

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

Flavie Letois, Thibault Mura, Jacqueline Scali, Laure-Anne Gutierrez, Catherine Feart, Claudine Berr

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

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4	Flavie Letois ^{ab} , Thibault Mura ^{a,c,d} , Jacqueline Scali ^{c,d} , Laure-Anne Gutierrez ^{a,c,d} , Catherine
5	Féart ^{e,f} , Claudine Berr ^{a,c,d,}
6	
7	^a CHRU Montpellier, F-34000 France
8	^b INSERM, CIC 1411, F-34000 Montpellier, France
9	^c INSERM U1061, La Colombière Hospital, F-34093 Montpellier, France.
10	^d Montpellier University, F-34090 Montpellier, France
11	^e INSERM, ISPED, Centre INSERM U1219-Bordeaux Population Health, F-33000 Bordeaux,
12	France.
13	^f Univ. Bordeaux, F- 33000 Bordeaux, France
14	
15	
16	Corresponding author
17	Dr Claudine BERR,
18	Inserm U1061, Hôpital La Colombière, F-34093 Montpellier Cedex 5, France.
19	Phone: 33 (0)4 99 61 45 66; Fax: 33 (0)4 99 61 45 79.
20	@address: claudine.berr@inserm.fr
21	
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24	

Abstract

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

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

Introduction

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

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

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

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

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Methods

- Data were extracted from the database of the 3C study, a prospective cohort study of vascular risk factors of dementia ⁽²⁹⁾. The present study was conducted according to the Declaration of Helsinki guidelines. The 3C study protocol was approved by the Consultative Committee for the Protection of Persons participating in Biomedical Research of the Kremlin-Bicêtre University Hospital (Paris, France). All participants signed a written informed consent.
- 85 *Participants*
- A sample of community dwellers aged 65 years and older was selected in 1999-2000 from the 86 electoral rolls of Bordeaux (South-West of France), Montpellier (South-East of France) and Dijon 87 (North-East of France). To be eligible for recruitment into the study (29), persons had to be (1) living 88 in these cities or their suburbs and registered on the electoral rolls, (2) aged 65 years and over, and 89 90 (3) not institutionalized. The cohort size by center was set at 2,500 in Bordeaux, 5,000 in Dijon and 2,500 in Montpellier. A personal letter was sent to each potential subject inviting them to participate 91 and including a brief description of the study protocol and an acceptance/refusal form. The 92 spouse/partner was also invited to participate in the study if he/she met eligibility criteria. As 93 electoral rolls are occasionally inaccurate (persons who have moved may still be registered at their 94 95 previous address), no further correspondence was sent to persons who did not respond to the first letter, but an attempt was made to contact them by telephone. Twenty-four percent of the eligible 96 persons selected on the electoral rolls (n = 34,922) could not be reached; among those contacted, the 97 98 acceptance rate was 37%. A total of 9,693 persons were included; 7 persons aged less than 65 years were subsequently excluded. Participants who had subsequently refused to participate in the baseline medical 99 interview (n = 392) were excluded from all analyses leading to an original sample of 9294 community 100 101 dwellers.
 - The participants were administered standardized questionnaires and underwent clinical examinations at baseline and after 2, 4, 8 and 10 years. Baseline data were collected by standardized face-to-face interview. They included information on sociodemographic features, lifestyle (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,
- anthropometric data, neuropsychological testing and blood sampling.
- For the current study, the following participants were excluded: 132 (1.4%) subjects with missing
- data for at least one dietary variable, 214 (2.3%) people with a diagnosis of dementia at baseline,
- and 11 (0.12%) individuals with no available vital statistics data. The analysis was thus carried out
- 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
- participants' dietary habits concerning nine broad food categories: (1) meat and poultry, (2) fish
- (including seafood), (3) eggs, (4) milk and dairy products, (5) cereals (including bread and
- 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,
- 2–3 times per week, 4–6 times per week and daily. The dietary habits of the whole sample have
- been described previously (30). Participants were also invited to indicate the dietary fats used at least
- once per week for dressing, cooking, or spreading among those included in the following list:
- butter, margarine, maize oil, peanut oil, sunflower or grapeseed oil, olive oil, blended oil, duck or
- goose fat, lard, 'Vegetaline' (mainly saturated fat), colza oil, walnut oil, soybean oil. Caffeine
- consumption was calculated by multiplying the number of tea and coffee cups drunk per day by
- their estimated caffeine content (about 50mg/cup for tea and 100mg/cup for coffee, respectively)
- **125** (31).

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

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

Baseline covariates

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

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

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

Vital status

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

- the precise assessment of all causes of death that were coded according to the tenth revision of the International Classification of Diseases (ICD-10)⁽³⁹⁾. Mortality from cardiovascular disease (CVD) (ICD-10: I) and cancer (ICD-10: C), the two leading causes of death in aged populations, were considered for the analyses ⁽³⁹⁾.
- Statistical Analyses
- Survival analysis was carried out using the Kaplan Meier method. Comparisons of baseline characteristics and dietary habits were performed with the log-rank test.
- The associations between dietary habits, diet diversity and mortality risk were determined by using Cox proportional hazards regression with delayed entry, with age (in years) used as the time axis and left truncation at the age of study entry. The results of the survival analysis were expressed as hazard ratios (HRs) with 95% confidence intervals (CI).

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

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

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

Results

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

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

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

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

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As the interaction between sex and consumption of olive oil was significant, analyses were
stratified by sex (Supplementary Table 1). The use of olive oil was inversely correlated with the
mortality risk after adjustment for all covariates, but only in women (moderate olive 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, p=0.0002).

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

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

Discussion

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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- 379 Authorship
- F Letois: formulation of the research question, statistical analysis and interpretation of the data;
- 381 drafting the manuscript.
- T Mura; drafting/revising the manuscript
- 383 J Scali drafting/revising the manuscript
- 384 LA Gutierrez: statistical analysis, revising the manuscript
- 385 C Feart: drafting/revising the manuscript
- 386 C. Berr: data acquisition; analysis and interpretation of the data; study design; study supervision;
- 387 drafting/revising the manuscript.

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

	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%	6)	531(26%	b)
Secondary	2474 (36%	(6)	714 (36%	%)
High school	1403 (20%	(6)	389 (19%	%)
University	1287 (19%	(6)	377 (19%	%)
Monthly income higher than 1500€	4148 (64%	(6)	1153 (62	2%)
Occupation				
White collar	2790 (40%	6)	815 (41%	%)
Employee	2029 (29%	(6)	535 (27%	%)
Blue collar	1395 (20%	(6)	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 24g/d for women; \geq 36g/d for men)	643 (9%)	237 (12%)
History of cardiovascular diseases ^a	1752 (25%)	878 (44%)
BMI $<$ 27 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%)

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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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Table 2 - Baseline food habits of the 3C cohort (N=8937) subdivided according to their vital 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: ≥4-6 servings/week	6162 (89%)	1715 (85%)
Meat: ≥1 serving/day	1689 (24%)	558 (28%)
Fish: ≥2 servings/week	3569 (52%)	923 (46%)
Diversity diet score ≥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%)

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Table 3 - Association between 10-year overall mortality and dietary habits in the 3C elderly cohort (N=8937): crude and adjusted hazard 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	8937	0.82	[0.75-0.90]	***	0.84	[0.77-0.93]	***	0.90	[0.82-0.99]	*
or raw/day										
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]	**

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

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

^{410 *}P<0.05; **P<0.01; ***P<0.001

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

(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

^aCox proportional model adjusted for sex, centre, education (no or primary/secondary/ high school/university), income (<1500 or >1500

euros/monthly), occupation (white collar/employee/blue collar/housewife)

bCox proportional model adjusted for sex, centre, education, income, occupation and also smoking, alcohol consumption, history of cardiovascular

diseases, BMI, depression, diabetes, hypertension, hypercholesterolemia, dependence (IADL scale), self-rated health, self-rated diet quality, number of

418 drugs, number of chronic diseases

*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
All	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]	**
Women	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]	***
Men	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	5273	0.83	[0.73-0.94]	**	0.85	[0.74-0.96]	*	0.90	[0.79-1.03]	ns
cooked or raw/day										
Cooked fruits or vegetables: $\geq 4-6$	5273	0.71	[0.59-0.85]	***	0.76	[0.63-0.91]	**	0.75	[0.62-0.90]	**
servings/week										
Meat: ≥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: ≥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 <u>physical activity</u>

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 $> 3 \le 3$	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