mortality have been carried out in countries with
283 traditional high fish consumption (Japan and Scandinavia). Other studies included fish consumption
284 in the diet scores (e.g., the Mediterranean Diet Score) or in “healthy” diet patterns ^(14; 16; 45) with
285 contrasting results. Hoffman et al. did not find any significant association between these dietary
286 patterns and mortality ⁽⁴⁵⁾. Conversely, Anderson et al ⁽¹⁶⁾ observed a positive link between survival
287 and a healthy dietary pattern (consumption of low-fat dairy products, fruit, whole grains, poultry,
288 fish and vegetables). The protective effect of fish consumption on health has been linked to the anti-
289 inflammatory effects of the essential omega-3 fatty acids ^(13; 22).

290 Olive oil is the main source of fat in the traditional Mediterranean diet. Our study reported a
291 beneficial effect only among women. This finding is in agreement with the findings in an elderly
292 British cohort ⁽⁷⁾ where the Mediterranean style dietary pattern was associated with reduced
293 mortality only in women. This sex-specific effect could be explained by the women’s longer life
294 expectancy. Many studies support the beneficial effect of the Mediterranean diet on mortality ^{(2; 3; 4;}
295 ^{5; 6; 7; 8; 12; 46)}. Masala et al. observed that the ‘Olive Oil & Salad’ dietary pattern (high consumption
296 of olive oil) is inversely associated with all-cause mortality in the elderly ⁽¹⁸⁾. The PREDIMED
297 study found that higher consumption of olive oil was associated with a specific reduction in the
298 cardiovascular mortality risk in an elderly Mediterranean population ⁽⁴⁷⁾. The beneficial effect of
299 olive oil could be explained by its high concentration in **mono**-unsaturated fatty acids and phenolic
300 compounds that improves endothelium function and reduces oxidative stress, thereby promoting
301 healthy aging and longevity ⁽¹³⁾.

302 On the other hand, we found that daily consumption of meat, as a broad category, had a
303 negative effect on survival. Most previous studies showing a deleterious effect of meat consumption
304 on lifespan ^(17; 45) also found that high meat consumption patterns were often associated with
305 unhealthy dietary habits, such as high levels of fat consumption. However, in other studies, red
306 meat consumption was not associated with increased mortality risk after correction for confounding

307 factors ⁽¹⁶⁾. Comparisons with previous findings are limited by the different definitions of meat
308 consumption groups. In some works red meat with high content of fatty acids was considered on its
309 own, whereas poultry or lean meat was not included in the analysis. Anderson et al. suggested that
310 high consumption of animal foods could increase the mortality risk, only if meat replaces protective
311 plant foods in the diet ⁽¹⁶⁾. The link between red meat and dietary fat could affect the lipid and
312 lipoprotein profile and thus the cardiovascular disease risk ⁽⁴⁵⁾.

313 The association between diet diversity and mortality did not remain significant after
314 adjustment for confounders, unlike in other studies ^(27; 28). However, comparisons are difficult
315 because these studies used different methods of food collections and different food groups.

316 The data from our study should be interpreted in the light of the following limitations. First,
317 the 3C sample is not representative of the French population. Indeed, compared with the whole
318 French population, this cohort included more urban dwellers, in better health and living together ⁽³⁰⁾.
319 Therefore, extrapolation of our results to the general population of elderly should be made with
320 caution. The FFQ did not record quantitative data (portions, grams), but only frequencies of
321 consumption. Low frequency consumption does not necessarily mean lower energy intake, but
322 simply suggests a lack of diversity in eating habits. Moreover, the FFQ did not allow calculating the
323 total energy intake, as recommended to better control for confounding factors and to reduce
324 extraneous variation ⁽⁴⁸⁾. In a previous article exclusively on the population from the Bordeaux
325 centre (N=1660) of the 3C study, daily energy intake was calculated in a sub-sample by using the
326 24-hour dietary recall technique. In this sub-sample, daily energy intake was not affected by the
327 frequency of consumption of fish, or of fruits and vegetable (frequent vs less frequent), or by the
328 use of omega-3 or omega-6 rich oils (regular vs non-regular) ⁽⁴⁹⁾. Moreover, the baseline energy
329 intake among the Bordeaux sub-sample was not significantly different between those who were
330 dead (N=375) or still alive (N=1422) at the end of the 10-year follow-up (data not shown). This
331 suggests that the energy intake is not a major confounder in the present analyses. According to the
332 literature, mainly studies with the most accurate data on food consumption (in daily amount) ^{(3; 7; 15;}
333 ^{16; 18; 20; 21; 22; 43; 46)} found significant associations between dietary patterns and mortality. Our data
334 did not allow this level of detail. However, our results confirm the benefit of several food categories
335 on survival. Moreover, in our study, the assessment of dietary intake covered only broad food
336 groups. This limitation is important for the interpretation of the association between meat and
337 survival, because the meat group included both white meat (lean, healthy) and red meat (fat,
338 deleterious). The limitations the food questionnaire (FFQ) used in this study (few items, absence of
339 validation, only baseline administration) could have led to non-differential misclassification bias.

340 However, previous studies using this questionnaire reported innovative results that are in agreement
341 with the literature or have been successively confirmed by other independent analyses ^(30; 34; 49; 50).
342 Finally in our sensitivity analysis including physical activity, only the association with fruits and
343 vegetables remains significant. But the variable physical activity did not rely on a detailed physical
344 activities questionnaire and these analyzes are conducted in a limited sample (n=5273) reducing
345 statistical power. The interpretation of this result is therefore limited.

346 Strengths of this study include the prospective population-based study design, with a large
347 sample size, the completeness of the collected dietary data (data provided by more than 99% of
348 subjects, possibly due to the use of a simple and short questionnaire) and the low number of drop-
349 outs (0.1%). Many variables were investigated as potential confounders, such as socio-demographic
350 factors, health behaviours, BMI, drug use, self-rated health status and diet. The FFQ used in the 3C
351 study has already allowed highlighting many interesting associations between diet habits and
352 diseases ^(31; 33; 34; 49; 50; 51; 52; 53). Chrysohoou et al. insisted on the importance of taking into account
353 socio-economic factors when considering the relationship between food habits and life expectancy,
354 as healthy habits are associated with financial and educational status ⁽¹³⁾. In our study, we
355 considered simultaneously education, occupation and income.

356 In conclusion, this study on the associations between dietary habits and mortality in a large
357 population-based elderly cohort brings reliable evidence that could be used for developing
358 nutritional programmes. Specifically, a diet with a daily intake of fruits and vegetables, regular
359 consumption of fish, as recommended by the French Nutrition and Health Programme ⁽²⁶⁾, and
360 regular use of olive oil promotes longevity among an elderly community-living population. Diet
361 quality is an important component of a healthy lifestyle that has beneficial effects on survival ⁽¹⁾.
362 Additional studies should investigate the association between survival, diet and healthy behaviours,
363 but this does not limit the importance of this simple public health message.

364

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378

379 Authorship

380 F Letois: formulation of the research question, statistical analysis and interpretation of the data;
381 drafting the manuscript.

382 T Mura; drafting/revising the manuscript

383 J Scali drafting/revising the manuscript

384 LA Gutierrez: statistical analysis, revising the manuscript

385 C Féart: drafting/revising the manuscript

386 C. Berr: data acquisition; analysis and interpretation of the data; study design; study supervision;
387 drafting/revising the manuscript.

388

389 **Table 1 - Baseline socio-demographic and medical characteristics of the 3C cohort (N=8937)**
 390 **subdivided according to their vital status (dead or alive) at the end of the 10-year follow-up**
 391

	Alive N=6921 (77%)		Dead N=2016 (23%)	
	N (%)	mean (sd)	N (%)	mean (sd)
Age (years)		73 (4.9)		77 (6.1)
Women	4507 (65%)		941 (47%)	
Education				
No or primary	1747 (25%)		531(26%)	
Secondary	2474 (36%)		714 (36%)	
High school	1403 (20%)		389 (19%)	
University	1287 (19%)		377 (19%)	
Monthly income higher than 1500€	4148 (64%)		1153 (62%)	
Occupation				
White collar	2790 (40%)		815 (41%)	
Employee	2029 (29%)		535 (27%)	
Blue collar	1395 (20%)		496 (25%)	
Housewife	687 (10%)		164 (8%)	
Smoking				
Never	4436 (65%)		1047 (53%)	
0-10 packets/year	902 (13%)		274 (14%)	
10-29 packets/year	898 (13%)		308 (15%)	
> 30 packets/year	586 (9%)		340 (17%)	

Alcohol ($\geq 24\text{g/d}$ for women; $\geq 36\text{g/d}$ for men)	643 (9%)	237 (12%)
History of cardiovascular diseases ^a	1752 (25%)	878 (44%)
BMI $< 27\text{ kg/m}^2$	4668 (68%)	1280 (65%)
Depression	879 (13%)	333 (17%)
Diabetes	568 (9%)	287 (15%)
Hypertension	5235 (76%)	1684 (84%)
Hypercholesterolemia	2405 (35%)	553 (28%)
Dependence ^b	431 (6%)	398 (20%)
Low/regular physical activity	2119 (34%)	373 (22%)
Self-rated health		
Poor	276 (4%)	182 (9%)
Fair	2337 (34%)	828 (41%)
Good	4275 (62%)	988 (49%)
Number of drugs		
None	651 (9%)	103 (5%)
1-4	3433 (50%)	752 (37%)
≥ 5	2837 (41%)	1161 (58%)
Number of chronic diseases ^c		
None	5850 (85%)	1567 (78%)
1	975 (14%)	396 (20%)
2 or more	91(1%)	50 (2%)

392 ^a Coronary heart disease was reported by 671 (9.7%) of subjects alive and 398 (20%) of subjects dead at the end
393 of the follow-up.

394 ^b Assessed with the IADL scale (at least 1 impairment).

395 ^c Chronic diseases included mainly respiratory diseases and dyspnoea (n=477, 5.8% of people still alive; n=285,
396 14.1% of subjects dead at the end of the follow-up), Parkinson's disease (n=46, 0.66% of alive; n=59, 2.9% of
397 dead subjects), and hyperthyroidism (n=6, 18.9% of alive; n=143, 7.1% of dead).

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401 **Table 2 - Baseline food habits of the 3C cohort (N=8937) subdivided according to their vital**
 402 **status (alive or dead) at the end of the 10-year follow-up**

	Alive N=6921 (77%)	Dead N=2016 (23%)
	N (%)	N (%)
At least 1 fruit and 1 vegetable, cooked or raw /day	2782 (40%)	663 (33%)
Cooked fruits/vegetables: \geq 4-6 servings/week	6162 (89%)	1715 (85%)
Meat: \geq 1 serving/day	1689 (24%)	558 (28%)
Fish: \geq 2 servings/week	3569 (52%)	923 (46%)
Diversity diet score \geq 4	4986 (72%)	1371 (68%)
Olive oil use		
None	1543 (23%)	644 (32%)
Moderate	2768 (40%)	755 (37%)
Intensive	2610 (38%)	617 (31%)
Different fats $>$ 3	1523 (22%)	345 (17%)
Caffeine (mg/day)		
<250	4781 (69%)	1489 (74%)
250-375	1441 (21%)	370 (18%)
>375	699 (10%)	157 (8%)
Self- rated diet quality		
Bad	589 (9%)	171 (9%)
Good	6174 (91%)	1790 (91%)

403 **Table 3 - Association between 10-year overall mortality and dietary habits in the 3C elderly cohort (N=8937): crude and adjusted hazard**
 404 **ratios (HR) and 95% CI**

	N	Crude	(95% CI)	p	Model 1 ^a	(95% CI)	p	Model 2 ^b	(95% CI)	p
At least 1 fruit and 1 vegetable, cooked or raw/day	8937	0.82	[0.75-0.90]	***	0.84	[0.77-0.93]	***	0.90	[0.82-0.99]	*
Cooked fruits or vegetables: ≥4-6/ week	8937	0.73	[0.65-0.83]	***	0.78	[0.69-0.89]	***	0.80	[0.70-0.90]	***
Meat: ≥1 serving/day	8937	1.22	[1.11-1.34]	***	1.16	[1.05-1.28]	**	1.12	[1.01-1.24]	*
Fish: ≥2 servings/week	8937	0.83	[0.76-0.91]	***	0.87	[0.80-0.96]	**	0.89	[0.81-0.97]	**

405 ^aCox proportional model adjusted for sex, centre, education (no or primary/secondary/ high school/university), income (<1500 or >1500 euros/month),
 406 occupation (white collar/employee/blue collar/housewife)

407 ^bCox proportional model adjusted for sex, centre, education, income, occupation and also smoking, alcohol consumption, history of cardiovascular
 408 diseases, BMI, depression, diabetes, hypertension, hypercholesterolemia, dependence (IADL scale), self-rated health, self-rated diet quality, number of
 409 drugs, number of chronic diseases.

410 *P<0.05; **P<0.01; ***P<0.001

411

412 **Table 4 - Association between 10-year overall mortality and diet diversity in the 3C elderly cohort (N=8937): crude and adjusted hazard ratios**
 413 **(HR) and 95% CI**

Diet Diversity	N	Crude	(95% CI)	p	Model 1 ^a	(95% CI)	p	Model 2 ^b	(95% CI)	p
Diversity diet score 4-5 vs 0-3	8937	0.89	[0.81-0.98]	*	0.90	[0.82-0.99]	*	0.94	[0.85-1.04]	ns
Various fats >3 vs ≤3	8937	0.84	[0.75-0.95]	**	0.86	[0.76-0.97]	*	0.90	[0.80-1.01]	ns

414 ^aCox proportional model adjusted for sex, centre, education (no or primary/secondary/ high school/university), income (<1500 or >1500
 415 euros/monthly), occupation (white collar/employee/blue collar/housewife)

416 ^bCox proportional model adjusted for sex, centre, education, income, occupation and also smoking, alcohol consumption, history of cardiovascular
 417 diseases, BMI, depression, diabetes, hypertension, hypercholesterolemia, dependence (IADL scale), self-rated health, self-rated diet quality, number of
 418 drugs, number of chronic diseases

419 *P<0.05; **P<0.01; ***P<0.001; ns=not significant

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Supplementary Table 1 - Association between 10-year overall mortality and olive oil use stratified on sex in the elderly 3C Study cohort (8937): crude and adjusted hazard ratios (HR) and 95% CI

Olive oil use	N	Crude	(95% CI)	p	Model 1 ^a	(95% CI)	p	Model 2 ^b	(95% CI)	p
<i>All</i>	8937									
Moderate / None		0.79	[0.71-0.88]	***	0.84	[0.76-0.94]	**	0.89	[0.80-0.99]	*
Intensive / None		0.76	[0.68-0.84]	***	0.80	[0.71-0.90]	***	0.83	[0.74-0.63]	**
<i>Women</i>	5448									
Moderate / None		0.75	[0.64-0.87]	***	0.77	[0.64-0.90]	***	0.80	[0.68-0.94]	**
Intensive / None		0.67	[0.57-0.79]	***	0.69	[0.58-0.81]	***	0.72	[0.60-0.85]	***
<i>Men</i>	3489									
Moderate / None		0.87	[0.75-1.01]	ns	0.90	[0.78-1.05]	ns	0.97	[0.83-1.13]	ns
Intensive / None		0.87	[0.75-1.01]	ns	0.91	[0.78-1.06]	ns	0.94	[0.80-1.10]	ns

^a Cox proportional model adjusted for sex, centre, education (no or primary/middle/ high school/university), income (<1500, >1500 euros/month), occupation (white collar/employee/blue collar/housewife)

^b Cox proportional model adjusted for sex, centre, education, income, occupation, smoking, alcohol consumption, history of cardiovascular diseases, BMI, depression, diabetes, hypertension, hypercholesterolemia, dependence (IADL), self-rated health, self-rated diet quality, number of drugs, number of chronic diseases.

*P<0.05; **P<0.01; ***P<0.001; ns=not significant

Supplementary Table 2 - Association between 10-year overall mortality (event N=1033) and dietary habits in the subgroup of the elderly cohort of the 3C Study with data on physical activity (only Dijon and Montpellier; N=5273): crude and adjusted hazard ratios (HR) and 95% CI

Dietary habits	N	Crude	(95% CI)	p	Model 1 ^a	(95% CI)	p	Model 2 ^b	(95% CI)	p
At least 1 fruit and 1 vegetable cooked or raw/day	5273	0.83	[0.73-0.94]	**	0.85	[0.74-0.96]	*	0.90	[0.79-1.03]	ns
Cooked fruits or vegetables: \geq 4-6 servings/week	5273	0.71	[0.59-0.85]	***	0.76	[0.63-0.91]	**	0.75	[0.62-0.90]	**
Meat: \geq 1 serving/day	5273	1.10	[0.96-1.27]	ns	1.03	[0.89-1.19]	ns	1.01	[0.87-1.16]	ns
Fish: \geq 2 servings/week	5273	0.85	[0.75-0.96]	**	0.88	[0.78-1.00]	*	0.92	[0.81-1.04]	ns
Olive oil use	5273									
Moderate / None§		0.85	[0.72-0.99]	*	0.89	[0.76-1.04]	ns	0.97	[0.83-1.15]	ns
Intensive / None§		0.81	[0.69-0.95]	**	0.85	[0.72-1.00]	*	0.90	[0.76-1.06]	ns

^a Cox proportional model adjusted for sex, centre, education (no or primary/middle/high school/university), monthly income (<1500, >1500 euros), occupation (white collar/employee/blue collar/housewife)

^b Cox proportional model adjusted for sex, centre, education, income, occupation, smoking, alcohol consumption, history of cardiovascular diseases, BMI, depression, diabetes, [hypertension](#), [hypercholesterolemia](#), dependence, self-rated health, self-rated diet quality, number of medication, number of chronic diseases and [physical activity](#)

§reference *P<0.05; **P<0.01; ***P<0.001; ns=not significant

Supplementary Table 3 - Association between 10-year overall mortality (event N=1033) and diet diversity in the subgroup of the elderly cohort of the 3C Study with data on physical activity (only Dijon and Montpellier; N=5273): crude and multivariate adjusted of hazard ratios (HR) and 95%

	N	Crude	(95% CI)	p	Model 1 ^a	(95% CI)	p	Model 2 ^b	(95% CI)	p
Diversity diet score 4-5 / 0-3	5273	0.90	[0.79-1.02]	ns	0.89	[0.78-1.02]	ns	0.92	[0.80-1.05]	ns
Various fats > 3/≤ 3	5273	0.86	[0.74-1.01]	ns	0.88	[0.75-1.02]	ns	0.90	[0.77-1.05]	ns

^a Cox proportional model adjusted for sex, centre, education (no or primary/middle/high school/university), monthly income (<1500, >1500 euros), occupation (white collar/employee/blue collar/housewife)

^b Cox proportional model adjusted for sex, centre, education, income, occupation, smoking, alcohol consumption, history of cardiovascular diseases, BMI, depression, diabetes, hypertension, hypercholesterolemia, dependence, self-rated health, self-rated diet quality, number of medication, number of chronic diseases and physical activity

*P<0.05; **P<0.01; ***P<0.001; ns=not significant