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Adherence to French dietary guidelines is associated with a reduced risk of mortality in the E3N French prospective cohort

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Abstract

Background Diet is a modifiable risk factor for non-communicable diseases which are the major causes of death worldwide. French dietary guidelines, updated in 2017, provide recommendations for a healthier diet. We aimed to study the association between adherence to these dietary guidelines and mortality in the E3N (Etude Epidémiologique auprès de femmes de l'Education Nationale) French cohort. A secondary objective was to investigate the role of dietary exposure to chemical contaminants in this association.

Methods We studied 72 585 women of the E3N prospective cohort, which completed a food frequency questionnaire in 1993. We estimated adherence to French dietary guidelines using the simplified "*Programme National Nutrition Santé*—guidelines score 2" (sPNNS-GS2, range -20.4 to 12.6). We estimated the association between sPNNS-GS2 and all-cause or cause-specific mortality using Cox proportional hazard models. Causes of death were coded and validated by the French Epidemiology Center on Medical Causes of Death (Inserm-CépiDc).

Results During follow-up (1993–2014), we identified 6 441 deaths. The mean sPNNS-GS2 was 3.8 (SD 3.0). In the fully adjusted model, we found a non-linear association between sPNNS-GS2 and all-cause, all-cancer, breast cancer and lung cancer mortality (*p*-values for the overall association < 0.001), with a diminution of the risk as sPNNS-GS2 increases up to its median or 65th percentile (depending on the outcome), and then a plateau (for all-cause and breast cancer mortality) or an inversion of the trend (for all-cancer and lung cancer mortality). Furthermore, we identified a linear inverse association with cardiovascular diseases mortality (HR_{oneSTD} [95%CI]: 0.86 [0.76; 0.97]), and no association with colorectal cancer mortality. We observed similar results when additionally adjusting on dietary exposure to chemical contaminants.

Conclusions This study conducted in a large prospective cohort following more than 70 000 women for over 20 years suggested that higher adherence to French dietary guidelines was associated with a reduced risk of mortality from all-cause, cardiovascular diseases, all-cancer, breast cancer, and lung cancer, except for high values of adherence for lung cancer mortality. These results contribute to informing on the importance of following the French nutritional recommendations.

Keywords Diet, Guidelines, PNNS, Mortality, Cohort, Women

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Introduction

Non-communicable diseases (NCDs), such as cancers or cardiovascular diseases (CVDs), are major causes of death worldwide. In 2019, according to the World Health Organisation (WHO), seven of the ten worldwide leading causes of death were NCDs. Moreover, NCDs accounted for 74% of all deaths reported in 2019 [1]. In France in the same year, NCDs represented nine out of the ten major causes of death [2]. The risk of dying from an NCD increases with several modifiable risk factors, with unhealthy diet standing out as a major one [3]. Prevention and promotion of a healthy diet is therefore of major public health interest. In this context, food-based dietary guidelines (FBDGs) are developed to provide food consumption advice to the general population in order to promote health through a quality diet and prevent chronic diseases.

To investigate the association between diet and health, nutritional epidemiology focuses on different scales: the scale of nutrients, food items, or dietary patterns. As we never consume exclusively one food item (since food is part of a more complex diet), the first two approaches present some difficulties. Indeed, depending on the nutrient or food consumed, the association with different health outcomes can be positive or inverse [4]. Moreover, nutrients can interact with each other [5], resulting in non-additive health effects. In a real-life perspective, it is therefore essential to study the effect of the overall diet. To achieve this goal, one possibility is to develop a priori scores quantifying the quality of the whole diet, for example by measuring the degree of adherence to FBDGs. Moreover, in a public health perspective, it is important to confirm that FBDGs are relevant by studying the effect of adherence to these recommendations on various health outcomes.

French FBDGs, updated in 2017, were provided in the framework of the 4th National Nutrition and Health Program 2019–2023 (PNNS). To study the association between French dietary guidelines and health, a score of adherence to these guidelines was developed in 2019: the *Programme National Nutrition Santé* – guidelines score 2 (PNNS-GS2) [6, 7]. This score was an update of the PNNS-GS based on the previous recommendations included in the PNNS 2001–2005 [8].

In the NutriNet-Santé French cohort, PNNS-GS2 was associated with a lower risk of overweight and obesity [9] and type 2 diabetes [10]. PNNS-GS2 was also associated with a lower risk of death, CVDs, cancer and colorectal cancer [11]. This study also reported no association with breast cancer risk. In the E3N (Etude Epidémiologique auprès de femmes de l'Education Nationale) cohort, an inverse association was highlighted between adherence to the 2017 French dietary guidelines and type 2 diabetes [12]. Despite the evidence on the associations between this score and NCDs or all-cause mortality, there are no studies on mortality from these NCDs, notably cancer-specific mortality. Given the observed inverse associations of this score with NCDs, we hypothesised that there might be an inverse association between adherence to these guidelines and the risk of mortality attributed to these NCDs.

Finally, foods are a source of nutrients, but also contain chemical contaminants. However, FBDGs take only partially into account the dietary exposure to food chemical contaminants. For example, fish or fruits and vegetables, both promoted by FBDGs for their beneficial nutrients, are also the main sources of dietary exposure to polychlorinated biphenyls (PCBs) and pesticides, respectively. Moreover, some studies showed that complying with nutritional recommendations may lead to higher dietary exposure to chemical contaminants [13–16].

The main objective of our study was to investigate the effect of adherence to the 2017 French dietary guidelines on the risk of all-cause and cause-specific mortality in the E3N French prospective cohort. The secondary objective was to investigate the role of dietary exposure to chemical contaminants in this association by adjusting on dietary exposure to food chemical mixtures in order to estimate the direct effect of French dietary guidelines on mortality.

Material and methods

E3N cohort

The French E3N-Générations cohort initially included 98 995 women followed prospectively since 1990. It was then extended by including the women's children and the biological fathers of their children. The present study focuses only on the first generation of women, initially called the E3N cohort. Women were born between 1925 and 1950 and were covered by the French health insurance for workers of the national education system (MGEN). They received self-administered questionnaires every 2 or 3 years to collect lifestyle, anthropometric and health information [17, 18]. All participants provided consent to this study, which was approved by the French National Commission for Data Protection and Privacy (CNIL).

Dietary questionnaire

The dietary questionnaire (third questionnaire, Q3), sent in 1993, was a semi-quantitative food frequency questionnaire divided into two parts and containing 208 food items. The first part was divided into eight meal occasions and collected the frequency and amount of food and drinks consumed during the previous year. The second part requested more details about the food items

included in the food groups appearing in the first part. The validity and reproducibility of the E3N dietary questionnaire were previously confirmed [19].

The quantity consumed of each food item was multiplied by the frequency of consumption of this food item to estimate daily food intakes. Daily nutrient intakes were estimated through the French food composition table of the French Information Centre on Food Quality (CIQUAL) [20]. Adherence to a healthy or a western dietary pattern was calculated from principal component analysis (PCA), as previously described [21]. Moreover, adherence to the Mediterranean diet was also estimated [22]. Finally, the healthful plant-based diet index (hPDI) was developed [23].

Adherence to French dietary guidelines

The PNNS-GS2 is a validated score aiming to measure adherence to the 2017 French dietary guidelines [6, 7]. Following Chaltiel et al. protocol to build the PNNS-GS2, we adapted this score to the E3N cohort. As there was no information on organic food consumption in the E3N cohort, we used the simplified version of the PNNS-GS2, named sPNNS-GS2, which included only the main PNNS recommendations and thus no distinction between organic and non-organic food consumption. This score was based on 13 components: seven adequacy components ("fruits and vegetables", "nuts", "legumes", "wholegrain food", "milk and dairy products", "fish and seafood", "added fat") leading to positive or null points, and six moderation components ("red meat", "processed meat", "sugary foods", "sweet-tasting beverages", "alcoholic beverages", "salt") leading to positive, negative or null points. Each component food items, specific recommendation, cut-offs, translation into servings and scoring can be found in Chaltiel et al. and in Supplementary tables 1 and 2. We estimated the sugar content of sugary foods on the basis of their nutritional composition (CIQUAL, [20]). To obtain sPNNS-GS2, we calculated the sum of the 13 components, which were beforehand standardised (to avoid overrating components with a higher scoring) and weighed (to take into account the strength of evidence of the effect of this component on health). Finally, to avoid overestimating the score of overconsumers, we penalised the score on energy intake. The score sPNNS-GS2 can be positive or negative. Its maximum is 14.25. A higher sPNNS-GS2 reflects higher adherence to 2017 French dietary guidelines [6, 7].

Ascertainment of mortality

We collected deaths during the follow-up period, i.e., from baseline (date of answer to the dietary questionnaire sent in 1993) to the most recent update of the mortality database (i.e., November 2014). We obtained the vital status through the MGEN, postal services, municipal registries, physicians, or next of kin. The French centre of epidemiology on medical causes of death (Inserm-CépiDc) coded the causes of death according to the 9th (deaths before 2000) or 10th (deaths after 2000) international classification of diseases, respectively, as follows: 390–459 and I00-I99 for CVDs mortality, 140–208 and C00-C97 for all-cancer mortality, 174 and C50 for breast cancer mortality, 162 and C33-C34 for lung cancer mortality, and 153, 154.0–154.1 and C18-C20 for colorectal cancer mortality.

Study population

We included the 74 522 women who answered to the dietary questionnaire. We excluded 1 491 women considered as outliers as they were in the 1st or 99th percentile of the ratio of energy intake to energy requirements, and 446 women lost to follow-up. Our study population was therefore composed of 72 585 women for the all-cause mortality analyses. For all-cancer or CVDs mortality analyses, we further excluded 169 participants with unknown causes of death, resulting in a study population of 72 416 women. For specific-cancer mortality analyses, the study population included 72 238 participants as we additionally excluded 178 women because of unknown primary location of cancer leading to death. The flow chart is presented in Supplementary Fig. 1.

Statistical analyses

Covariates

When possible, we selected adjustment covariates in the 2nd questionnaire (Q2) sent in 1992 in order to respect temporality, as the dietary questionnaire (Q3) sent in 1993 collected dietary information of the previous year.

We defined covariates as follows: body mass index (BMI) at Q2 (continuous, kg/m^2), birth cohort ($\leq$1930, (1930 – 1935], (1935 – 1940], (1940 – 1945], $>$1945), education level ($<$12 years, 12 to 14 years, $>$14 years), smoking status at Q2 (never smoker, former smoker, current smoker), physical activity at Q3 (continuous, MET-hours/week), menopausal status combined with recent (i.e., during the last year) use of menopausal hormone therapy (MHT) at Q2 (premenopausal, menopausal and recent MHT use, menopausal and no recent MHT use, menopausal and no information on whether and when MHT was used), total energy intake at Q3 (continuous, kcal/day), and adherence to dietary scores (healthy dietary pattern, western dietary pattern, Mediterranean diet and healthful plant-based diet index) at Q3 (continuous).

In our analyses, we also considered dietary exposure to mixtures of food chemical contaminants. Food contamination levels were derived from the second French total diet study (TDS2) performed by the French Agency for

Food, Environmental and Occupational Health & Safety [24]. Briefly, between 2007 and 2009, 20 280 food items were purchased in 8 French regions to obtain 1 352 composite samples prepared as consumed (i.e., pealing, frying, etc.), according to French cooking habits, in order to analyse the presence of more than 400 food chemical contaminants [25]. We then merged the E3N dietary consumption database with the TDS2 food contamination database. We obtained the dietary intake of a given contaminant (in g of contaminant/day) by summing, over all food items, the product of the consumed quantity of the food item (in g of food/day) by the concentration of the contaminant in the food item (in g of contaminant/g of food) [26]. Finally, based on the dietary intake of 197 contaminants and using the sparse non-negative matrix under-approximation (SNMU dimension reduction method, we identified six mixtures of contaminants to which the E3N participants were most frequently exposed through the diet. Overall, the 6 mixtures explained 81% of the variance and were all correlated with each other. Mixture 1 was mostly composed of minerals, inorganic contaminants, and furans,mixture 2 of brominated flame retardants (BFRs), dioxins, PCBs, and furan; mixture 3 of mycotoxins, pesticide, and polycyclic aromatic hydrocarbons (PAHs); mixtures 4 and 5 of pesticides; mixture 6 of per- and polyfluoroalkyl substances (PFAS), BFRs, PCBs, selenium (Se), mercury (Hg), and furan [27]. More details on the methodology applied, the mixtures and their association with mortality risk can be found elsewhere [27, 28].

There was no missing data on dietary variables. We imputed covariates with less than 5% of missing values by the median for continuous variables or the modal category for categorical variables. When there were more than 5% of missing values, we created an "unknown value" category (only for menopausal status and recent MHT use).

Descriptive analyses

We described the baseline characteristics (mean and standard deviation (STD) for continuous variables, number and proportion for categorical variables) of the overall population, according to quartiles of sPNNS-GS2 and according to vital status. We also estimated the Spearman rank correlation coefficients between sPNNS-GS2 and 24 food groups' consumption, four dietary scores or weights of adherence to the six mixtures of contaminants.

Main analyses

We used Cox proportional hazard models with age (continuous, years) as the time-scale to estimate hazard ratios (HR) and their 95% confidence intervals (CI) of the association between sPNNS-GS2 and the risk of all-cause, CVDs, all-cancer, and breast, lung or colorectal cancer mortality. We followed participants from the age of answer to the dietary questionnaire sent in 1993 to the age at death, at the last completed questionnaire, or at the end of the follow-up (i.e., last update of the mortality database in November 2014), whichever came first. For cause-specific mortality analyses, we censored all other causes of death at the age of death.

We divided our main exposure variable sPNNS-GS2 by its STD to estimate HR per one STD increment.

We tested four different models, selecting adjustment variables through literature knowledge and through a directed acyclic graph (DAG, https://www.dagitty.net/) (Supplementary Fig. 2). We only adjusted model 1 on age as time-scale. We additionally adjusted model 2 on BMI, birth cohort, education level, smoking status, physical activity, and menopausal status combined with recent MHT use. We further adjusted model 3, our main model, on total energy intake. Finally, we also performed model 4, corresponding to model 3 with an additional adjustment on the weights of adherence to the six mixtures of contaminants, to close the indirect causal path through chemical mixtures in order to estimate the direct effect of sPNNS-GS2 on mortality (Supplementary Fig. 2).

To take potential non-linear relationships into account, we modelled continuous variables with restricted cubic spline functions when the *p*-value of the non-linearity test was below 0.1, or as a linear term otherwise. For the main exposure variable, we tested models with 3 (at the 10^{th}, 50^{th} and 90^{th} percentiles), 4 (at the 5^{th}, 35^{th}, 65^{th} and 95^{th} percentiles) or 5 nodes (at the 5^{th}, 27.5^{th}, 50^{th}, 72.5^{th} and 95^{th} percentiles) and selected the one with the smallest Akaike information criterion (AIC) value. We modelled continuous covariates with 4 knots, as suggested by Harrell [29].

We considered as statistically significant a *p*-value strictly lower than 0.05. We used the Statistical Analysis System software package version 9.4 to build the database (SAS Institute, Cary, North California), and R version 4.1.2 to perform the statistical analyses. The STROBE-nutreporting guidelines were used [30].

Sensitivity analyses

We performed the analyses between sPNNS-GS2 and mortality risk in models 1, 2, 3 and 4 in quartile groups to compare the association between the highest versus the lowest (as reference) category of sPNNS-GS2 and mortality. Finally, on model 3 and for all-cause mortality, we studied the potential reverse causation bias by 1) including a 5-year exposure lag and 2) excluding participants who died or were censored during the first five years of follow-up.

Results

General characteristics

During an average of 19.0 years (STD 4.1) of follow-up, we identified 6 441 deaths, among which 896 from CVDs, 3 473 from all-cancer, 953 from breast cancer, 364 from lung cancer, and 317 from colorectal cancer.

We presented baseline characteristics of the study population overall and among each quartile group of sPNNS-GS2 in Table 1, and according to vital status in Supplementary Table 3. In our study population, sPNNS-GS2 was on average 3.8 (STD 3.0). It ranged from −20.4 to 12.6, with a median of 3.9 (IQR 1.9–5.9). Compared to women in the 1st quartile group of sPNNS-GS2, women in the 4th quartile group were on average older (53.8 years vs 52.0 years), more frequently never smokers (59.8% vs 50.4%), and they had a lower mean total energy intake (1 795.9 kcal/day vs 2 723.2 kcal/day).

We presented the estimated Spearman rank correlation coefficients between sPNNS-GS2 and food groups, four dietary scores or weights of adherence to the six mixtures of contaminants in Supplementary Table 4. We identified positive correlations with fruits and vegetables consumption and tea consumption, and negative correlations with all other food groups, such as dairy products,

Table 1 Baseline characteristics[a] of the study population overall and among each quartile group of sPNNS-GS2 in the E3N cohort (*N* = 72 585)

		sPNNS-GS2			
	All	**Q1 (−20.4–1.9)**	**Q2 (1.9–3.9)**	**Q3 (3.9–5.9)**	**Q4 (5.9–12.6)**
	(*N* = 72 585)	**(*N* = 18 146)**	**(*N* = 18 188)**	**(*N* = 18 070)**	**(*N* = 18 181)**
sPNNS-GS2	3.8 (3.0)	0.0 (1.9)	2.9 (0.6)	4.9 (0.6)	7.4 (1.2)
Age (years)	52.9 (6.7)	52.0 (6.5)	52.8 (6.7)	53.1 (6.7)	53.8 (6.8)
Follow-up duration (years)	19.0 (4.1)	19.0 (4.2)	19.0 (4.2)	19.0 (4.2)	19.0 (4.1)
Follow-up duration (person-years)	1 378 046	344 149	345 461	343 360	345 076
BMI (kg/m^2)	22.7 (3.1)	22.8 (3.2)	22.7 (3.1)	22.7 (3.1)	22.8 (3.1)
< 18.5	2 645 (3.6)	670 (3.7)	658 (3.6)	661 (3.7)	656 (3.6)
[18.5 – 25)	56 794 (78.2)	14 156 (78.0)	14 298 (78.6)	14 147 (78.3)	14 193 (78.1)
≥ 25	13 146 (18.1)	3 320 (18.3)	3 232 (17.8)	3 262 (18.1)	3 332 (18.3)
Birth cohort					
≤ 1 930	7 295 (10.1)	1 475 (8.1)	1 777 (9.8)	1 908 (10.6)	2 135 (11.7)
(1 930 – 1 935]	9 996 (13.8)	2 020 (11.1)	2 422 (13.3)	2 569 (14.2)	2 985 (16.4)
(1 935 – 1 940]	14 710 (20.3)	3 325 (18.3)	3 631 (20.0)	3 757 (20.8)	3 997 (22.0)
(1 940 – 1 945]	17 811 (24.5)	4 640 (25.6)	4 466 (24.6)	4 416 (24.4)	4 289 (23.6)
> 1 945	22 773 (31.4)	6 686 (36.9)	5 892 (32.4)	5 420 (30.0)	4 775 (26.3)
Education level					
< 12 years	8 190 (11.3)	2 007 (11.1)	2 010 (11.1)	2 073 (11.5)	2 100 (11.6)
12 to 14 years	38 408 (52.9)	9 270 (51.1)	9 596 (52.8)	9 662 (53.5)	9 880 (54.3)
> 14 years	25 987 (35.8)	6 869 (37.9)	6 582 (36.2)	6 335 (35.1)	6 201 (34.1)
Smoking status					
Never	40 286 (55.5)	9 136 (50.4)	9 969 (54.8)	10 315 (57.1)	10 866 (59.8)
Former	23 139 (31.9)	5 926 (32.7)	5 867 (32.3)	5 733 (31.7)	5 613 (30.9)
Current	9 160 (12.6)	3 084 (17.0)	2 352 (12.9)	2 022 (11.2)	1 702 (9.4)
Physical activity (MET-hours/week)	46.4 (43.4)	47.5 (44.4)	46.1 (43.0)	45.4 (41.5)	46.6 (44.3)
Menopausal status and recent use of MHT					
Premenopausal	37 313 (51.4)	10 406 (57.4)	9 553 (52.5)	9 007 (49.9)	8 347 (45.9)
Menopausal and recent MHT use	10 047 (13.8)	2 253 (12.4)	2 494 (13.7)	2 570 (14.2)	2 730 (15.0)
Menopausal and no recent MHT use	21 671 (29.9)	4 624 (25.5)	5 271 (29.0)	5 636 (31.2)	6 140 (33.8)
Menopausal and no information on whether and when MHT was used	3 554 (4.9)	863 (4.8)	870 (4.8)	857 (4.7)	964 (5.3)
Total energy intake (kcal/day)	2 210.6 (560.8)	2 723.2 (570.7)	2 301.5 (447.7)	2 021.4 (386.5)	1 795.9 (321.6)

[a] Mean (std) for continuous variables, N (%) for categorical variables

sweet products, starch foods, meat and charcuterie, fats, fish and seafood or alcohol consumption. Moreover, we found positive correlations with Mediterranean diet (0.09), healthful plant-based diet index (0.49) and healthy dietary pattern (0.10), and negative correlation with western dietary pattern (−0.66). We also highlighted negative correlations with the weights of adherence to mixtures 1 (−0.50), 2 (−0.44), 3 (−0.42) and 6 (−0.17), and positive correlations with the weights of adherence to mixtures 4 (0.08) and 5 (0.16).

sPNNS-GS2 and mortality

We presented the results of the association between sPNNS-GS2 and mortality risk in models 1, 2, 3 and 4 in Table 2, and the related restricted cubic spline graphs in Fig. 1.

In our main model (model 3), we observed a statistically significant and non-linear association between sPNNS-GS2 and all-cause, all-cancer, breast cancer and lung cancer mortality risk (*p*-values for the overall association < 0.001), with a diminution of the risk as

Table 2 Hazard ratios (95% CI) estimated by Cox multivariable regression models for the association between sPNNS-GS2 and mortality risk in the E3N cohort (*N* = 72 585)

		N deaths / Person-years	Model 1 HR [95% CI][a]	Model 2 HR [95% CI][a]	Model 3 HR [95% CI][a]	Model 4 HR [95% CI][a]
All-cause mortality (*N* = 72 585)	**sPNNS-GS2 (spline with 4 knots)**	6 441 / 1 378 046				
	p-value for the overall association		< 0.001	< 0.001	< 0.001	< 0.001
	p-value for the non-linearity test		0.012	0.026	0.004	0.002
All-cancer mortality (*N* = 72 416)	**sPNNS-GS2 (spline with 4 knots)**	3 473 / 1 375 276				
	p-value for the overall association		< 0.001	< 0.001	< 0.001	< 0.001
	p-value for the non-linearity test		0.010	0.015	0.001	0.001
Cardiovascular diseases mortality (*N* = 72 416)	**sPNNS-GS2 (linear term)**	896 / 1 375 276	0.93 [0.85; 1.02]	0.96 [0.87; 1.05]	0.86 [0.76; 0.97]	0.84 [0.74; 0.95]
	p-value		0.135	0.355	0.012	0.007
	p-value for the non-linearity test		0.986	0.847	0.993	0.973
Breast cancer mortality (*N* = 72 238)	**sPNNS-GS2 (spline with 3 knots)**	953 / 1 373 148				
	p-value for the overall association		0.004	0.002	< 0.001	< 0.001
	p-value for the non-linearity test		0.090	0.100	0.007	0.007
Lung cancer mortality (*N* = 72 238)	**sPNNS-GS2 (spline with 4 knots)**	364 / 1 373 148				
	p-value for the overall association		< 0.001	0.003	< 0.001	0.001
	p-value for the non-linearity test		< 0.001	0.001	< 0.001	< 0.001
Colorectal cancer mortality (*N* = 72 238)	**sPNNS-GS2 (linear term)**	317 / 1 373 148	0.85 [0.73; 0.99]	0.86 [0.74; 1.00]	0.86 [0.70; 1.04]	0.90 [0.73; 1.12]
	p-value		0.036	0.052	0.120	0.343
	p-value for the non-linearity test		0.133	0.120	0.121	0.106

Model 1: Adjustment on age (years) as time-scale

Model 2: M1 + BMI (kg/m^2), physical activity (MET-hours/week), birth cohort (≤ 1930, (1930 – 1935], (1935 – 1940], (1940 – 1945], > 1945), education level (< 12 years, 12 to 14 years, > 14 years), smoking status (never smoker, former smoker, current smoker), menopausal status and recent MHT use (premenopausal, menopausal and recent MHT use, menopausal and no recent MHT use, menopausal and no information on whether and when MHT was used)

Model 3: M2 + total energy intake (kcal/day)

Model 4: M3 + weights of adherence to the six mixtures of food chemical contaminants

[a] We present the results of linear associations between sPNNS-GS2 and mortality risk with HR [95% CI] per one standard deviation, *p*-value and *p*-value for the non-linearity test, and of non-linear associations with *p*-values for the overall association and for the non-linearity test

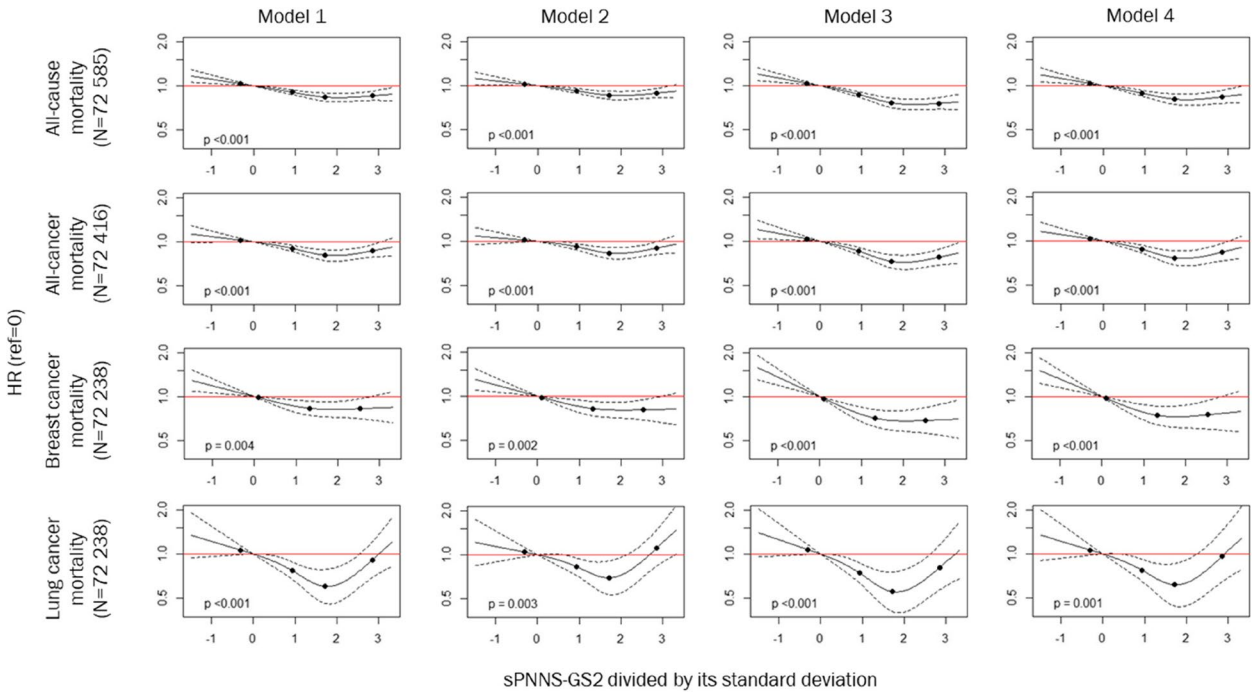

Fig. 1 Restricted cubic splines of sPNNS-GS2 in models 1, 2, 3 and 4 in association with mortality risk in the E3N cohort (*N* = 72 585). The null is taken as reference. The "p" represents the *p*-value for the overall association. Solid lines indicate HR, and dashed lines indicate 95% CI. The points represent percentiles as follows: 3 nodes at the 10th, 50th and 90th percentiles, 4 nodes at the 5th, 35th, 65th and 95th percentiles, or 5 nodes at the 5th, 27.5th, 50th, 72.5th and 95th percentiles. To facilitate the readability of the results, the graph represents the association between sPNNS-GS2 and mortality for sPNNS-GS2 values ranging from the 1st to the 99th percentile

sPNNS-GS2 increases up to its median (for breast cancer mortality) or its 65th percentile (for all-cause, all-cancer and lung cancer mortality), and then a plateau (for all-cause or breast cancer mortality) or an inversion of the trend (for all-cancer or lung cancer mortality) (Table 2 and Fig. 1). Moreover, we observed linear associations between sPNNS-GS2 and CVDs or colorectal cancer mortality. We highlighted a statistically significant inverse association between sPNNS-GS2 and CVDs mortality (model 3: HR 0.86, 95%CI 0.76–0.97), and no statistically significant association with colorectal cancer mortality (model 3: HR 0.86, 95%CI 0.70–1.04) (Table 2).

In model 4, corresponding to model 3 additionally adjusted on the weights of adherence to the six mixtures of contaminants, we observed similar results to those obtained in model 3 in terms of statistical significance and shapes of the associations (Table 2 and Fig. 1).

Sensitivity analyses

In the analyses investigating the associations between quartile groups of sPNNS-GS2 and mortality risk, we observed similar results to those obtained with continuous sPNNS-GS2, except for CVDs mortality for which the association was not statistically significant in any of the quartile groups, probably partly due to limited statistical power (Supplementary Table 5). Finally, we highlighted unchanged results when including a 5-year exposure lag, and excluding participants who died or were censored during the first five years of follow-up (data not shown).

Discussion

In this large prospective study, we observed non-linear associations between sPNNS-GS2 and all-cause, all-cancer, breast cancer and lung cancer mortality. We also highlighted a linear inverse association with CVDs mortality, and no association with colorectal cancer mortality. We also noted unchanged results when additionally adjusting our model on the weights of adherence to six mixtures of food chemical contaminants.

Our estimation of mean sPNNS-GS2 was 3.8 (STD 3.0), which was close to the estimation of sPNNS-GS2 in women in the NutriNet-Santé cohort (mean 2.2, STD 3.3) [6].

Only one study, conducted in the NutriNet-Santé cohort, investigated the association between PNNS-GS2 and mortality [11]. Our results on all-cause mortality were very similar to those obtained in this study, as the authors observed that PNNS-GS2 was inversely associated with non-accidental mortality. However, contrary

to our results, the authors observed a linear association between PNNS-GS2 and non-accidental mortality. This difference may come from the different study populations, the different exposure variables and outcomes (PNNS-GS2 and non-accidental mortality in the NutriNet-Santé study vs sPNNS-GS2 and all-cause mortality in our study), and the linearity test applied (in the unadjusted model with Martingale residuals in the NutriNet-Santé study vs restricted cubic spline functions in the fully adjusted model in our study). Moreover, in this study, the authors also observed an inverse association between PNNS-GS2 and the incidence of cancer and CVDs, consistent with our results that showed an inverse association with cancer and CVDs mortality risk. Finally, the authors observed no association with the incidence of breast cancer and an inverse association with the incidence of colorectal cancer, contrasting with the present study findings of an inverse association with breast cancer mortality and no association with colorectal cancer mortality.

A systematic review of 153 studies highlighted that a healthy dietary pattern (high in fruits and vegetables, legumes, nuts, whole grains, vegetable oils, fish, lean meat or poultry, and low in red and processed meat, high-fat dairy and refined carbohydrates) was associated with a lower risk of all-cause mortality, which is in line with our results on all-cause mortality, as the sPNNS-GS2 would probably be high in participants following this healthy dietary pattern [31]. Consistent with our results, some systematic reviews and meta-analyses focusing on adherence to diets from specific geographic areas characterised by high-quality diets, such as the Mediterranean Diet (consisting of a high intake of olive oil, legumes, fruits, vegetables, nuts, and fish, moderate intake of dairy products, and low intake of meat and processed meat products), the Nordic diet (rich in fruits, vegetables, whole grains, fish, rapeseed oil, fish and low-fat dairy products, and poor in processed meat and alcohol) and the Japanese-style diet (characterised by the intake of vegetables, fruits, fish, soy products, green tea, seaweed, mushrooms, pickles, rice, and meat) observed inverse associations with all-cause mortality [32], all-cause, cancer and CVDs mortality [33], and CVDs mortality [34], respectively. Finally, several systematic reviews and meta-analyses studying Healthy Eating Index (HEI), Alternate Healthy Eating Index (AHEI), healthy plant-based diet (hPDI) and Dietary Approaches to Stop Hypertension Score (DASH), four diet quality scores, concluded that these scores are associated with a lower risk of all-cause, cancer and CVDs mortality [35–38]. In their study, Soltani et al. highlighted that these inverse associations were monotonic but non-linear [37].

As far as we know, no other studies investigated the association between PNNS-GS2 and specific-cancer mortality. However, our results are indirectly consistent with some previous studies performed on dietary patterns and specific cancer incidence. A systematic review on dietary patterns and cancer incidence observed an inverse association between postmenopausal breast cancer incidence and dietary patterns rich in vegetables, fruits, and whole grains, and poor in animal products and refined carbohydrates (with moderate evidence), which was in line with our results on breast cancer mortality [39]. The authors also concluded (with limited evidence) for an inverse association between lung cancer incidence and a diet rich in vegetables, fruits, seafood, grains and cereals, legumes and lean fat meats and poor in dairy products and fat meats, which was consistent with our results on lung cancer mortality [39]. Finally, in contrast to our findings on colorectal cancer mortality, these authors highlighted an inverse association between colorectal cancer incidence and a diet rich in vegetables, fruits, legumes, whole grains, lean meats, seafood, and low-fat dairy, and low in red and processed meats, saturated fat, sugar-sweetened beverages and sweets, with moderate supporting evidence [39].

Adherence to French dietary guidelines was inversely associated with many causes of death. If these results are confirmed in other studies, its adequacy components (fruits and vegetables, nuts, legumes, whole-grain food, milk and dairy products, fish and seafood, and added vegetable fat) should be promoted, and its moderation components (red meat, processed meat, sugary foods, sweet-tasting beverages, alcoholic beverages, and salt) should be limited: this is thus in adequacy with other dietary guidelines, reflecting the widespread benefits of applying French dietary recommendations, beyond just the French population.

Moreover, our results remained unchanged after additionally adjusting the main model on the weights of adherence to six mixtures of food chemical contaminants to which the E3N participants were most frequently exposed through their diet. To our knowledge, this was the first study considering dietary exposure to chemical mixtures in an epidemiological setting investigating the association between dietary guidelines and health. Some studies observed that complying with nutritional recommendations may lead to higher dietary exposure to contaminants [13–16], which was consistent with our descriptive results concerning mixtures 4 and 5, mainly characterised by dietary intake of pesticides, but contrary to our results on other mixtures. However, we didn't highlight harmful health implications of this increase of exposure to mixtures 4 and 5 when better complying with French

dietary guidelines. One possibility is that the levels of chemical contaminants in the recommended foods are still within acceptable safety limits, thereby not posing an immediate health risk. Another hypothesis could be that the potential health risks associated with dietary exposure to chemical contaminants may be mitigated by the protective effects of other components present in the recommended foods. Further research is warranted to explore these hypotheses and better understand the complex interplay between adherence to dietary guidelines, dietary exposure to chemical contaminants, and overall health outcomes.

We have to take into account some limitations when interpreting the results obtained by the present study. The first one is that the E3N cohort is composed of volunteer women, with a probable interest for health, and who are leaner and with a higher school education level compared to the general population, which limits the generalisability of our results [17]. However, comparisons between high and low adherence to French dietary guidelines remain possible. Moreover, dietary data in the E3N cohort are self-reported, which may have resulted in measurement errors, especially due to memory bias and social desirability bias. In addition, we have only one estimate of the diet (at baseline), while we cannot exclude that the dietary habits may have changed during the long follow-up. Therefore, it would be useful to have dietary estimates at various time points of the follow-up and to study the trajectories of sPNNS-GS2 over time. However, a previous study suggested that the diet of middle-aged women remains stable over time [40], which would result in a stable sPNNS-GS2. Finally, despite our many adjustment variables, we cannot completely exclude the risk of residual confounding, especially when studying a dietary score, as dietary habits are closely linked to lifestyle and health consciousness.

Our study also benefits from several strengths. Its prospective design enables us to study more than 70 000 women for an average of 19 years, allowing to investigate the long-term health effects of diet. The large number of participants and cases ensures a good statistical power. The stable results of the sensitivity analyses suggest the robustness of the results. All death cases are validated by the Inserm-CépiDc. Thanks to the large number of deaths, we are able to obtain results on specific-cancer mortality. Moreover, the dietary questionnaire of the E3N cohort was previously validated, which limits measurement errors [19]. The PNNS-GS2 was previously validated by experts [6]. Finally, the large number of quality data available in the E3N cohort allows to take into account a large number of confounding factors in our analyses.

Conclusion

To conclude, we observed that higher adherence to French dietary guidelines is associated with a reduced risk of mortality from all-cause, CVDs, all-cancer, breast cancer and lung cancer, except for high values of adherence for lung cancer mortality. Our results further confirmed the importance of following the French dietary guidelines and highlighted their importance in preventing mortality from NCDs. Finally, the reduced risk observed for numerous and various mortality outcomes highlighted the public health importance of these guidelines.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12937-025-01099-4.

Supplementary Material 1.

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Authors' contributions
All authors contributed to the study conceptualization and methodology. CM performed statistical analyses. CM wrote the first draft of the manuscript and all authors reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets analysed during the current study are not publicly available due to privacy reasons but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All participants provided consent to this study, which was approved by the French National Commission for Data Protection and Privacy (CNIL).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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