# Association between nutritional profiles of foods underlying Nutri-Score front-of-pack labels and mortality: EPIC cohort study in 10 European countries

# Association between the nutritional profile of foods underlying the front-of-pack label "Nutri-Score" and mortality: EPIC cohort study in 10 European countries

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**ABSTRACT**

**Objectives:** To study if the FSAm-NPS (Food Standards Agency nutrient profiling system) associates with mortality in the EPIC study. The FSAm-NPS grades the nutritional quality of food products and is currently used in several European countries to derive the Nutri-Score label, a tool to guide consumers towards healthier food choices.

**Design:** population-based cohort study

**Setting and participants:** 501,594 adults from the EPIC cohort (10 European countries, median follow-up: 17.2y) were included in the analyses. Usual food intakes were assessed with country-specific diet assessment methods. The FSAm-NPS was calculated for each food item using its 100g content in terms of energy, sugars, saturated fatty acids, sodium, fibre and protein, and of fruits, vegetables, legumes and nuts. The FSAm-NPS dietary index (DI) was calculated for each individual as an energy-weighted mean of the FSAm-NPS score of all foods consumed. The higher the FSAm-NPS DI score the lower the overall diet nutritional quality.

**Main outcome measures:** The associations between the FSAm-NPS DI and mortality assessed using multivariable-adjusted Cox proportional hazards regression models.

**Results:** Participants with higher FSAm-NPS DI (quintile 5 vs. 1) showed an increased all-cause mortality (n=53,112 events, non-external causes; HR=1.07 [95%CI 1.03 to 1.10], P-trend<0.001), and, in cause-specific analyses, of mortality from cancer (HR=1.08 [1.03 to 1.13], P-trend<0.001) and from diseases of the circulatory (HR=1.04 [0.98 to 1.11], P-trend=0.06), respiratory (HR=1.39 [1.22 to 1.59], P<0.001) and digestive (HR=1.22 [1.02 to 1.45], P-trend=0.03) systems. The age-standardized absolute rates were 760 and 661 deaths per 10,000 persons over 10 years, for quintiles 5 and 1 of the FSAm-NPS DI, respectively.

**Conclusions:** In this large multinational European cohort, consuming foods with a higher FSAm-NPS score (i.e. lower nutritional quality) was associated with a higher mortality rate, supporting the relevance of the FSAm-NPS to characterize healthier food choices in the context of public health policies (e.g., the Nutri-Score) for European populations. This is important considering ongoing discussions regarding the potential implementation of a unique nutrition labelling system at the EU level.

**SUMMARY BOX**

**What is already known on this topic**

-Helping consumers make healthier food choices is a major challenge for the prevention of non-communicable diseases and related deaths

-The FSAm-NPS, a nutrient profiling system grading the nutritional quality of food products based on their 100g content in terms of energy, sugars, saturated fatty acids, sodium, fibre and protein, and of fruits, vegetables, legumes and nuts, underlies the Nutri-Score, a simple nutrition label selected by several countries in Europe and considered at the EU level as a candidate for the harmonization of food labelling systems

-The nutritional quality of foods, as defined by the FSAm-NPS, has been studied in relation to human health but not mortality in French cohorts, and, recently to cancer risk in the large multinational EPIC cohort; evidence in an international setting regarding other health outcomes and especially mortality is still needed

**What this study adds**

-This study used data from EPIC, a large cohort comprising 501,594 adults from 10 European countries (53,112 deaths), with diverse profiles and nutritional habits and showed that the consumption of foods with higher FSAm-NPS scores, reflecting lower nutritional quality, was associated with increased mortality (all-cause and cause-specific)

-These results add support to the relevance of using the FSAm-NPS (and the derived Nutri-Score) to characterize healthier food choices as a basis for public health nutritional policies in Europe, which is important considering ongoing and future debates at the EU level on the harmonization of food labelling systems on the front of food product packaging

## PRINT ABSTRACT

**Study question:** This study aimed to assess the association between the FSAm-NPS, a nutrient profiling system grading the nutritional quality of food products and underlying the Nutri-Score label, and mortality in the multinational framework of the EPIC cohort.

**Methods:** A total of 501,594 adults from the EPIC cohort, originating from 10 European countries were included in the analyses. Usual food intakes were assessed with country-specific diet assessment methods. The FSAm-NPS was calculated for each food item using its 100g content in terms of energy, sugars, saturated fatty acids, sodium, fibre and protein, and of fruits, vegetables, legumes and nuts. The FSAm-NPS dietary index (DI) was calculated for each individual as an energy-weighted mean of the FSAm-NPS score of all foods consumed. The higher the FSAm-NPS DI score the lower the overall diet nutritional quality. The associations between the FSAm-NPS DI and mortality (all-cause and cause-specific) were assessed using multivariable-adjusted Cox proportional hazards regression models.

**Study answer and limitations:** Higher FSAm-NPS DI scores (reflecting a lower nutritional quality of foods consumed as graded by a higher FSAm-NPS score) were associated with increased all-cause mortality (n=53,112 events), including mortality from cancer and from diseases of the circulatory, respiratory and digestive systems, suggesting that the FSAm-NPS is able to characterize healthier food choices. These results were obtained from an observational study using self-reported dietary intakes. Hence, despite their robustness, consistence and plausibility, misclassifications and residual confounding cannot be entirely ruled out.

| FSAm-NPS DI (continuous, per 1-SD increment) | n for cases/ person-years | HR (95%CI) | P-value |
|---|---|---|---|
| **Mortality, all causes** | 54,951/8,162,730 | 1.02 (1.01 to 1.03) | <0.001 |
| **Mortality, non-external causes** | 53,112/8,162,730 | 1.03 (1.02 to 1.04) | <0.001 |
| **Mortality, external causes** | 1,839/7,783,132 | 1.00 (0.95 to 1.05) | 0.93 |
| **Mortality from cancer** | 23,143/7,783,132 | 1.03 (1.01 to 1.04) | <0.001 |
| **Mortality from diseases of the circulatory system** | 13,246/7,783,132 | 1.02 (1.00 to 1.04) | 0.03 |
| **Mortality from diseases of the respiratory system** | 2,857/7,783,132 | 1.11 (1.06 to 1.15) | <0.001 |
| **Mortality from diseases of the digestive system** | 1,561/7,783,132 | 1.08 (1.02 to 1.14) | 0.01 |

**INTRODUCTION**

Poor nutrition is a major well-known risk factor for non-communicable diseases (NCDs), with an estimated 11 million NCD-related deaths attributed to unbalanced diets in 2017 worldwide [1]. While it is now well-established that, for better health, one should eat less sugars, saturated fats, salt, energy and more dietary fibers or fruit and vegetables, putting these recommendations into practice remains an important challenge. Helping consumers make healthier food choices could therefore serve as one of the key strategies to prevent NCD-related mortality. Affixing a front-of-pack nutrition label providing user-friendly summary information on the nutritional quality of food products has been identified as one possible answer to tackle this issue. Such labels have indeed the potential to help consumers choose food products with a better nutritional quality at the point of purchase and at the same time, to incentivize food manufacturers to improve the nutritional quality of their products thus contributing to a healthier food environment [2,3]. The Nutri-Score five-colour labelling system [4], considered promising for use in a broad international context, classifies food products into 5 categories reflecting their nutritional quality (from A – higher nutritional quality, to E – lower) assessed with the FSAm-NPS, an adapted version of a nutrient profiling system initially developed by the British Food Standards Agency [5–7]. This scoring system was developed with the aim of preventing a large range of nutrition-related NCDs, allocating a score to a given food/beverage from its content per 100g of energy, saturated fatty acids, sugars, sodium, dietary fibre, and protein and of fruit, vegetables, legumes, and nuts.

The Nutri-Score was officially adopted in France in 2017 by public health authorities [8,9], following a series of studies that demonstrated the validity, scientific relevance and potential public health impact of the use of the FSAm-NPS [10–12] and of the Nutri-Score label as a tool for public health nutrition policies [13–21] (reviewed in [22]). Subsequently, governments in Belgium, Spain, and recently in Germany, the Netherlands, Switzerland and Luxembourg also adopted the Nutri-Score. Medical professionals and academic societies in Europe have also recognized its importance and potential public health impact as a tool that can be recommended to the general public and patients to guide them towards food choices of higher nutritional quality.

Yet, in the context of current EU labelling regulations, Member States cannot make a front-of-pack nutrition label such as the Nutri-Score mandatory, leaving the choice to food manufacturers to affix it on their products. There are therefore high stakes to the possible harmonization of nutritional labelling systems at the EU level, with the selection of a unique mandatory front-of-pack nutrition label. Similar discussions are also ongoing in America and in Australia. Since most of the original studies assessing the validity of the FSAm-NPS underlying the Nutri-Score have been performed in France [22–25], it is important to extend the validity of the model to international settings [26] to provide relevant scientific evidence for ongoing discussions in the EU and beyond.

In particular, one aspect of the validity assessment of the FSAm-NPS is to study the association between the nutritional quality of the food products consumed as graded by the FSAm-NPS and health outcomes. Such studies have been performed in the French SU.VI.MAX and NutriNet-Santé cohorts and showed that consuming on average more food products with lower FSAm-NPS scores (corresponding to higher nutritional quality) was associated with more favourable health outcomes with regard to weight gain [27], asthma symptoms [25], metabolic syndrome [28], cardiovascular diseases [29,30] and cancer [31,32]. Recently, we showed that similar observations could be made regarding cancer risk in a large multinational European cohort, the European Prospective Investigation into Cancer and Nutrition (EPIC) study [33]. The objective of the current study was to investigate if the FSAm-NPS scores of the food products consumed associate with mortality in this large and diverse European population.

## METHODS

### Study population: the EPIC cohort

The study was conducted within the framework of the EPIC cohort (http://epic.iarc.fr/) which enrolled over 500,000 volunteers (25-70 years) from 23 centres located in 10 European countries (Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden and the UK) between 1992 and 2000. This cohort study aims to investigate metabolic, dietary, lifestyle, and environmental factors associated with the development of cancer and other NCDs in Europe. All participants gave their written informed consent and the study was approved by the local ethics committees and by the Internal Review Board of the International Agency for Research on Cancer. Details of the study design, recruitment, and data collection have been previously published [34–36].

### Baseline data collection

Participants were extensively characterized upon their enrolment using questionnaires covering information on sociodemographic characteristics, lifestyle factors, personal and familial history of diseases, and menstrual and reproductive history for women. Anthropometric measurements (e.g. height, weight) were performed in all centres at baseline using standard procedures except in France, Oxford and Norway, where self-reported data were collected. Updated data on weight during follow-up were obtained for a subsample of participants involved in the EPIC-PANACEA study [37].

**Dietary intake assessment**

Country-specific and validated dietary questionnaires were used to assess usual dietary intakes for each participant at recruitment, taking into account the specificities across countries. Depending on the study centres, the dietary questionnaires used were self- or interviewer-administered semi-quantitative food frequency questionnaires (FFQs) with an estimation of individual average portions or with the same standard portion assigned to all participants, or diet history questionnaires, some combining an FFQ and 7-day dietary records [36]. The EPIC food composition database comprises more than 10,000 food and beverage items reflecting the specificities of the type of food consumed in each country [38]. A subset of the EPIC cohort (random samples of 5-12% of participants from each EPIC center) also completed one computer-assisted 24-hour dietary recall (EPIC-SOFT), as part of a calibration study [39].

**FSAm-NPS dietary index computation**

The FSAm-NPS is a modified version of the original FSA-NPS, with slight adaptations in the allocation of points for specific foods (beverages, cheese and added fats) recommended by the French High Council for Public Health (HCSP) to ensure a proper discrimination of the nutritional quality of products within these groups and a high consistency of the FSAm-NPS score with nutritional recommendations [12]. Details of the FSAm-NPS score computation have been previously published [6,10,12,33] and can be found in Supplementary Methods. The FSAm-NPS score (food-level score) was calculated for each food and beverage in the EPIC food composition database based on its composition per 100g: ‘A points’ were allocated for total sugars (g), saturated fatty acids (g), sodium (mg), and energy (kJ) [i.e. nutrients that should be consumed in limited amounts], and ‘C points’ were allocated for dietary fibre (g), protein (g) and fruits, vegetables, legumes and nuts (%) [i.e. nutrients/components that should be promoted]. The percentage content of fruit, vegetables, legumes, and nuts was derived using standard recipes. ‘A points’ (range: 0-10 for each of the 4 items) and ‘C points’ (range:0-5 for each of the 3 items) are allocated following specific grids for each item (provided in Supplementary Methods) and summed. The sum of ‘C points’ is then subtracted from the sum of ‘A points’ (rules provided in Supplementary Methods) to obtain the FSAm-NPS. The FSAm-NPS score for each food/beverage is based on a unique discrete continuous scale ranging theoretically from -15 (highest nutritional quality) to +40 points (lowest nutritional quality). Cut-offs are then applied to the FSAm-NPS to derive the Nutri-Score.

Examples of FSAm-NPS calculation, Nutri-Score cut-offs, and examples of food products classified according to the Nutri-Score are provided in Supplementary Methods.

In a second step, a dietary index (FSAm-NPS DI) was computed to characterize the nutritional quality of an individual's diet. The FSAm-NPS DI (individual-level score) was obtained as the sum of FSAm-NPS score for each food/beverage consumed multiplied by the amount of energy brought by this product (energy content per 100g multiplied by the estimated daily intake assessed using the baseline dietary questionnaires), divided by the total amount of energy intake. The following equation was used [40] where $FS_i$ is the score of food/beverage i, $E_i$ the energy intake from food/beverage i, and $n$ the number of food/beverage consumed:

$$\text{FSAm-NPS DI} = \frac{\sum_{i=1}^{n}(FS_i E_i)}{\sum_{i=1}^{n} E_i}$$

By construction, a higher FSAm-NPS DI reflects an overall lower nutritional quality of consumed foods.

**Follow-up for vital status**

Data on vital status and originating cause of death were obtained through linkage to mortality registries in combination with data collected during active follow-up of the cohort. The end of follow-up/closure dates of the study period varied between 2012 and 2015 depending on the country. The originating cause of death was coded using the International Statistical Classification of Diseases, Injuries and Causes of Death, 10th revision (ICD-10) [41]. In this study, in addition to mortality from all causes we more specifically considered cancer-related mortality (C00–D48), mortality from diseases of the circulatory system (I00–I99), mortality from diseases of the respiratory system (J00–J99), mortality from diseases of the digestive system (K00–K93) and, as a negative control, mortality due to external causes (injury, poisoning and other consequences of external causes: S00-T98, and external causes of morbidity and mortality: V01–Y98). Mortality from all non-external causes (main exposure) was defined as mortality from all causes but external causes of death.

**Statistical analyses**

Of the 521,324 study participants, we excluded those with missing lifestyle and/or dietary information (n=6,902), along with those with an extreme ranking on the ratio of energy intake/energy requirement (highest and lowest percentiles, n=10,241), participants with null follow-up (n=2,516) or those with missing date of death (n=71). A total of 54,951 death events were recorded during follow-up, among which 1,839 were due to external causes. A flowchart is presented in Supplementary Figure 1.

Age-standardized absolute rates were calculated as the number of cases per 10,000 persons over 10 years in the highest and in the lowest quintile of the FSAm-NPS DI score.

The FSAm-NPS DI was considered as a continuous variable (increment of 1 standard deviation, i.e. 2.1 points of score) and as sex-specific quintiles. Tests for linear trends were performed assigning the median for each FSAm-NPS DI quintiles. Non-linear associations were explored using restricted cubic spline modelling. Cox proportional hazards regression models were computed to analyse the associations between the FSAm-NPS DI and all-cause mortality as well as cause-specific mortality. We confirmed that the assumptions of proportionality were satisfied through examination of the Schoenfeld residuals (Supplementary Figure 2). Participants contributed person-time to the model until date of death, date of emigration/loss to follow-up, or end-of-follow-up, whichever occurred first. For analyses of cause-specific mortality, participants who died from another cause than the one under study were included and censored at the date of the competing death event. Similarly, for analyses on mortality from all non-external causes, participants dying from external causes were included in the model and censored at their date of death. Competing risks were also tested using Fine and Gray models [42]. Hazard ratios [HRs] and their 95% confidence interval [95% CI] were derived from multivariable Cox regression models using age as the underlying time variable. Models were stratified (using Cox model 'strata') by age at recruitment (1-year intervals) and study centre [34] to take into account a possible heterogeneity between study centres (and therefore countries). The main model accounted for all major potential confounders available through an adjustment for the following covariates, pertaining to sociodemographic characteristics (sex, educational level (longer education, including university degree; technical/professional school; secondary school; primary school)), lifestyle (combined total physical activity (sex-specific categories: active; moderately active; moderately inactive; inactive), smoking status and intensity (current, 1–15 cigarettes/d; current, 16–25 cigarettes/d; current, 26+ cigarettes/d; current, pipe/cigar/occasional; current/former, missing; former, quit ≤10 y; former, quit 11–20 y; former, quit 20+y; non-smoker), alcohol and energy intakes at baseline), anthropometric characteristics (body mass index (BMI), height) and prevalent disease status (personal history of cancer, cardiovascular diseases and diabetes).

Missing data on covariates (physical activity: n=34,400, 6.9%, smoking status and intensity: n=8,527, 1.7%; educational level: n=18,383, 3.7%; personal history of cardiovascular diseases: n=78,400, 15.6%, personal history of diabetes: n=39,892, 7.9%, BMI: n=91,412, 18.2%; height: n=90,258, 18%) were handled using Multiple Imputation by Chained Equations (MICE method [43]) by fully conditional specification (FCS, 10 imputed datasets). A complete case approach, i.e. excluding participants with missing data on covariates, was also conducted.

BMI was considered as a confounding factor in the analyses and was therefore adjusted for in the multivariable models. However, BMI could also be considered as an intermediate mediating factor. Thus, sensitivity analyses were conducted without adjustment for BMI and analyses of mediation through BMI variation were also implemented using the method proposed by Lange et al. [44].

To test the robustness of the associations, the following sensitivity analyses were performed: 1) energy intake was removed from the models (assessing a potential collider bias), 2) coffee and soft drink intakes were included in the models (assessing if these two dietary factors recently found to be strongly associated with mortality in EPIC [45,46] would entirely explain the associations), 3) participants with a previous history of cancer, cardiovascular diseases, and diabetes were excluded from the analyses (assessing a potential bias due to modified dietary behaviours following these major health events: e.g., indications to follow a healthier diet), 4) participants whose death occurred during the first 5 years of follow-up were excluded from the analyses (allowing a longer delay between baseline dietary assessment and mortality event). Subgroup analyses according to major potential confounders (sex, BMI, physical activity, educational level, smoking status, alcohol intake, energy intake) were also conducted to assess the potential for residual confounding. Potential residual confounding from unmeasured confounders was assessed using E-values [47,48].

All tests were two-sided and $P<0.05$ was considered statistically significant. SAS version 9.4 (SAS Institute) and R version 3.6.2 were used for the analyses.

### Patient and public involvement

The research question developed in this article corresponds to concerns of the participants involved in the EPIC cohort, and of the public in general. Participants to the study are thanked in the Acknowledgements section. The results of the present study will be disseminated through institutional websites and through media.

## RESULTS

A total of 501,594 participants (70.8% females, median age: 51.6 years) were included in this study (see flowchart in Supplementary Figure 1). After a median follow-up of 17.2 years

(8,162,730 person-years) 54,951 deaths occurred, among which 23,143 from cancer, 13,246 from diseases of the circulatory system, 2,857 from diseases of the respiratory system, 1,561 from diseases of the digestive system, and 1,839 from external causes.

Baseline characteristics of the study participants overall and according to sex-specific quintiles of the FSAm-NPS DI are presented in Table 1. The FSAm-NPS DI reflects the overall nutritional quality of one's diet based on the intrinsic nutritional quality of each food consumed, regardless the cultural context. The diverse dietary habits in the 10 countries participating in the EPIC cohort resulted in lower FSAm-NPS DI scores, indicating diets of overall higher nutritional quality, in Spain (median: 4.06), Greece (4.49), Norway (4.92) and Italy (5.34), and in higher scores in the UK (6.01), Sweden (6.19), the Netherlands (6.22), Denmark (6.25), Germany (6.73) and France (7.25).

As expected, participants with higher FSAm-NPS DI scores were more likely to have less healthy dietary intakes (lower intakes of dietary fibres, fruit and vegetables, and fish, and higher intakes of red and processed meat) and higher energy intakes. Still, a broad range of energy intakes was observed within each quintile. They were also more likely to smoke, to be less physically active, to have higher alcohol intakes and a higher level of education, as well as a personal history of cancer. In contrast, we observed a higher proportion of existing cardiovascular diseases or diabetes and a higher BMI in participants with a lower FSAm-NPS DI score, which may reflect a diet change for disease management in these participants.

Associations between the FSAm-NPS DI and mortality are displayed in Table 2.

A higher FSAm-NPS DI score was associated with higher mortality overall ($HR_{Q5vs.Q1}$=1.06, [95% CI 1.03 to 1.09], P-trend<0.001, P-non-trend<0.001). Mortality from external causes was not associated with FSAm-NPS DI ($HR_{Q5vs.Q1}$=0.99, [0.84 to 1.16], P-trend=0.9, P-non-trend=0.9). Mortality from all non-external causes (main exposure, referred to as "all-cause" mortality) was positively associated with FSAm-NPS DI (n=53,112 cases, $HR_{Q5vs.Q1}$=1.07, [1.03 to 1.10], P-trend<0.001, P-non-trend<0.001). Corresponding age-standardized absolute rates for all-cause mortality in those with high (quintile 5) and low (quintile 1) FSAm-NPS DI scores were 760 (men: 1,237; women: 563) and 661 (men: 1,008; women: 518) death events per 10,000 persons over 10 years, respectively.

Overall, results were consistent across all countries (Supplementary Figure 3), with however only borderline significant associations (restricted sample size). Results for Norway may be related to the distribution of the FSAm-NPS DI scores in this country, with overall low FSAm-NPS DI scores and a resulting small contrast between individuals with higher and lower scores (median: 4.92, IQR: 3.87-5.98).

Cause-specific analyses showed that a higher FSAm-NPS DI score was associated with higher mortality related to cancer ($HR_{Q5vs.Q1}$=1.08 [1.03 to 1.13], P-trend<0.001, P-non-trend<0.001), diseases of the circulatory system ($HR_{Q5vs.Q1}$=1.04 [0.98 to 1.11], P-trend=0.06, P-non-trend=0.02), diseases of the respiratory system ($HR_{Q5vs.Q1}$=1.39 [1.22 to 1.59], P-trend<0.001, P-non-trend<0.001), and diseases of the digestive system ($HR_{Q5vs.Q1}$=1.22 [1.02 to 1.45], P-trend=0.03, P-non-trend=0.2).

Some evidence of non-linearity was observed for all-cause mortality, mortality from cancer and mortality from diseases of the circulatory system. Such non-linearity was mainly observed for the very low values of the FSAm-NPS DI score whereas the association had a linear shape for higher FSAm-NPS DI scores (Supplementary Figure 4).

Similar results were observed across all sensitivity analyses (Supplementary Table 1). Overall, subgroup analyses also illustrate the robustness of our results across categories of major potential confounders (Figure 1): associations with all-cause mortality were consistent across strata for men and women, non-smokers and smokers, and according to energy or alcohol intakes and education levels (although strengthened in highly educated participants); associations were stronger in non-obese participants and in those less physically active. Mediation analyses suggested limited mediation effect of BMI variation during follow-up in the association between FSAm-NPS DI and mortality (Supplementary Table 2). Removing BMI from the models did not change the results of the main models (Supplementary Table 1). Finally, E-values obtained suggest that the residual confounding due to potential unmeasured confounding factors is likely moderate (Supplementary Table 3).

## DISCUSSION

### Principal findings

This study conducted in a large population from 10 European countries aimed at assessing the relevance of the FSAm-NPS score to characterize healthier food choices in the European context. Our results found that a higher consumption of food products with higher FSAm-NPS scores (i.e. higher FSAm-NPS DI scores at the individual level), was positively associated with mortality from all causes and mortality from cancer and from diseases of the circulatory, respiratory and digestive systems.

### Comparison with other studies

This work builds upon prior analyses conducted on cancer incidence in the EPIC cohort [33] to investigate the association between the FSAm-NPS DI and health outcomes in a large

European population and complements the analyses conducted in the French SU.VI.MAX and NutriNet-Santé cohorts [25,27–32]. All these studies consistently reported poorer health outcomes (weight gain [27], metabolic syndrome [28], cancer [31–33], cardiovascular diseases [29,30], asthma symptoms [25]) associated with higher FSAm-NPS DI scores.

Prior studies in the UK also investigated the association between the FSA-NPS score (i.e. the original score not including the slight adaptations made in the FSAm-NPS, see Methods) and mortality, applying to the FSA-NPS a cut-off to categorize food products as 'healthier' or as 'less healthy' (Ofcom threshold used for advertising regulation [7]). The results of these studies were consistent with ours, showing a lower all-cause and cancer mortality associated with the intake of a greater variety of 'healthier' food items in the Whitehall II cohort [49], and a higher all-cause mortality associated with a higher consumption of 'less healthy' food items in EPIC-Norfolk ($HR_{Q5vs.Q1}$=1.11 [1.02-1.20]) [50]. Both studies observed no association with mortality related to cardiovascular diseases while ours observed a borderline significant association. This may be related to the larger sample size in our study or to a better ranking of participants using the continuous FSAm-NPS, allowing for a more refined discrimination of food products nutritional quality likely resulting in a better ranking of participants according to the overall nutritional quality of their diets.

The approach used in our study, in which a dietary index at the individual level (the FSAm-NPS DI) stems from the nutrient profile of the foods consumed (the FSAm-NPS) and is studied in relation to health outcomes, was also implemented with different nutrient profiling systems in two studies. In the Nurses' Health Study and the Health Professionals Follow-up Study, the Overall Nutritional Quality Index translated at the individual level (ONQI-f) was associated with a lower mortality rate [51]. In the Rotterdam Study, the Nutrient-Rich Food (NRF) 9.3 score at the individual level was inversely associated with all-cause mortality but not with mortality from cardiovascular diseases [52]. These scores nonetheless differ by the number and types of nutritional items considered for their calculation. The FSAm-NPS was designed to be easily computable by industrial and public stakeholders in a transparent manner to serve as a basis for tools of public health nutritional policies (such as the Nutri-Score label). Hence, it consists of a unique scale applicable to all food products (raw or manufactured) and to all countries (as was done in the present study) and is deliberately focused on 7 items only (energy, saturated fatty acids, sodium, sugars, dietary fibre, and protein, and fruits, vegetables, legumes and nuts). These items are those generally found in the nutritional facts of all food labels, and were selected based on their association with NCDs and/or their ability to reflect the nutritional value of foods, in line with dietary guidelines

[6,40]. In contrast, the ONQI is based on 30 items and the NRF9.3 is based on 12 items, both including macronutrients, vitamins, and minerals, but also polyphenols (ONQI) or reference values of intake (NRF9.3) that may differ across countries.

The FSAm-NPS is also consistent with the two recent reports from the *Global Burden of Disease Study* and the *EAT-Lancet Commission*, estimating that about 11 million deaths worldwide could be prevented with healthier diets, including notably more dietary fibre and whole grains, fruit, vegetables, legumes, and nuts, and less sodium, sugars and saturated fats [1,53]. Of note, our results showed a strong association of the FSAm-NPS DI with mortality from respiratory diseases. Beyond the well-established impact of nutrition on cancer and cardiometabolic risks [1], mounting evidence also supports a substantial impact of nutrition on respiratory health through several pathways involving oxidative stress and inflammation, epigenetic, and the gut microbiome. Notably, dietary fibers – involved in anti-inflammatory response, fruit and vegetables – source of antioxidants (part of a "healthy diet") have been suggested to play a beneficial role for respiratory health while components such as saturated fats and red or processed meat – pro-inflammation, or more generally a "Western diet", would have detrimental effects [54–59]. The FSAm-NPS DI has also been associated to asthma symptoms in the NutriNet-Santé cohort study [25]. Similar strong associations with mortality from respiratory diseases (as compared to mortality from other causes) have been observed in previous studies looking at saturated fatty acids [60] or vegetables and red meat intakes [61]. These results are consistent with the items building the FSAm-NPS DI score.

**Non-linearity and associations between the FSAm-NPS DI and BMI**

In our study, evidence of non-linearity was observed for all-cause mortality and for mortality from cancer or diseases of the circulatory system for very low values of the FSAm-NPS DI. Such values reflect very healthy food choices that may actually have been adopted by individuals with high disease risks (and thus high underlying mortality risks). Hence, individuals exhibiting the best diets (lowest FSAm-NPS DI scores) would be the one with higher mortality rates, thus blurring the association overall. Evidence of this can be seen in Table 1 where participants in the first quintile of the FSAm-NPS DI have a higher baseline BMI (cross-sectional analyses) and were more likely to have a prevalent cardiovascular disease or a diabetes at baseline (probably partly because of their past diet). This may also contribute to explain why weaker (though significant) associations were observed for mortality from circulatory diseases or why we observed stronger results in non-obese individuals at baseline since mechanisms leading to premature death have to some extent already played out for obese individuals. Finally, our analyses showed little mediation effect of BMI variation in the association between the FSAm-NPS DI and mortality. This suggests that the overall nutritional quality might have an impact on mortality rates beyond weight gain.

**Associations between the FSAm-NPS DI and educational level**

The positive cross-sectional association between the FSAm-NPS DI score and educational level may seem counterintuitive but was also made in prior studies conducted in the independent SU.VI.MAX and NutriNet-Santé cohorts [40,62]. Several hypotheses can explain this finding. In EPIC, countries with a higher proportion of participants with lower mean educational level (e.g., Greece, Spain, Italy) also had the lowest FSAm-NPS DI scores (reflecting trends towards a Mediterranean / healthier diet in countries of Southern Europe [63,64]). At least in these countries, people with lower education may lean more on traditional diets which may include food of better nutritional quality. This trend could also be due to an age and/or generation effect. Younger people tend to have a higher educational level but also to have a higher consumption of "junk food", leading to higher FSAm-NPS DI scores (i.e., diets with lower nutritional quality). Associations were statistically significant for all categories of educational level but slightly strengthened in highly educated participants. The latter may be related to more contrasted FSAm-NPS DI scores in the "longer education" category. Another hypothesis is that participants with longer education may be less exposed to other risk factors linked to occupation or environment compared to those with a lower socioeconomic position.

**Strengths and limitations of this study**

Strengths of our study notably pertained to its prospective design with a long follow-up of a very large number of participants from different European countries with various phenotypes, and for which collected data have been standardized. This provided a unique opportunity to study the nutritional quality of food choices in relation to mortality in a broad European context with diverse dietary habits. Additionally, a large array of lifestyle data was available which allowed adjustment for major potential confounding factors in our main model and to perform in-depth sensitivity analyses.

Yet our study also comes with some limitations. First, due to the observational design, potential residual confounding or unmeasured confounding (from other factors such as genetics or environmental factors that could not be taken into account) cannot be ruled out. In addition, in this study, data were collected using questionnaires. Hence, misclassification bias from imprecision in the measure of dietary data and covariates cannot be excluded. Because data were collected prior to the studied outcome (prospective design), any misclassification resulting from measurement errors is likely to have been non-differential as regards case/non-case status. Nonetheless, this may have resulted in biased estimates of effect (underestimation or overestimation) [65,66]. In particular, the tools used to estimate an individual's usual diet are subject to imprecision and inaccuracy (such as misreporting bias, inherent to challenges in assessing usual dietary intakes) and therefore could have induced some misclassification of participants regarding the nutritional quality of the foods they consumed. In this regard, most EPIC centres used an FFQ to assess dietary intakes, which, while allowing good estimations of usual dietary intakes, still limits the discrimination of the nutritional quality of individual food products (compared for example to repeated 24-h dietary records, as used in the SU.VI.MAX and NutriNet-Santé cohorts where larger effect estimates were observed for associations between the FSAm-NPS DI and health outcomes [29–32,59]). In the subsample from the EPIC calibration study (n=34,367), the FSAm-NPS DI score calculated from the dietary questionnaires (mainly FFQ) and from the calibration 24h-dietary recall showed good concordance (68% of participants were classified either in the same quintile or in the adjacent quintile, only 3% were classified in extreme opposite quintiles, data not tabulated). However, only one day of 24h recall was available for EPIC participants in the calibration study. Hence, although the dietary questionnaires available for the whole EPIC cohort may come with some limitations as regards the level of detail available for each food item, they still provide a better picture of the usual diet of participants compared to the single 24h recall. In addition, dietary intakes were only assessed at baseline. Although changes in food consumption might have occurred during follow-up, it is usually hypothesized that the baseline estimation reflects general eating behaviour throughout middle-aged adult life [67]. Next, participants of the EPIC cohort were volunteers involved in a long-term cohort study investigating the association between nutrition and health and likely had more health-conscious behaviours and less unhealthy dietary behaviours compared to the general population. This might have resulted in weaker observed associations (hence a smaller effect size) due to smaller contrast between high and low FSAm-NPS DI scores. EPIC participants have also been recruited from 10 countries in Western Europe which warrants caution when extrapolating the results to other populations or ethnicities worldwide. Finally, the order of magnitude obtained for the association between the FSAm-NPS DI and mortality in our study was relatively modest but still in line with the one traditionally observed in nutritional epidemiology, and similar to the one observed in the study on cancer incidence in EPIC [33]. In terms of public health perspective, the opportunity of preventing 7% of premature deaths through healthier food choices may nonetheless be of high interest.

These limitations, identifying potential sources of bias in our study warrant for overall caution in interpreting our findings. Still, despite the rather low HR, the following arguments allow some confidence in our results and are in favour of a ‘true’ association supporting possible causality, beyond residual confounding: robustness of associations across sensitivity analyses, including across categories of major potential confounders; null results obtained for associations with mortality due to external causes which are unrelated to diet (“negative control”); E-values suggesting a moderate potential unmeasured confounding [47,48]; consistency of the results with prior studies on the association between the FSAm-NPS DI and health outcomes in independent cohorts [25,27–32]; consistency of the results with mechanistic hypotheses supporting biological plausibility.

**Conclusions and policy implications**

To conclude, in this large cohort study involving 10 European countries, a diet composed on average of more food products with higher FSAm-NPS scores, which reflected poorer nutritional profiles, was associated with higher all-cause and cause-specific mortality. Overall, the fact that a higher FSAm-NPS DI, obtained with different dietary patterns in different countries from a diverse European population, leads to higher mortality rates, suggest that the FSAm-NPS is a relevant tool to characterize more or less healthy food products, no matter the food category or the specificities of the national dietary habits.

This study adds to the current body of evidence surrounding the FSAm-NPS score and/or the Nutri-Score, a nutrition label derived from the FSAm-NPS: studies linking the FSAm-NPS DI to health outcomes, including one in the EPIC cohort [25,27–33]; studies on the perception and understanding of the Nutri-Score and its actual impact on food choices [22–24,26,68]. Altogether, these results back up the relevance of using the FSAm-NPS to grade the nutritional quality of food products in the framework of public health nutritional measures such as the Nutri-Score label, a tool aimed at the general public and patients to help them choose food products with a higher nutritional quality. This is important considering ongoing and future debates at the EU level regarding the harmonization of food labelling systems on the front of food product packaging.

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**Authors' contribution:** The authors' contributions were as follows – MD, MT, SH, CJ and, IH conceptualised the study and defined the analytical strategy; MD, MT and IH performed statistical analyses and provided preliminary interpretation of findings; MD and writing group (IH, CJ, SH, ME, MJG, MT) drafted the manuscript; CB, CC, HAW, KO, ATj, ALR-H, M-CB-R, FRM, YM-S, TK, VK, MMB, MBS, ATr, AK, EP, GM, CA, MSDM, RT, CS, JMAB, WMMV, YTvdS, GS, TB, MLR, AA, DP, SMC-Y, AB, PA, ES, UE, JO, BSu, NJW, NGF, PV, KKT, AKn, KP, PF, ER and MJG played a key role in the acquisition of the data, and were active in searching for funding to continue the study. All authors (MD, IH, CJ, SH, ME, BSr, EK-G, PL-M, CB, CC, NM, MJ, HAW, EW, KO, ATj, ALR-H, M-CB-R, FRM, YM-S, TK, VK, MMB, MBS, ATr, AK, EP, GM, CA, MSDM, RT, CS, JMAB, WMMV, YTvdS, GS, TB, MLR, AA, DP, SMC-Y, AB, PA, ES, UE, JO, BSu, NJW, NGF, PV, KKT, AKn, KP, PF, ER, MJG, MT) critically helped in the interpretation of results, revised the manuscript and provided relevant intellectual input. They all read and approved the final manuscript. MD and MT had primary responsibility for the final content, they are the guarantors. The corresponding author (MD) attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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**Data sharing:** For information on how to submit an application for gaining access to EPIC data and/or biospecimens, please follow the instructions at http://epic.iarc.fr/access/index.php.

**Dissemination to participants and related patient and public communities:** The results of this article will be disseminated as lay summaries to the public through different channels including articles on the open web-platform The Conversation (in English and in French), press releases, social media accounts of our research team, IARC newsletter and communications through the French Nutrition and Cancer Research network (NACRe: www.inra.fr/nacre).

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**Table 1. Baseline characteristics of the study participants overall and by sex-specific quintiles of the FSAm-NPS DI score, EPIC cohort**

| | All (n=501,594) | Sex-specific quintiles of the FSAm-NPS DI score [a] | | | | |
|---|---|---|---|---|---|---|
| | | Q1 (n=100,318) | Q2 (n=100,319) | Q3 (n=100,319) | Q4 (n=100,319) | Q5 (n=100,319) |
| | Median (IQR) or N (%) [b] | Median (IQR) or N (%) [c] | Median (IQR) or N (%) | Median (IQR) or N (%) | Median (IQR) or N (%) | Median (IQR) or N (%) |
| FSAm-NPS DI Score | 5.95 (4.53-7.39) | 3.29 (2.52-3.79) | 4.84 (4.53-5.13) | 5.95 (5.67-6.22) | 7.07 (6.78-7.39) | 8.66 (8.14-9.44) |
| Sex | | | | | | |
| Men | 146,329 (29.2) | 29,265 (20.0) | 29,266 (20.0) | 29,266 (20.0) | 29,266 (20.0) | 29,266 (20.0) |
| Women | 355,265 (70.8) | 71,053 (20.0) | 71,053 (20.0) | 71,053 (20.0) | 71,053 (20.0) | 71,053 (20.0) |
| Age at recruitment (years) | 51.6 (45.3-58.4) | 52.1 (45.4-59.2) | 51.5 (44.9-58.3) | 51.5 (44.8-58.0) | 51.6 (45.4-58.3) | 51.5 (45.7-58.4) |
| Country | | | | | | |
| France | 72,980 (14.5) | 2,558 (3.51) | 6,812 (9.33) | 13,135 (18.0) | 21,795 (29.9) | 28,680 (39.3) |
| Italy | 45,700 (9.11) | 9,734 (21.3) | 13,945 (30.5) | 11,143 (24.4) | 7,295 (16.0) | 3,583 (7.84) |
| Spain | 40,619 (8.10) | 21,587 (53.1) | 8,708 (21.4) | 5,214 (12.8) | 3,098 (7.63) | 2,012 (4.95) |
| United Kingdom | 80,441 (16.0) | 18,826 (23.4) | 13,661 (17.0) | 13,936 (17.3) | 14,652 (18.2) | 19,366 (24.1) |
| The Netherlands | 38,195 (7.61) | 3,736 (9.78) | 7,725 (20.2) | 10,108 (26.5) | 9,999 (26.2) | 6,627 (17.3) |
| Greece | 26,651 (5.31) | 10,900 (40.9) | 10,032 (37.6) | 4,263 (16.0) | 1,206 (4.53) | 250 (0.94) |
| Germany | 52,010 (10.4) | 4,729 (9.09) | 7,718 (14.8) | 11,107 (21.4) | 13,735 (26.4) | 14,721 (28.3) |
| Sweden | 52,741 (10.5) | 8,495 (16.1) | 10,311 (19.5) | 11,043 (20.9) | 10,982 (20.8) | 11,910 (22.6) |
| Denmark | 55,818 (11.1) | 8,503 (15.2) | 10,461 (18.7) | 12,297 (22.0) | 13,171 (23.6) | 11,386 (20.4) |
| Norway | 36,439 (7.26) | 11,250 (30.9) | 10,946 (30.0) | 8,073 (22.1) | 4,386 (12.0) | 1,784 (4.90) |
| Body Mass Index (kg/m²) [d] | 25.3 (22.8-28.2) | 26.0 (23.3-29.1) | 25.5 (23.1-28.5) | 25.2 (22.8-28.0) | 24.8 (22.5-27.6) | 24.7 (22.2-27.5) |
| Height (cm) [e] | 166 (160-173) | 164 (158-170) | 165 (159-172) | 166 (160-173) | 167 (161-174) | 167 (161-174) |
| Educational level [f] | | | | | | |
| None / Primary school | 149,580 (31.0) | 40,566 (27.1) | 33,650 (22.5) | 27,778 (18.6) | 23,976 (16.0) | 23,610 (15.8) |
| Technical/professional/ secondary school | 214,154 (44.3) | 35,580 (16.6) | 41,742 (19.5) | 44,933 (21.0) | 46,072 (21.5) | 45,827 (21.4) |
| Longer education (incl. University degree) | 119,477 (24.7) | 20,301 (17.0) | 21,935 (18.4) | 24,473 (20.5) | 26,653 (22.3) | 26,115 (21.9) |
| Physical activity [g] | | | | | | |
| Inactive | 76,414 (15.2) | 12,349 (16.2) | 13,864 (18.1) | 15,532 (20.3) | 16,969 (22.2) | 17,700 (23.2) |
| Moderately inactive | 159,880 (31.9) | 26,205 (16.4) | 27,882 (17.4) | 30,765 (19.2) | 35,200 (22.0) | 39,828 (24.9) |
| Moderately active | 185,968 (37.1) | 44,635 (24.0) | 40,824 (22.0) | 36,879 (19.8) | 33,180 (17.8) | 30,450 (16.4) |
| Active | 44,932 (8.96) | 9,819 (21.8) | 9,429 (21.0) | 9,178 (20.4) | 8,541 (19.0) | 7,965 (17.7) |
| Smoking status [h] | | | | | | |
| Non-smoker | 244,929 (48.8) | 51,476 (21.0) | 48,552 (19.8) | 47,992 (19.6) | 48,625 (19.8) | 48,284 (19.7) |
| Former smoker | 134,382 (26.8) | 27,306 (20.3) | 27,400 (20.4) | 27,459 (20.4) | 26,815 (19.9) | 25,402 (18.9) |
| Current smoker | 111,938 (22.3) | 19,756 (17.6) | 22,405 (20.0) | 22,851 (20.4) | 22,817 (20.4) | 24,109 (21.5) |
| Alcohol intake (g/d) | 5.29 (0.93-14.8) | 2.86 (0.35-11.8) | 4.56 (0.82-13.2) | 5.56 (1.08-15.0) | 6.64 (1.46-16.4) | 6.81 (1.49-17.0) |
| Energy (kcal/d) | 1992 (1628-2430) | 1745 (1432-2144) | 1899 (1568-2310) | 1984 (1645-2393) | 2092 (1736-2502) | 2253 (1863-2703) |
| Total dietary fibre (g/d) | 21.8 (17.4-27.0) | 24.2 (19.3-30.4) | 22.4 (18.1-27.5) | 21.7 (17.4-26.6) | 21.1 (16.9-25.9) | 19.9 (15.7-24.5) |
| Vegetables (g/d) | 175.4 (110.0-276.3) | 218.6 (133.6-339.7) | 183.2 (115.3-292.1) | 166.2 (107.0-260.4) | 160.6 (104.0-249.3) | 157.2 (98.4-243.5) |
| Fruits, nuts and seeds (g/d) | 200.5 (111.7-321.6) | 287.1 (173.5-434.6) | 234.1 (132.1-354.5) | 194.9 (111.6-308.1) | 171.9 (98.8-273.2) | 143.6 (80.1-234.0) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Dairy products (g/d) | 278.1 (161.3-445.9) | 269.8 (146.5-448.7) | 284.5 (164.5-463.6) | 294.9 (173.6-465.4) | 284.1 (168.2-445.5) | 258.3 (153.0-400.0) |
| Fish and shellfish (g/d) | 28.0 (13.8-49.7) | 32.9 (15.1-63.6) | 28.6 (14.4-53.0) | 27.3 (13.6-48.9) | 26.5 (13.2-44.8) | 25.5 (12.8-42.3) |
| Red meat (g/d) | 34.5 (16.1-62.7) | 26.1 (10.1-49.9) | 34.2 (16.6-60.3) | 37.3 (18.0-65.9) | 40.1 (19.0-69.0) | 36.6 (17.1-65.9) |
| Processed meat (g/d) | 24.3 (10.6-43.9) | 13.0 (3.22-27.4) | 19.9 (7.74-36.5) | 25.6 (12.5-44) | 30.5 (16.1-50.9) | 35.6 (18.5-59.9) |
| Personal history of cancer, Yes | 24,155 (4.82) | 4,359 (18.0) | 4,456 (18.4) | 4,708 (19.5) | 5,204 (21.5) | 5,428 (22.5) |
| Personal history of cardiovascular diseases, Yes [i] | 97,370 (19.4) | 22,211 (22.8) | 19,915 (20.4) | 18,997 (19.5) | 18,645 (19.2) | 17,602 (18.1) |
| Personal history of diabetes, Yes [j] | 13,311 (2.65) | 5,258 (39.5) | 2,853 (21.4) | 2,017 (15.1) | 1,692 (12.7) | 1,491 (11.2) |

[a] Cut-offs for sex-specific quintiles of the FSAm-NPS DI were, for women: 4.14/5.35/6.43/7.68, for men: 4.32/5.55/6.63/7.88. A higher FSAm-NPS DI indicates a lower nutritional quality of the foods consumed
[b] column percentages
[c] row percentages
[d] BMI missing for n=91,412 (18.2%)
[e] Height missing for n=90,258 (18.0%)
[f] Missing for n=18,383 (3.7%)
[g] Missing for n=34,400 (6.9%)
[h] Missing for n=10,345 (2.1%)
[i] Missing for n=78,400 (15.6%)
[j] Missing for n=39,892 (7.9%)

Abbreviations: DI, Dietary Index; EPIC, European Prospective Investigation into Cancer and Nutrition; FSAm-NPS, Nutrient Profiling System of the British Food Standards Agency (modified version); IQR, interquartile range.

**Table 2. Associations between the FSAm-NPS DI and mortality (all cause and cause-specific), from multivariable Cox proportional hazards regression models, EPIC cohort, 1992–2015.**

| | Continuous (per 1-SD increment) | | Quintiles [a] | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Q1 | Q2 | Q3 | Q4 | Q5 | | |
| | HR (95%CI) | P-value | | HR (95%CI) | HR (95%CI) | HR (95%CI) | HR (95%CI) | P-trend | P-non-trend |
| **Mortality, all causes** (n for cases/person-years) | 54,951/8,162,730 | | 10,887/1,605,206 | 9,934/1,585,846 | 10,275/1,626,056 | 11,098/1,662,098 | 12,757/1,683,523 | | |
| Sex-adjusted model [b] | 1.04 (1.03 to 1.05) | <0.001 | | 0.97 (0.94 to 1.00) | 0.98 (0.95 to 1.01) | 1.01 (0.98 to 1.04) | 1.10 (1.07 to 1.14) | <0.001 | <0.001 |
| Main model [c] | 1.02 (1.01 to 1.03) | <0.001 | 1.00 (ref) | 0.98 (0.96 to 1.01) | 0.99 (0.96 to 1.02) | 1.01 (0.98 to 1.04) | 1.06 (1.03 to 1.09) | <0.001 | <0.001 |
| **Mortality, non-external causes** (n for cases/person-years) | 53,112/8,162,730 | | 10,515/1,605,206 | 9,605/1,585,846 | 9,922/1,626,056 | 10,728/1,662,098 | 12,342/1,683,523 | | |
| Sex-adjusted model | 1.04 (1.03 to 1.05) | <0.001 | 1.00 (ref) | 0.97 (0.94 to 1.00) | 0.98 (0.95 to 1.01) | 1.01 (0.98 to 1.04) | 1.10 (1.07 to 1.14) | <0.001 | <0.001 |
| Main model | 1.03 (1.02 to 1.04) | <0.001 | 1.00 (ref) | 0.99 (0.96 to 1.02) | 0.99 (0.96 to 1.02) | 1.01 (0.98 to 1.04) | 1.07 (1.03 to 1.1) | <0.001 | <0.001 |
| **Mortality, external causes** (n for cases/person-years) | 1,839/7,783,132 | | 372/1,568,430 | 329/1,538,426 | 353/1,556,361 | 370/1,562,787 | 415/1,557,129 | | |
| Sex-adjusted model | 1.03 (0.98 to 1.09) | 0.23 | | 0.95 (0.81 to 1.10) | 1.00 (0.86 to 1.17) | 1.00 (0.86 to 1.17) | 1.08 (0.92 to 1.27) | 0.21 | 0.54 |
| Main model | 1.00 (0.95 to 1.05) | 0.93 | 1.00 (ref) | 0.94 (0.81 to 1.1) | 0.98 (0.84 to 1.15) | 0.96 (0.82 to 1.13) | 0.99 (0.84 to 1.16) | 0.98 | 0.93 |
| **Mortality from cancer** (n for cases/person-years) | 23,143/7,783,132 | | 4,550/1,568,430 | 4,288/1,538,426 | 4,482/1,556,361 | 4,700/1,562,787 | 5,123/1,557,129 | | |
| Sex-adjusted model | 1.06 (1.04 to 1.07) | <0.001 | 1.00 (ref) | 1.00 (0.96 to 1.04) | 1.04 (0.99 to 1.08) | 1.07 (1.03 to 1.12) | 1.16 (1.11 to 1.21) | <0.001 | <0.001 |
| Main model | 1.03 (1.01 to 1.04) | <0.001 | 1.00 (ref) | 0.99 (0.95 to 1.04) | 1.02 (0.98 to 1.07) | 1.03 (0.99 to 1.08) | 1.08 (1.03 to 1.13) | <0.001 | 0.003 |
| **Mortality from diseases of the circulatory system** (n for cases/person-years) | 13,246/7,783,132 | | 2,973/1,568,430 | 2,432/1,538,426 | 2,377/1,556,361 | 2,526/1,562,787 | 2,938/1,557,129 | | |
| Sex-adjusted model | 1.02 (1.00 to 1.04) | 0.04 | 1.00 (ref) | 0.91 (0.86 to 0.96) | 0.92 (0.87 to 0.97) | 0.95 (0.90 to 1.01) | 1.03 (0.97 to 1.09) | 0.11 | <0.001 |
| Main model | 1.02 (1.00 to 1.04) | 0.03 | 1.00 (ref) | 0.96 (0.91 to 1.01) | 0.96 (0.91 to 1.02) | 1.00 (0.94 to 1.06) | 1.04 (0.98 to 1.11) | 0.06 | 0.02 |
| **Mortality from diseases of the respiratory system** (n for cases/person-years) | 2,857/7,783,132 | | 508/1,568,430 | 501/1,538,426 | 507/1,556,361 | 591/1,562,787 | 750/1,557,129 | | |
| Sex-adjusted model | 1.16 (1.12 to 1.21) | <0.001 | 1.00 (ref) | 1.12 (0.98 to 1.27) | 1.15 (1.01 to 1.31) | 1.30 (1.14 to 1.47) | 1.56 (1.37 to 1.76) | <0.001 | <0.001 |
| Main model | 1.11 (1.06 to 1.15) | <0.001 | 1.00 (ref) | 1.15 (1.01 to 1.31) | 1.16 (1.01 to 1.32) | 1.27 (1.11 to 1.45) | 1.39 (1.22 to 1.59) | <0.001 | <0.001 |
| **Mortality from diseases of the digestive system** (n for cases/person-years) | 1,561/7,783,132 | | 294/1,568,430 | 286/1,538,426 | 282/1,556,361 | 326/1,562,787 | 373/1,557,129 | | |
| Sex-adjusted model | 1.09 (1.03 to 1.15) | 0.002 | 1.00 (ref) | 1.06 (0.89 to 1.25) | 1.03 (0.87 to 1.22) | 1.15 (0.97 to 1.36) | 1.25 (1.06 to 1.48) | 0.005 | 0.05 |
| Main model | 1.08 (1.02 to 1.14) | 0.01 | 1.00 (ref) | 1.08 (0.91 to 1.28) | 1.05 (0.88 to 1.25) | 1.15 (0.97 to 1.37) | 1.22 (1.02 to 1.45) | 0.03 | 0.19 |

[a] Cut-offs for sex-specific quintiles of the FSAm-NPS DI were, for women: 4.14/5.35/6.43/7.68, for men: 4.32/5.55/6.63/7.88. A higher FSAm-NPS DI indicates a lower nutritional quality of the foods consumed.
[b] The sex-adjusted model was stratified for age (1-y interval) and study centre and adjusted for age (time-scale) and sex.
[c] The main model was stratified for age (1-y interval) and study centre and adjusted for age (time-scale), sex, body mass index, height, educational level (longer education, including university degree; technical/professional school; secondary school; primary school; missing), combined total physical activity (sex-specific categories: active; moderately active; moderately inactive; inactive; missing), smoking status and intensity of smoking (current, 1–15 cigarettes/d; current, 16–25 cigarettes/d; current, 26+ cigarettes/d; current, pipe/cigar/occasional; current/former, missing; former, quit 11–20 y; former, quit 20+y; former, quit ≤10 y; non-smoker; missing), baseline alcohol intake, baseline energy intake and personal history of cancer (yes; no), cardiovascular diseases (yes; no; missing) and diabetes(yes; no; missing).

Abbreviations: DI, Dietary Index; EPIC, European Prospective Investigation into Cancer and Nutrition; FSAm-NPS, Nutrient Profiling System of the British Food Standards Agency (modified version).

**Figure 1. Associations between the FSAm-NPS DI and all-cause mortality, Subgroup analyses, from multivariable Cox proportional hazards regression models, EPIC cohort, 1992–2015.** A higher FSAm-NPS DI indicates a lower nutritional quality of the foods consumed. The main model was stratified for age (1-y interval) and study centre and adjusted for sex, body mass index, height, educational level (longer education, including university degree; technical/professional school; secondary school; primary school; missing), combined total physical activity (sex-specific categories: active; moderately active; moderately inactive; inactive; missing), smoking status and intensity of smoking (current, 1–15 cigarettes/d; current, 16–25 cigarettes/d; current, 26+ cigarettes/d; current, pipe/cigar/occasional; current/former, missing; former, quit 11–20 y; former, quit 20+y; former, quit ≤10 y; non-smoker; missing), baseline alcohol intake, baseline energy intake and personal history of cancer (yes; no), cardiovascular diseases (yes; no; missing) and diabetes(yes; no; missing). P for interaction, obtained for each subgroup analysis from the likelihood ratio test of models with and without the interaction term, were as follows: sex, P=0.04; weight status, P=0.22; physical activity, P=0.23; smoking status, P<0.001; energy intake, P=0.05; alcohol intake, P=0.07; educational level, P=0.27. Abbreviations: DI, Dietary Index; EPIC, European Prospective Investigation into Cancer and Nutrition; FSAm-NPS, Nutrient Profiling System of the British Food Standards Agency (modified version)