Cardiovascular disease risk and the balance between animal-based and plant-based foods, nutritional quality, and food processing level in the French NutriNet-Santé cohort: a longitudinal observational study

Clémentine Prioux,[a,*] Emmanuelle Kesse-Guyot,[a] Bernard Srour,[a] Léopold K. Fézeu,[a] Julia Baudry,[a] Sandra Wagner,[b] Serge Hercberg,[a] Mathilde Touvier,[a] and Benjamin Allès[a]

[a]Université Sorbonne Paris Nord and Université Paris Cité, Inserm, INRAE, CNAM, Nutritional Epidemiology Research Team (EREN), Center of Research in Epidemiology and StatisticS (CRESS), 74 Rue Marcel Cachin, F-93017, Bobigny, France
[b]University of Lorraine, Inserm CIC 1433, Nancy CHRU, Inserm U1116 DCAC, FCRIN, INI-CRCT, 4 Rue du Morvan, 54500, Vandoeuvre-lès-Nancy, France

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Summary

Background Few studies have evaluated the effects of plant-based diets combined with ultra-processed food on cardiovascular diseases (CVD). The objective of this study was to assess associations between CVD risk and novel diet indices that integrate balance between plant-based and animal-based foods, nutritional quality and processing level.

Methods We analyzed data from the French NutriNet-Santé prospective cohort. First, the two original healthy Plant-Based Diet and unhealthy Plant-Based Diet Indices (hPDI and uPDI) were computed. Four new indices were then built, based on the hPDI and uPDI computation, but with a multiplying factor to account for (i) the contribution of unprocessed food (UnPF) and (ii) the contribution of ultra-processed food (UPF), using the NOVA classification, culturally adapted. These two contributions (UnPF and UPF) were estimated using dietary data from 24 h records as percentages of total food consumed (g.day^{-1}). The association between each of the six resulting index scores and cardiovascular disease (cerebrovascular and coronary) was estimated using multivariate Cox proportional hazards models adjusted for confounding factors. Sensitivity analyses were also performed to assess the robustness of these novel indices.

Findings Among 63,835 participants, median follow-up time 9.0 years, IQR: 5–13 years, 76% women, mean age 51.4, SD = 10.2, no statistically significant protective or deleterious association was observed between those adhering to a nutritionally healthy but ultra-processed plant-based diet (hPDI-UPF), and a nutritionally unhealthy but unprocessed plant-based diet (uPDI-UnPF). When comparing participants with the highest adherence to a nutritionally healthy and unprocessed plant-based diet (hPDI-UnPF), to those with the lowest, we observed a 44% lower incidence of coronary heart disease ($HR_{D10\ vs.\ D1}$: 0.56, 95% CI: [0.42–0.75]) and 32% lower risk for CVD ($HR_{D10\ vs.\ D1}$: 0.68, 95% CI: [0.53–0.88]). Similarly, participants with the highest adherence to an unhealthy and ultra-processed plant-based diet (uPDI-UPF) had a 46% higher incidence of coronary heart disease ($HR_{D10\ vs.\ D1}$: 1.46, 95% CI: [1.11–1.93]), and a 38% higher incidence of CVD ($HR_{D10\ vs.\ D1}$: 1.38, 95% CI: [1.09–1.76]). This was the strongest association observed in our study.

Interpretation The findings of this study mark the importance of considering not only balance between plant-based and animal-based foods, but also nutritional quality and degree of processing when evaluating association between diet and cardiovascular risk.

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Abbreviations: BMI, Body mass index; CI, Confidence interval; CU, Consumption unit; CVD, Cardiovascular diseases; FFQ, Food frequency questionnaire; hPDI, Healthy plant-based diet index; HR, Hazard ratio; IPAQ, International Physical Activity Questionnaire; PDI, Plant-based diet index; SFA, Saturated fatty acid; uPDI, Unhealthy plant-based diet index; UPF, Ultra-processed food; UnPF, Unprocessed food

*Corresponding author. Université Sorbonne Paris Nord, Inserm, INRAE, CNAM, Nutritional Epidemiology Research Team (EREN), Center of Research in Epidemiology and StatisticS (CRESS), 74 Rue Marcel Cachin, F-93017, Bobigny, France.

E-mail address: clementine.prioux@eren.smbh.univ-paris13.fr (C. Prioux).

Keywords: Plant-based diets; Ultra-processed foods; Cardiovascular diseases

Research in context

Evidence before this study

Current evidence indicate that well-balanced plant-based diets are associated with a reduced risk of cardiovascular diseases (CVD), but not all plant-based diets are equivalent in terms of nutritional quality, and also in terms of levels of food processing. In May 2025, we conducted a PubMed search using the following terms: ((“ultra-processed foods” OR “ultra-processed foods” OR “ultra-processed food” OR “ultra-processed food” OR “unprocessed foods”) AND (“cardiovascular diseases” OR “cardiovascular diseases” OR “cardiovascular mortality” OR “cardiovascular health”) AND (“plant-based diet” OR “plant-based”)). We found two studies that considered, in their research, both the origin (plant-based vs. animal-based) and the level of food processing separately, but not integrated in a single diet indicator. The first study, was conducted in the EPIC-NL cohort and investigated the associations between nutritionally healthy (hPDI) and unhealthy (uPDI) plant-based diets and all-cause mortality, stratifying by the consumption of UPF. The second study, was conducted in the UK Biobank cohort and investigated with indicators the role of non ultra-processed and ultra-processed plant-based foods on cardiovascular outcomes.

Added value of this study

In contrast of these two studies, our approach aimed to provide a more comprehensive evaluation of plant-based diets developing new dietary indices that integrate altogether the rebalance between plant-based and animal-based foods, the nutritional quality (hPDI vs. uPDI), and the degree of processing (Unprocessed foods–UnPF vs. Ultra-processed Foods–UPF). We conducted validation analyses to assess the robustness of the PDI-food processing indices or scores that indicated a good internal validity of these scores. We then assessed the relationships between these indicators and CVD, no significant associations were found for hPDI-UPF or uPDI-UnPF; suggesting that UPF consumption “attenuates” somehow the protective role of healthy plant foods. The participants adhering the most to a nutritionally healthy and unprocessed plant-based diet (hPDI-UnPF) had a 44% lower incidence of coronary heart disease and 32% lower risk for CVD, whereas participants adhering the most to unhealthy and ultra-processed foods plant-based diet (uPDI-UPF) had a 46% higher incidence of coronary heart disease and a 38% greater incidence of CVD.

Implications of all the available evidence

Our findings reinforce the necessity of simultaneously considering the rebalance between plant- and animal-based foods, their nutritional quality and the degree of processing level of foods in dietary recommendations, advocating not only for a reduction in animal products but also encouraging again the consumption of minimally processed plant-based foods to improve cardiovascular health.

Introduction

Cardiovascular diseases (CVD) are the leading cause of mortality worldwide[1] and a major public health issue. In 2021, these conditions accounted for 21% of total mortality.[1] They are a substantial socioeconomic burden for many countries, especially in Europe and North and South America, where they are a significant source of morbidity and entail numerous hospitalizations and prolonged medical care.[2]

Preventing CVD is a recognized public health priority, and dietary guidelines play a key role in this effort.[3] An increasing number of national dietary guidelines from European countries,[4,5] from learned societies such as the American Heart Association[6] and from WCRF/AICR[7] (including the scores derived from these guidelines) advocate diets rich in plant-based foods, while also considering the degree of food processing using the NOVA classification. These diets are characterized by greater consumption of plant-based foods, including fruits, vegetables, whole grains, and legumes, with correspondingly lower consumption of red and processed meats, and of high-fat and high-salt dairy products (e.g., cheese).

Current evidence shows that plant-based diets, when well-balanced, are associated with a reduced risk of CVD.[8] However, not all plant-based diets are equivalent either in terms of nutrient profile[9] or in terms of how much ultra-processed/unprocessed food they contain, two separate dimensions of diet quality.[10] For example, diets that include a high proportion of ready-to-eat meals such as canned vegetable soups, or industrially packaged whole bread with additives, and a low proportion of minimally or unprocessed foods, may be healthy in terms of nutritional quality, but count as ultra-processed. In recent years, the consumption of ultra-processed foods has grown significantly worldwide.[11] An umbrella review highlighted that higher consumption of ultra-processed foods was associated with higher risks of cardiovascular, coronary heart, and cerebrovascular diseases.[12]

Thus nutritional quality (e.g., the quantity of sugar or fibers in foods) and the level of food-processing (unprocessed vs. ultra-processed) are now acknowledged as two separate and complementary dimensions to be considered when assessing beneficial or detrimental effects of diets on human health.[10,13,14]

Few studies have specifically integrated level of processing of plant-based foods when correlating plant-based diets to risk of CVD, particularly in Europe. To our knowledge, only two studies have considered both dimensions in their research.[15,16] The first study, conducted in the EPIC-NL cohort, investigated the associations between nutritionally healthy (hPDI) and unhealthy (uPDI) plant-based diets and all-cause mortality, stratifying by consumption of UPF.[15] This study reported that a decreased risk of mortality for hPDI was observed only in the three lowest quartiles of UPF consumption, with a nonsignificant association among the highest consumers of UPF. The second study, conducted in the UK Biobank cohort, found that a higher intake of plant-based non-UPF was associated with a lower risk of CVD. By contrast, the consumption of plant-based UPF and animal UPF was linked to an increased risk of CVD.[16] However, these studies did not use indicators for the following three components: proportion of nutritionally healthy and unhealthy plant food, limited intake of animal-based foods, and level of food processing. Such indicators could be used to directly assess the relationship between diets that are both plant-sourced and mostly composed of UPF or UnPF, and cardiovascular outcomes in a single model, instead of conducting complex stratified analyses[15] or using substitution analyses.[16]

The purpose of the present study was to develop novel indices to characterize diet by integrating balance between dietary proportions of plant-based foods and their nutritional quality (healthy vs. unhealthy), and processing level of foods (unprocessed vs. ultra-processed). Our study used data from the NutriNet-Santé cohort to assess the potential association of these variables with the risk of incident cardiovascular diseases. Specifically, it estimated the associations between four plant-based diet indices, namely (i) healthy plus ultra-processed, (ii) healthy plus unprocessed, (iii) unhealthy plus ultra-processed, and (iv) unhealthy plus unprocessed (noted hPDI-UPF, hPDI-UnPF, uPDI-UPF, and uPDI-UnPF), and incidence of CVD.

Methods

Study population

The study population was selected from the NutriNet-Santé cohort, a prospective observational web-based cohort study launched in May 2009 in France. Its main purpose was to analyze the relationships between nutrition and health, together with the determinants of eating behaviors and nutritional status. This cohort includes volunteers aged 15 years or older, recruited continuously from the general population, provided they have Internet access.

The study complies with the Declaration of Helsinki and was approved by the Inserm Ethics Evaluation Committee (IRB Inserm No. 0000388FWA00005831) and the French National Commission on Informatics and Liberty (CNIL) (Nos. 908450 and 909216). Electronic informed consent is systematically obtained from participants. The clinical trial registration number is NCT03335644. The methodological details of this study are described elsewhere.[17]

Data collection

Health data

Participant health data were collected through multiple channels: an extensive annual health questionnaire, a follow-up questionnaire every six months, and a dedicated interface on the study website enabling participants to report a health event, medical examinations and treatments at any time. When a new health issue was reported, participants were asked to provide their medical records (diagnoses, hospital discharge summaries, radiological examinations, electrocardiograms). If these documents were unavailable or additional information was needed, the research team contacted the referring healthcare professionals (general practitioners, specialists, and hospital facilities) to gather more details. A medical committee then reviewed these data to validate and code major health events. Additionally, to ensure comprehensive identification of cases, the study received authorization from the French Council of State (No. 2013-175) to link participant data with the French National Health Insurance administrative databases (SNIIRAM). Vital status and causes of death were obtained via the National Registry of Medical Causes of Death (CépiDC), accessible without specific authorization. Cardiovascular events were classified according to the International Classification of Diseases, 10th Revision (ICD-10). The study focused on the first validated incident cases of CVD, including myocardial infarction, acute coronary syndrome, angioplasty, and both ischemic and hemorrhagic strokes.

Dietary data

Participant dietary intake was assessed using three 24-h dietary records, completed at baseline and then every six months. These recording days were randomly assigned over a two-week period and included two weekdays and one weekend day to account for variations in eating habits across different days.[18] During each reporting period, participants recorded all foods and beverages consumed, including the three main meals (breakfast, lunch, and dinner) and any snacks and beverages between meals. Portion sizes were estimated using photographs from a previously validated photo booklet[19] or standardized containers, or entered directly in grams or milliliters through a dedicated web platform. Daily intakes of energy, macronutrients, fiber, micronutrients, and alcohol were calculated using a food composition database that includes approximately 3500 foods and beverages.[20] For mixed dishes, nutrient contributions were estimated based on standardized

French recipes, validated by nutrition professionals. To ensure data quality, the dietary records were validated by comparing them with interviews conducted by dieticians, and with blood and urinary biomarkers.[21] Participants who underreported their energy intake were identified using Black's method.[22] The average food intake from 24-h dietary records collected during the first two years of follow-up was calculated to set the indices, using the mean of at least three completed records within this period.

Plant-based diet indices (PDIs): Healthy Plant-Diet Index (hPDI) and Unhealthy Plant-Diet Index (uPDI)

The healthy Plant-Diet Index (hPDI) and the unhealthy Plant-Diet Index (uPDI) were developed according to the methodology used by Sajita et al.[23] to assess the consumption of nutritionally "healthy" plant-based foods (hPDI), known to be associated with a lower risk of certain diseases, and the consumption of nutritionally "unhealthy" plant-based foods (uPDI), known to be associated with a higher risk of those diseases.[8] This methodology was adapted and applied to the NutriNet-Santé dietary databases (Supplementary Tables S1 and S2).[24] The hPDI and uPDI values ranged from 18 to 90, with higher scores indicating a greater proportion of healthy (hPDI) or unhealthy (uPDI) plant-based foods in the diet. Both high hPDI and high uPDI scores reflect a lower proportion of animal-source products in the diet.

Processing level determination

Food classification by level of processing was carried out using the NOVA system. This categorizes foods and beverages into four groups according to their industrial processing level,[25] culturally adapted. This classification was applied to the dietary data collected through 24-h records. The first group comprises unprocessed or minimally processed foods (fresh, dried, or frozen fruits and vegetables, cereals, pasta, plain milk, fresh or frozen meat and fish, etc.). The second group comprises processed culinary ingredients (sugar, vegetable oils, butter, salt, etc.). The third group comprises processed foods (canned vegetables, cheese, plain bread like plain baguettes from bakery, fruit in syrup, canned fish, etc.). The fourth group comprises ultra-processed foods (UPF) (poultry and fish nuggets and sticks and other reconstituted meat products transformed with addition of preservatives other than salt, such as nitrites, instant noodles and dehydrated soups, industrial bread and plain bread like plain sliced breads, carbonated diet and regular sodas, instant desserts, most breakfast "cereals", cooked seasoned vegetables with ready-made sauces, and meat-substitute vegetable patties, containing food additives).

Trained dietitians classified the 3500 foods from the NutriNet-Santé food composition database into the four NOVA groups. This classification was validated by a committee of nutritional epidemiology experts consisting of three dietitians and five researchers. In cases of uncertainty, the researchers made the classification according to the proportion of homemade or artisanal foods vs. industrial brands reported by participants. Standardized recipes were used to identify and break down the ingredients for homemade or artisanal preparations, which were then classified according to the NOVA system. Given the level of detail in the dietary data available, we applied a cultural adaptation of the NOVA classification to better reflect the specificities of the French food context (e.g., classification of wholegrain foods and yogurt). Supplementary Appendix 1 details the NOVA classification with some examples (see Supplementary Table S3), and more details have been published elsewhere.[25] Ultra-processed foods (NOVA 4) are noted "UPF" and unprocessed foods (NOVA 1) "UnPF". The first three NOVA groups (unprocessed foods, culinary ingredients, and processed foods) are noted "non-UPF".

Computation of nutritionally healthy and unhealthy PDI/ultra-processed and unprocessed scores

To create new scores which reflect the balance between plant-based and animal-based foods, their nutritional quality and processing level of foods in combination, we combined the hPDI/uPDI and unprocessed)/ultra-processed, indices already validated and commonly used in the literature. To do that, food processing level (unprocessed or ultra-processed) was included in the hPDI and uPDI scores to give healthy PDI-unprocessed (hPDI-UnPF), healthy PDI-ultra-processed (hPDI-UPF), unhealthy PDI-unprocessed (uPDI-UnPF), and unhealthy PDI-ultra-processed (uPDI-UPF).

To compute these scores at the diet level, we calculated the contribution (%) of unprocessed/minimally processed and ultra-processed foods in the total weight (g/day) of foods and beverages consumed. This contribution was determined using a weight-based rather than an energy-based ratio to account for ultra-processed foods that do not provide energy (e.g., artificially sweetened beverages) and for non-nutritional factors related to food processing (e.g., additives and modifications to the structure of raw foods). Examples of food items considered in each food group are given in Supplementary Table S3.

These contributions were computed for the 18 food groups used in the PDI score calculation and aggregated to obtain an overall contribution of unprocessed or ultra-processed foods consumed for each group in total weight (g/day). Participants were then classified into quintiles of unprocessed or ultra-processed food consumption for these 18 food groups. Each quintile, from first to fifth, was assigned a multiplier coefficient of 1, 1.25, 1.5, 1.75, and 2, respectively. To calculate hPDI-UnPF, hPDI-UPF, uPDI-UnPF, and uPDI-UPF, the scores obtained for each of the 18 food groups (ranging from 1 to 5, as described in the "PDI score" method) were multiplied by the coefficient corresponding to the quintile of unprocessed or ultra-processed consumption (1, 1.25, 1.5, 1.75, or 2). For a food group i, a person obtaining X_i points based on the quintile corresponding to their score for the original PDI and having a multiplier coefficient Y_i, corresponding to their quintile of consumption of unprocessed or ultra-processed foods, will obtain a score of $\boldsymbol{X_i Y_i}$. Supplementary Table S4 details the method used to construct the score. This operation was applied to all food groups of PDIs, and all the scores of the food groups were then summed as follows:

PDI-food processing scores (hPDI-UPF, uPDI-UPF, hPDI-UnPF and uPDI-UnPF):

$\sum_{i=1}^{18} X_i Y_i$, ranging from 18 to 180

A higher hPDI-UnPF score reflected a diet richer in plant-based foods that were both nutritionally healthy and unprocessed. A higher hPDI-UPF score reflected a diet richer in plant-based foods that were nutritionally healthy but ultra-processed, and conversely for uPDI-UnPF and uPDI-UPF.

The hPDI-UnPF, hPDI-UPF, uPDI-UnPF and uPDI-UPF scores were categorized into deciles and continuous (per 10% increase) variables. hPDI and uPDI ranged from 18 to 90. hPDI-UnPF, hPDI-UPF, uPDI-UnPF, and uPDI-UPF ranged from 18 to 180.

We also created indicators representing the dietary contribution of plant-sourced non-UPF, plant-sourced UPF, animal-sourced non-UPF, and animal-sourced UPF, following the methods developed in a previous study to enhance comparability of our results.[16] To do this, we categorized foods into two categories (plant/animal) and then separated them into non-UPF and UPF. These scores were categorized into quartiles (% of total energy) and continuous (per 10% in total energy contribution) variables.

Other covariates

On entering the study, participants completed a series of validated online questionnaires (during the same period as the initial 24-h dietary records), covering various aspects such as health, anthropometric data, lifestyle, and sociodemographic characteristics. The information collected included sex, age at recruitment, education level, marital status, occupation, and household income. Household income per month was divided by the number of consumption units (CU) calculated: 1 CU for the first adult in the household, 0.5 CU for each additional person aged 14 or older, and 0.3 CU for children under 14. Physical activity levels were assessed using the International Physical Activity Questionnaire (IPAQ), a validated tool for quantifying the intensity and duration of physical activities. The activities reported by participants were converted into metabolic equivalents of task (MET) in minutes/week. Daily energy expenditure was classified as follows: low physical activity (<30 min of physical activity, equivalent to brisk walking), moderate physical activity (≥30 min and <60 min), or high physical activity (≥60 min). Smoking status was also recorded (never smoker/former smoker/current smoker). Participants self-reported their height and weight, which were used to calculate body mass index (BMI, in kg/m^2).[26] A participant was considered to be on a diet for medical reasons or weight management (lose weight or keep it off, or stay in shape) at baseline, the closest instance to 24-h records used in this study. Personal medical history (diabetes, hypertension, hypercholesterolemia, and hypertriglyceridemia) and family medical history (angina, myocardial infarction, ischemic or hemorrhagic stroke, arthritis, high blood pressure, hypercholesterolemia, and diabetes) were also collected for parents and siblings.

Sample selection

Participants recruited between February 2009 and September 2023 who completed at least three validated 24-h dietary records within the first two years following their inclusion were included. Those who did not complete at least three validated 24-h records among all of the bi-annual instances during the two first years following their inclusion were excluded. Participants who experienced a CVD event during the first two years of follow-up were included in the main analysis, and dietary indices were computed using the mean of their 24-h dietary records collected during this period. Participants identified as underreporting or who had a BMI below 13 or above 55 or did not respond to the health questionnaire were excluded from the study. Given the very low prevalence of major MCV and cardiometabolic risk factors such as hypertension and hypercholesterolemia before age 35,[27–29] only participants aged over 35 years were included. Analyses of the risk of coronary, cerebrovascular diseases and overall CVD were conducted on 63,831, 63,835, and 63,830 participants, respectively (Supplementary Figure S1).

Statistical analyses

We evaluated the relationship between each of the PDI-food processing scores and the incidence of cerebrovascular diseases and coronary diseases, separately and combined (overall CVD). All scores were modeled continuously (per 10-point increase) and by deciles for hPDI, uPDI, and PDI-food processing scores, consistent with the original studies that developed and used these indicators, for external validity assessment and comparison.[30] The p for trend value was obtained by including the exposure variable as a continuous variable in the model. We used multivariable Cox proportional hazard models to obtain HRs and 95% CIs. Age was used as the time scale. Participants contributed person-time until date of diagnosis, date of death, date of last completed questionnaire, or January 1, 2024, whichever came first. The proportional hazards assumption was confirmed by examining Schoenfeld residuals. We did not observe any violation for the models (Figures were presented only for main model (Supplementary Figures S2–S7)). The linearity of the associations between the scores and the risk of cerebrovascular and coronary diseases, separately and combined, was tested using restricted cubic spline (RCS) functions with the SAS macro[31] given the log-profile of the associations suggested by the RCS curves. Except for plant-sourced non-UPF for overall CVD and cerebrovascular diseases, the restricted cubic spline and decile analyses of the scores confirmed the linearity assumptions between these scores and risks of overall CVD, coronary and cerebrovascular diseases (Supplementary Figures S8–S13).

The main models were adjusted for known potential confounding factors: age (time scale), sex, educational level (below high-school degree, <3 yr after high-school degree, ≥3 yr after high-school degree), occupational status (unemployed/farmer, merchant, artisan, self-employed, manual worker/students or retired people/intermediate profession/managerial staff, intellectual profession), monthly household income (refused to declare, <1200 €, between 1200 € and 1800 €, between 1800 € and 2700 €, ≥2700 €), marital status (single/civil union, cohabiting, married/separated, divorced, widowed), physical activity (missing data, low, moderate, high), BMI (kg/m^2, continuous variable), height (cm), diet currently followed (yes/no), smoking status (never smoker, former smoker, current smoker), energy intake without alcohol (kcal/d, continuous variable), number of completed 24 h dietary records (continuous variable), alcohol consumption (g/d, continuous variable), and family history of CVD (yes/no).

We verified that sex did not affect the association between the scores and the occurrence of CVD by including sex as an interaction term in the main models. No significant effect was found.

In supplementary analyses, we assessed the dietary contribution of plant-sourced UPF, non-UPF and animal-sourced UPF, non-UPF and total daily energy intake on cerebrovascular and coronary diseases and overall CVD. They were modeled continuously (per 10-point increase) and by quintiles.

We also conducted sensitivity analyses by computing additional models. First, we tested reverse causality by excluding subjects diagnosed during the first 2 yr of follow-up and subjects with <2 yr of follow-up. Reverse causality refers here to the possibility that individuals with preclinical or recently diagnosed CVD may have changed their dietary habits in response to their condition, potentially biasing associations towards the null.

Second, we repeated the main models without adjusting for BMI. Finally, the we repeated the main models with adjusting for personal history of diabetes, hypertension, hypertriglyceridemia and hypercholesterolemia at inclusion.

Substitution analyses were performed by creating a model to evaluate the effect of replacing 10% of the plant-sourced UPF, animal-sourced non-UPF, and animal-sourced UPF, with 10% of plant-sourced non-UPF, on cardiovascular disease risk, keeping the other groups constant, and using the methods proposed in a previous study.[16] Cox proportional hazards regression with the same covariates used in the main analyses were modeled only for outcomes that showed significant associations with the dietary exposures in the main analyses.

Finally, we assessed the robustness of the PDI-food processing scores. We computed new versions of these indices with three different types of modification: (i) slight modifications in the multipliers testing two scenarios: +0.10 points (coefficients for the scenario A (coef A)) and –0.10 points (coefficients for the scenario B (coef B)) for each multiplier except for the first one, which has to remain neutral as it represents the lowest consumptions of each NOVA category, (ii) replacing quintiles by quartiles for the part of the score corresponding to the multiplying effect by NOVA categories, and (iii) grouping NOVA categories 1, 2 and 3 together. We then ran the main model once more with all indices (see Supplementary Tables S18–S20 for more details and results).

In each multivariable model, if a covariate had <2% missing values, these were imputed by their modal values.

All statistical analyses were conducted using R® version 4.0.4 (R Foundation) and SAS® version 8.3 (SAS Institute). All tests were two-sided, and a *p*-value of <0.05 was considered statistically significant. To account for multiple testing, we applied the Benjamini-Hochberg correction for the false discovery rate.

Role of funding source

This study was funded by a grant for the French national research agency (a governmental non profit agency) which had no role nor in study design, data collection, data analysis, interpretation, writing of the report.

Results

The total number of participants included in the study was 65,355, comprising 24% men and 76% women. Their mean age at baseline was 51.4 years (SD 10.2). A description of the participants is given in Table 1.

During follow-up (575.258 person-years, median follow-up period of 9.0 years (IQR: 5–13 years)), 1397 first incident CVD events were documented, including

	All (*n* = 63,835)		With MCV (n = 1397)		Without MCV (n = 62,438)	
	n/mean	%/SD	n/mean	%/SD	n/mean	%/SD
Sex (female)	48.2	75.6	558	39.9	47.7	76.3
Age, year	51.4	10.2	60.3	8.9	51.2	10.4
Education level						
<High-school degree	15,189	23.8	548	39.2	28,781	46.1
<3 yr after high-school degree	29,329	45.9	460	32.9	14,729	23.6
≥3 yr after high-school degree	19,317	30.3	389	27.8	18,928	30.3
Occupation						
Unemployed	7776	12.2	106	7.6	7670	12.3
Farmer, merchant. Artisan, company director, manual worker	12,441	19.5	112	8.02	12,329	19.7
Students or retired people	18,585	29.1	869	62.2	17,716	28.4
Intermediate profession	10,673	16.7	113	8.14	10,560	16.9
Managerial staff, intellectual profession	14,360	22.5	197	14.1	14,163	22.7
Monthly household income per consumption unit, €						
Not communicated	6785	10.6	122	8.7	6663	10.7
<1200	10,163	15.9	170	12.2	9993	16.0
1200–1800	14,981	23.5	283	20.3	14,698	23.5
1800–2700	15,184	23.8	361	25.8	14,823	23.7
≥2700	16,722	26.2	461	33.0	16,261	26.0
Marital status						
Civil union, cohabiting, married	48,313	75.7	1091	78.1	47,222	75.6
Separated or divorced, widowed	9353	14.6	223	16.0	9130	14.6
Single	6169	9.7	83	5.9	6086	9.7
Smoking status						
Never smoker	29,143	45.6	702	50.5	28,632	45.9
Former smoker	26,132	40.9	511	36.6	25,430	40.7
Current smoker	8560	13.4	184	13.2	8376	13.4
Family history of diseases[a]	29,124	45.6	894	64.0	28,230	45.2
Diet currently followed (%)[b]	12,401	19.4	270	19.3	12,131	19.4
Energy intake without alcohol, kcal/day	1842.9	439.7	1955.1	443.4	1840.3	439.4
24 h records, *n*	6.4	3.2	7.6	2.8	6.4	3.2
Alcohol consumption, g/day	8.9	12.4	13.6	15.4	8.8	12.3
Physical activity						
Missing data	7737	12.1	170	12.2	7567	12.1
Low	12,632	19.8	549	39.3	12,395	19.8
Moderate	22,680	35.5	441	31.6	22,239	35.6
High	20,786	32.6	237	17.0	2037	32.4
BMI, kg/m^2	24.3	4.5	25.6	4.1	24.3	4.5

[a]Family history of arteritis, stroke, heart attack, high blood pressure, high cholesterol, diabetes in father, brother, mother and sister. BMI, body mass index. [b]Diet currently followed: A participant was considered to be on a diet for medical reasons or weight management (to lose weight or keep it off, or to stay in shape).

Table 1: **Description of anthropometric, sociodemographic and lifestyle characteristics at inclusion, NutriNet-Santé study, France, 2009–2023.**

1051 cases of coronary diseases and 346 instances of cerebrovascular diseases.

The mean contribution of all plant-based foods to the total daily energy intake (kcal/day) was 62.7%, with 42.7% coming from non-UPF and 20.0% from UPF. Animal-based foods accounted for 37.2% of the total, with 26.2% of this percentage being non-UPF and 11.0% UPF (Supplementary Table S5).

The mean daily food group consumptions for the last deciles of hPDI, uPDI, hPDI-UnPF, hPDI-UPF, uPDI-UnPF, and uPDI-UPF are described in Supplementary Table S6.

Figs. 1–6, and Supplementary Tables S7–S12 present the associations and statistical tests for trends between hPDI, uPDI, PDI-food processing scores, and cerebrovascular and coronary diseases separately and combined (overall CVD).

A higher adherence to a healthy and unprocessed plant-based diet was associated with a 32% lower incidence of overall CVD ($HR_{D10\ vs.\ D1}$: 0.68, 95% CI: [0.53–0.88], p for trend = 0.006) and a 44% lower incidence risk of coronary heart disease ($HR_{D10\ vs.\ D1}$: 0.56, 95% CI: [0.42–0.75], p for trend = 0.003). The presence of a significant p for trend suggests the existence of a

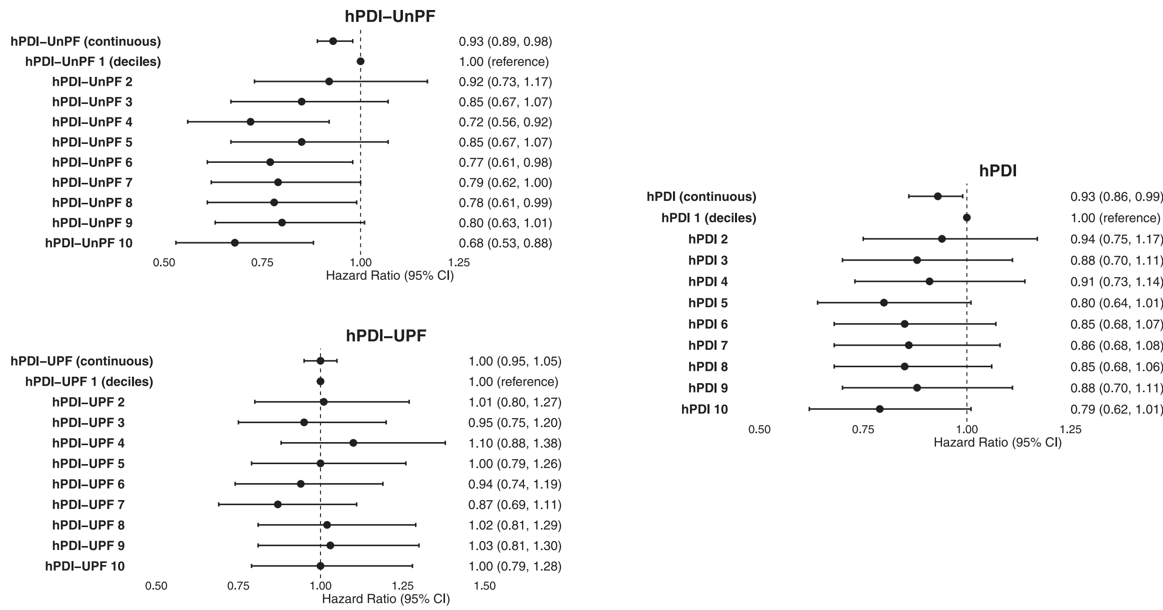

***Fig. 1:* Prospective association between hPDI, hPDI-UnPF and hPDI-UPF scores and risk of overall CVD, n = 63,830, NutriNet-Santé study, France, 2009–2023.** [1]Overall CVD: incident cases of cardiovascular diseases (CVD), including myocardial infarction, acute coronary syndrome, angioplasty, and both ischemic and hemorrhagic strokes. Cox proportional hazard model adjusted for age (time scale), sex, and energy intake (without alcohol, kcal/d), adjusted for education level (below high-school degree, high-school degree or greater, <3 yr after high-school degree, ≥3 yr after high-school degree), occupation (unemployed/farmer, merchant, artisan, company director, manual worker/employee/intermediate profession/managerial staff/students or retired people), monthly household income (not communicated, <1200 €, between 1200 € and 1800 €, between 1800 € and 2700 €, ≥2700 €), marital status (single/married, civil union, cohabiting/separated, divorced, widowed), number of completed 24 h dietary records, physical activity (high, moderate, low, calculated according to International Physical Activity Questionnaire recommendations), diet currently followed for weight management (lose weight or keep it off or stay in shape) or for medical reasons, alcohol consumption (g/d), BMI (kg/m^2), smoking status (never smoker, former smoker, current smoker) and family history of arteritis and/or stroke and/or heart attack and/or high blood pressure and/or high cholesterol and/or diabetes in father and/or brother and/or mother and/or sister. Range for hPDI: 29.0–85.0. Range for hPDI-UnPF: 33.0–122.25. Range for hPDI-UnPF: 34.0–121.0.

dose–response relationship (Supplementary Tables S7 and S8). This relationship was weakest for participants with the highest adherence to a healthy plant-based diet without considering UPF or UnPF food (hPDI score). It was significantly associated only for coronary heart disease, but with only a 26% lower risk of incidence ($HR_{D10\ vs.\ D1}$: 0.74, 95% CI: [0.55–0.98], p for trend = 0.013). This relationship was not observed for participants adhering most closely to a healthy and ultra-processed plant-based diet (CVD: $HR_{D10\ vs.\ D1}$: 1.00, 95% CI: [0.79; 1.28], p for trend = 0.86; coronary diseases: $HR_{D10\ vs.\ D1}$: 0.96, 95% CI: [0.73–1.27], p for trend = 0.251).

Individuals with the highest adherence to unhealthy and ultra-processed plant-based diet had a 38% higher risk of overall CVD ($HR_{D10\ vs.\ D1}$: 1.38, 95% CI: [1.09–1.76], p for trend = 0.004), and a 46% higher risk of developing a coronary heart disease ($HR_{D10\ vs.\ D1}$: 1.46, 95% CI: [1.11–1.93], p for trend = 0.015). A significant p for trend suggests a dose–response relationship (Supplementary Tables S10 and S11). This relationship was not observed for participants adhering most closely to an unhealthy plant-based diet without considering UPF (CVD: $HR_{D10\ vs.\ D1}$: 1.15, 95% CI: [0.90–1.48], p for trend = 0.09; coronary diseases: $HR_{D10\ vs.\ D1}$: 1.22, 95% CI: [0.92–1.61], p for trend = 0.097) or UnPF intakes (CVD: $HR_{D10\ vs.\ D1}$: 1.22, 95% CI: [0.95–1.55], p for trend = 0.192; coronary diseases: $HR_{D10\ vs.\ D1}$: 1.37, 95% CI: [1.04–1.82], p for trend = 0.06).

There was no association between any of the scores and cerebrovascular diseases.

The main models excluding participants diagnosed within the first two years of follow-up or followed for less than two years showed results consistent with the main analyses (Supplementary Tables S13 and S14). Additional adjustment for personal history of diabetes, hypertension, hypercholesterolemia, and hypertriglyceridemia yielded results broadly consistent with the main model, although the association between hPDI (modelled in deciles and continuous) and overall CVD only was no longer statistically significant (Supplementary Tables S15 and S16). When models were adjusted without BMI, associations remained

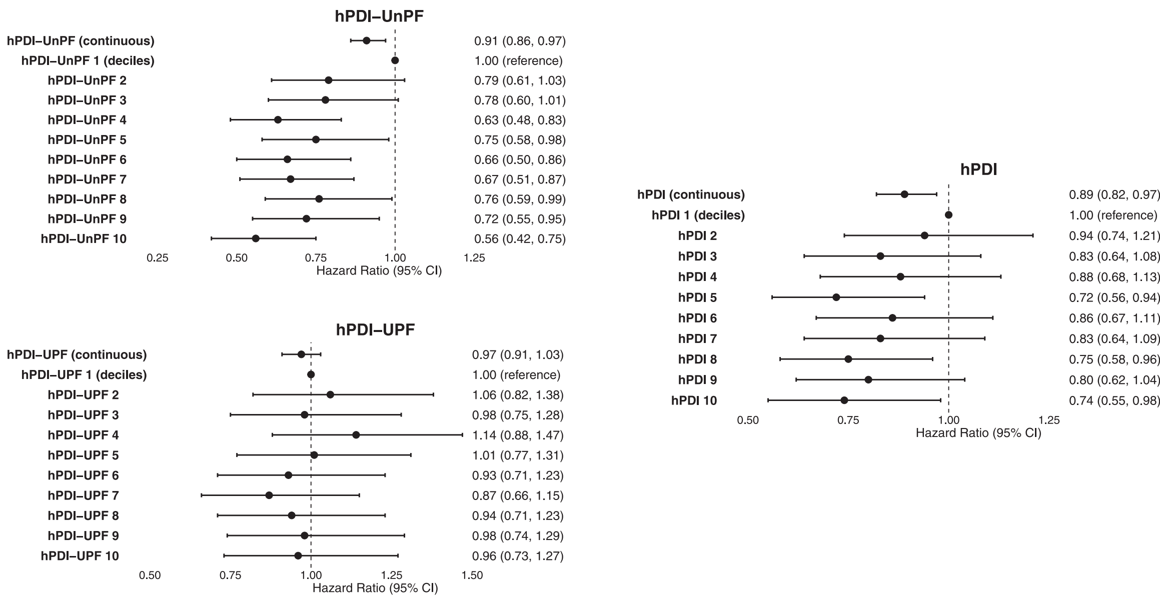

Fig. 2: **Prospective association between hPDI, hPDI-UnPF and hPDI-UPF scores and risk of coronary diseases, n = 63,831, NutriNet-Santé study, France, 2009–2023.** [1]Coronary diseases: incident cases of myocardial infarction, acute coronary syndrome and angioplasty. Cox proportional hazard model adjusted for age (time scale), sex, and energy intake (without alcohol, kcal/d), adjusted for education level (below high-school degree, high-school degree or greater, <3 yr after high-school degree, ≥3 yr after high-school degree), occupation (unemployed/farmer, merchant, artisan, company director, manual worker/employee/intermediate profession/managerial staff/students or retired people), monthly household income (not communicated, <1200 €, between 1200 € and 1800 €, between 1800 € and 2700 €, ≥270 0€), marital status (single/married, civil union, cohabiting/separated, divorced, widowed), number of completed 24 h dietary records, physical activity (high, moderate, low, calculated according to International Physical Activity Questionnaire recommendations), diet currently followed for weight management (lose weight or keep it off or stay in shape) or for medical reasons, alcohol consumption (g/d), BMI (kg/m^2), smoking status (never smoker, former smoker, current smoker) and family history of arteritis and/or stroke and/or heart attack and/or high blood pressure and/or high cholesterol and/or diabetes in father and/or brother and/or mother and/or sister. Range for hPDI: 29.0–85.0. Range for hPDI-UnPFhPDI-UnPF: 33.0–122.25. Range for hPDI-UnPF: 34.0–121.0.

overall similar to the main model, except that a significant inverse association was observed between hPDI (modelled in deciles) and CVD risk (Supplementary Tables S17 and S18).

A 10% increase in the dietary contribution of plant-sourced non-UPF was associated with a 10% reduced risk of overall CVD (HR: 0.90, 95% CI: [0.85–0.95]) and an 11% reduced risk of coronary heart disease (HR: 0.89, CI 95%: [0.83–0.95], Supplementary Tables S19–S21). Conversely, a 10% increase in the dietary contribution of animal-sourced UPF was associated with a 24% increased risk of overall CVD (HR 1.24, 95% CI: [1.12–1.37]) and a 25% increased risk of coronary heart disease (HR 1.25, 95% CI: [1.11–1.40], Supplementary Tables S19–S21).

In the substitution analysis (Supplementary Table S22), replacing 10% of the energy intake from either of the two groups (animal-based non-UPF, or animal-based UPF) with an equivalent amount from plant-based non-UPF was associated with a lower risk of cardiovascular and coronary heart diseases. Replacing plant-based UPF by plant-based non-UPF was not significantly associated with cardiovascular or coronary heart diseases.

Finally, robustness analyses of the PDI-food processing indices or scores (Supplementary Tables S23–S25) indicated that there were only small differences both for estimates and AIC/BIC criteria (mostly around 1%, and up to 16% for a few estimates/criteria), representing a good internal validity of these scores.

The sensitivity analyses where we included participants in the 15–35 yr age group yielded the same results as our principal analyses (Supplementary Tables S26 and S27).

Discussion

Our findings indicate that level of food processing can influence the association between plant-based diets and incidence of CVD. Adherence to a nutritionally healthy plant-based diet richer in unprocessed food was associated with a 44% lower risk of developing a coronary disease and 32% for overall CVD, while no significant association was observed for healthy plant-based diets rich in ultra-processed foods. We also observed that unhealthy and ultra-processed plant-based diets were associated with a 48% increased risk of coronary disease and 38% for overall CVD, while no significant

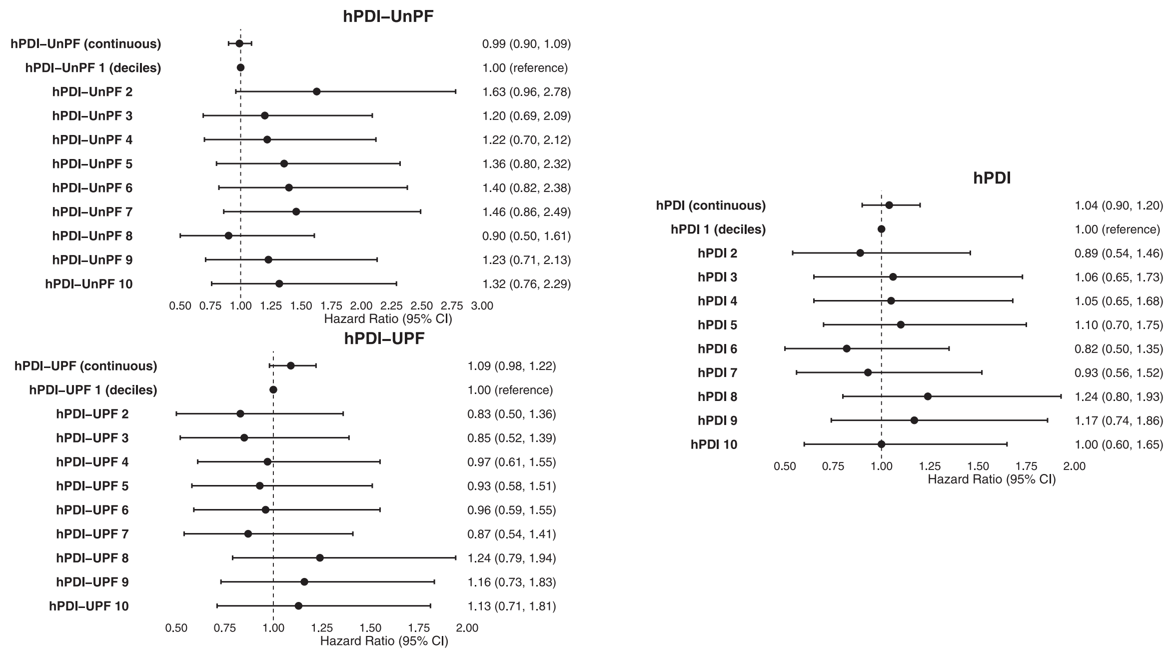

Fig. 3: **Prospective association between hPDI, hPDI-UnPF and hPDI-UPF scores and risk of cerebrovascular diseases, n = 63,835, NutriNet-Santé study, France, 2009–2023**. [1]Cerebrovascular diseases: incident cases of both ischemic and hemorrhagic strokes. Cox proportional hazard model adjusted for age (time scale), sex, and energy intake (without alcohol, kcal/d), adjusted for education level (below high-school degree, high-school degree or greater, <3 yr after high-school degree, ≥3 yr after high-school degree), occupation (unemployed/farmer, merchant, artisan, company director, manual worker/employee/intermediate profession/managerial staff/students or retired people), monthly household income (not communicated, <1200 €, between 1200 € and 1800 €, between 1800 € and 2700 €, ≥2700 €), marital status (single/married, civil union, cohabiting/separated, divorced, widowed), number of completed 24 h dietary records, physical activity (high, moderate, low-calculated according to International Physical Activity Questionnaire recommendations), diet currently followed for weight management (lose weight or keep it off or stay in shape) or for medical reasons, alcohol consumption (g/d), BMI (kg/m^2), smoking status (never smoker, former smoker, current smoker) and family history of arteritis and/or stroke and/or heart attack and/or high blood pressure and/or high cholesterol and/or diabetes in father and/or brother and/or mother and/or sister. Range for hPDI: 29.0–85.0. Range for hPDI-UnPF: 33.0–122.25. Range for hPDI-UnPF: 34.0–121.0.

association was observed for unhealthy plant-based diets without considering UPF intake. Taken together, these results point to the importance of taking into account three dimensions to define healthy diets for the prevention of cardiovascular diseases, namely (i) the balance between plant-based and animal-based foods, (ii) their nutritional quality, and (iii) processing level of foods.

To our knowledge, only two studies have investigated the role of plant foods according to their degree of processing on the risk of CVD or all-cause mortality. Overall, our findings are mostly consistent with those based on the UK Biobank[16] and EPIC-NL[15] cohorts. In a previous study based on the UK Biobank cohort, a 10% increase in the proportion of non-ultra-processed plant-based foods was associated with a 7% reduction in CVD risk and a 13% reduction in CVD-related mortality, and a higher intake of ultra-processed animal-based foods was associated with a 6% increased risk of CVD. However, unlike ours, those studies found that a higher intake of ultra-processed plant-based foods was associated with a 5% increase in CVD risk and a 12% increase in CVD mortality. Several hypotheses could explain this discrepancy, such as variations in food classification criteria and differences in dietary habits, and the availability of ultra-processed plant-based products across populations.[32] More specifically, there is a greater range of ultra-processed products with low nutritional quality and less choice of ultra-processed products with better nutritional quality on the food market in the UK than in France. The populations in the study from UK Biobank consumed twice as much ultra-processed plant-based products as our study population[16] with, for example, five times more industrially packaged breads and almost three times more biscuits (Supplementary Table S5).

No association was observed for hPDI-UPF, suggesting that the UPF offset the protective role of healthy plant foods. This observation can be compared to the results from the EPIC-NL study, which reported a significantly lower risk of mortality among individuals in the quartile with greater adherence to a nutritionally

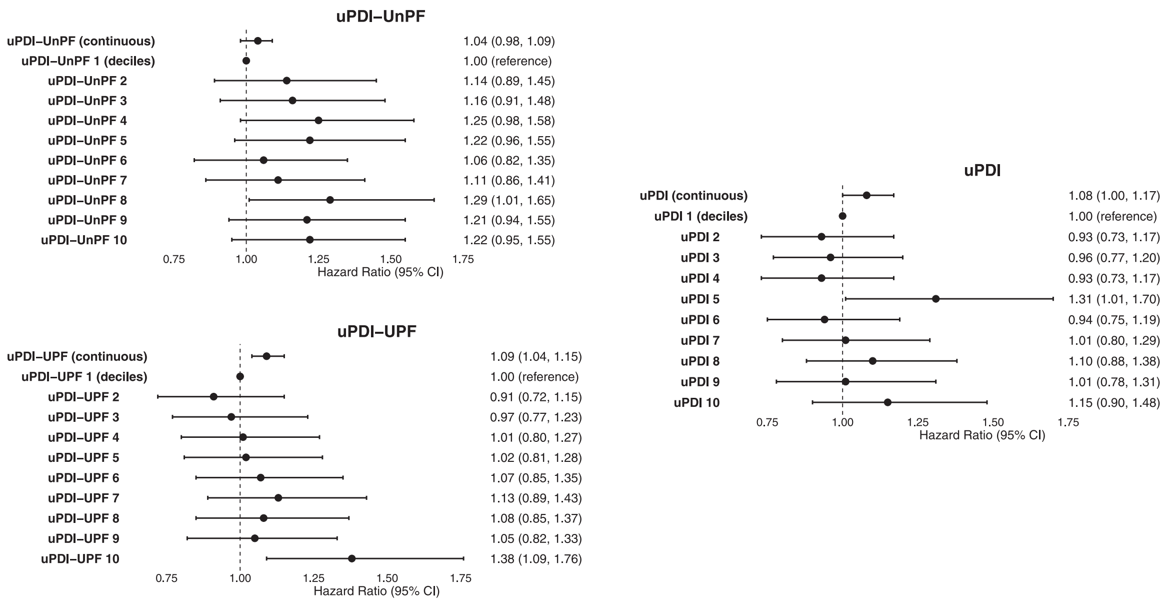

Fig. 4: **Prospective association between uPDI, uPDI-UPF and uPDI-UnPF and risk of overall CVD, n = 63,830, NutriNet-Santé study, France, 2009–2023**. [1]Overall CVD: incident cases of cardiovascular diseases (CVD), including myocardial infarction, acute coronary syndrome, angioplasty, and both ischemic and hemorrhagic strokes. Cox proportional hazard model adjusted for age (time scale), sex, and energy intake (without alcohol, kcal/d), adjusted for education level (less than high-school degree, high-school degree or greater, <3 yr after high-school degree, ≥3 yr after high-school degree), occupation (unemployed/farmer, merchant, artisan, company director, manual worker/employee/ intermediate profession/managerial staff/students or retired people), monthly household income (not communicated, <1200 €, between 1200 € and 1800 €, between 1800 € and 2700 €, ≥2700 €), marital status (single/married, civil union, cohabiting/separated, divorced, widowed), number of completed 24 h dietary records, physical activity (high, moderate, low, calculated according to International Physical Activity Questionnaire recommendations), diet currently followed for weight management (lose weight or keep it off or stay in shape) or for medical reasons, alcohol consumption (g/d), BMI (kg/m^2), smoking status (never smoker, former smoker, current smoker) and family history of arteritis and/or stroke and/or heart attack and/or high blood pressure and/or high cholesterol and/or diabetes in father and/or brother and/ or mother and/or sister. Range for uPDI: 29.0–81.0. Range for uPDI-UPF: 30.5–121.25. Range for uPDI-UnPF: 29.75–107.0.

healthy plant-based diet low in ultra-processed products ($HR_{(Q1hPDI/Q4UPF)/(Q4hPDI/Q1UPF)}$: 0.78, 95% CI: 0.66–0.89). This study also found that the protective association between hPDI and CVD was not significant in individuals with higher intakes of UPF.[15] However, comparison with our study could be specious because different methods were used; the earlier study did not combine the two dimensions (contribution of both UPF and plant food) in one indicator, but conducted stratified analyses.[15] Additionally, no association was observed between the uPDI score and all-cause mortality.[15] Our results can also be compared with those from a study that estimated both level of adherence to the Mediterranean diet and level of food processing in combination. This study reported that individuals with the highest adherence to a Mediterranean diet, which could also be considered as a plant-based diet, and with the lowest intake of UPF, had improved survival rates and lower non-cancer-related mortality.[14] This is in line with the recommendation that sustainable diets, including Mediterranean and other types of plant-based diets, should include low levels of UPF to have potential benefits on longevity and health.

In this study, we used PDI-food processing scores, aligned with previous research highlighting the relevance of evaluating overall dietary quality rather than focusing solely on isolated, specific food groups.[16] The consumption of a given food is embedded within an overall dietary pattern, reflecting preferences, habits, and overall nutritional behaviors, as previously underlined.[33] A food is not consumed in isolation but is associated with a preference for other foods leading to correlation and/or synergy within the dietary matrix. A diet richer in unhealthy and UPF plant-based foods contains not only more sugar and fat, but also multiple food additives, and correspondingly less fiber, protein, and essential micronutrients. Our findings are evidence that the source of food (plant or animal), its nutritional quality, and its level of processing can have combined effects on cardiovascular disease risk. Healthy, minimally or non-processed plant-based foods, such as whole grains, fruits, vegetables, and legumes, have been consistently associated with cardiovascular benefits reported in many studies included in meta-analyses[34,35] and one umbrella review.[12] Our results argue for using combined indicators to obviate complex

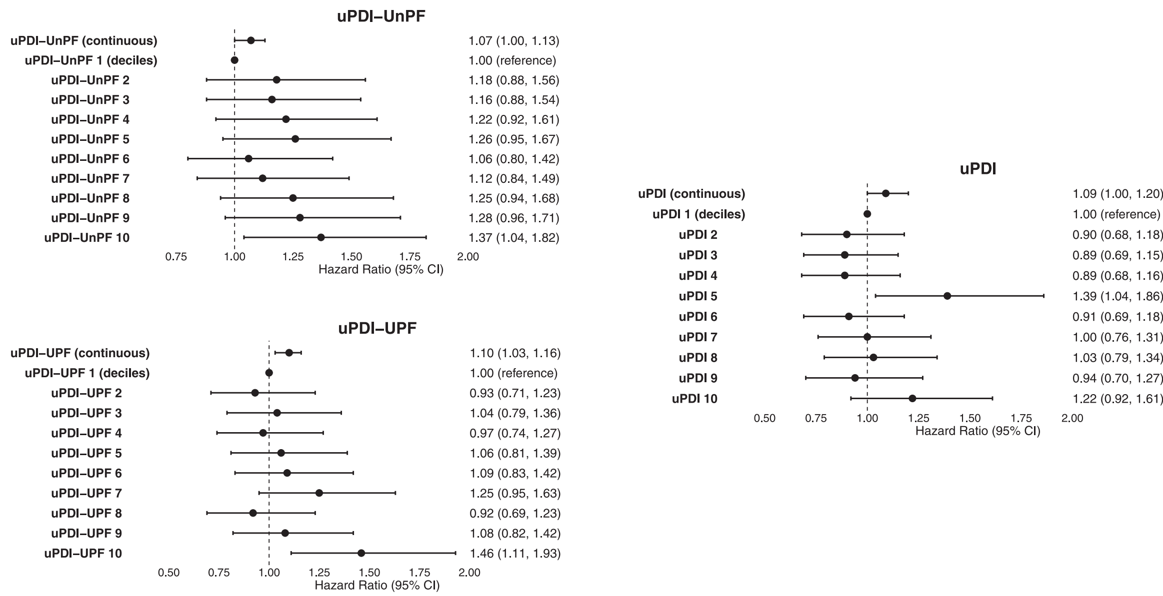

Fig. 5: **Prospective association between uPDI, uPDI-UPF and uPDI-UnPF and risk of coronary diseases, n = 63,831, NutriNet-Santé study, France, 2009–2023**. [1]Coronary diseases: incident cases of myocardial infarction, acute coronary syndrome and angioplasty. Cox proportional hazard model adjusted for age (time scale), sex, and energy intake (without alcohol, kcal/d), adjusted for education level (less than high-school degree, high-school degree or greater, <3 yr after high-school degree, ≥3 yr after high-school degree), occupation (unemployed/farmer, merchant, artisan, company director, manual worker/employee/intermediate profession/managerial staff/students or retired people), monthly household income (not communicated, <1200 €, between 1200 € and 1800 €, between 1800 € and 2700 €, ≥2700 €), marital status (single/married, civil union, cohabiting/separated, divorced, widowed), number of completed 24 h dietary records, physical activity (high, moderate, low-calculated according to International Physical Activity Questionnaire recommendations), diet currently followed for weight management (lose weight or keep it off or stay in shape) or for medical reasons, alcohol consumption (g/d), BMI (kg/m^2), smoking status (never smoker, former smoker, current smoker) and family history of arteritis and/or stroke and/or heart attack and/or high blood pressure and/or high cholesterol and/or diabetes in father and/or brother and/or mother and/or sister. Range for uPDI: 29.0–81.0. Range for uPDI-UPF: 30.5–121.25. Range for uPDI-UnPF: 29.75–107.0.

statistical modeling strategies, such as stratification, which increase the number of required comparisons and statistical tests. Another randomized controlled crossover clinical trial conducted in the UK reported results in line with our findings.[36] In this study, participants who followed a diet which was both balanced following dietary guidelines from the UK, and contained only minimally processed foods, had a greater weight loss and fat mass reduction, compared to those who followed a similarly balanced diet but containing only ultra-processed foods.[36] The result of this study add evidence about the relevance of considering both food processing in addition to diet quality for dietary guidelines.[36]

Several mechanisms support a beneficial effect of a diet rich in nutritionally healthy and minimally processed plant-sourced food for the prevention of CVD.[37,38] A diet rich in minimally processed plant foods provides dietary fiber, which lowers cholesterol, improves glycemic control, and promotes satiety, supporting weight management. Plant foods are sources of antioxidants, vitamins (e.g., C and E), minerals (e.g., potassium and magnesium), and phytochemicals (including polyphenols and flavonoids), which collectively reduce oxidative stress and inflammation. Dietary fiber and phytosterols, found for example in seeds and nuts, reduce the reabsorption of cholesterol and bile acids in the small intestine, which stimulates the expression of LDL receptors in the liver, increasing the clearance of LDL-C from the blood and thereby lowering circulating cholesterol levels. The fermentation of plant fibers by the gut microbiota produces short-chain fatty acids, which have beneficial effects on glucose metabolism, lipid profiles, and immune function. These combined effects of plant-based nutrients, bioactive compounds, and the absence (or low presence) of compounds derived from industrial processes (such as additives and newformed contaminants)[11] may contribute to the observed associations between minimally processed plant-rich diets and lower cardiovascular disease risk.

The harmful impact of a diet rich in unhealthy plant sourced foods may be explained by several factors.[11] These include high energy density, excessive amounts of sugar, sodium, and saturated fats, the presence of additives such as artificial sweeteners and emulsifiers, hyper-palatability leading to overconsumption, and a

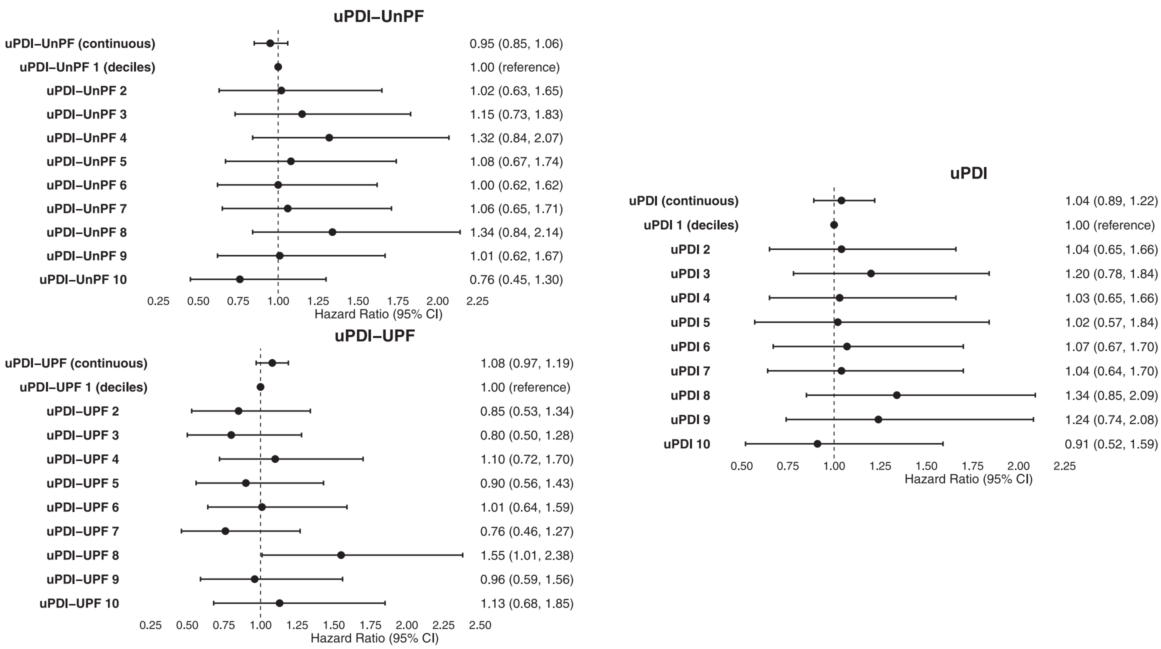

Fig. 6: **Prospective association between uPDI, uPDI-UPF and uPDI-UnPF and risk of cerebrovascular diseases, n = 63,835, NutriNet-Santé study, France, 2009–2023**. [1]Cerebrovascular diseases: incident cases of both ischemic and hemorrhagic strokes. Cox proportional hazard model adjusted for age (time scale), sex, and energy intake (without alcohol, kcal/d), adjusted for education level (below high-school degree, high-school degree or greater, <3 yr after high-school degree, ≥3 yr after high-school degree), occupation (unemployed/farmer, merchant, artisan, company director, manual worker/employee/intermediate profession/managerial staff/students or retired people), monthly household income (not communicated, <1200 €, between 1200 € and 1800 €, between 1800 € and 2700 €, ≥2700 €), marital status (single/married, civil union, cohabiting/separated, divorced, widowed), number of completed 24 h dietary records, physical activity (high, moderate, low, calculated according to International Physical Activity Questionnaire recommendations), diet currently followed for weight management (lose weight or keep it off or stay in shape) or for medical reasons, alcohol consumption (g/d), BMI (kg/m^2), smoking status (never smoker, former smoker, current smoker) and family history of arteritis and/or stroke and/or heart attack and/or high blood pressure and/or high cholesterol and/or diabetes in father and/or brother and/or mother and/or sister. Range for uPDI: 29.0–81.0. Range for uPDI-UPF: 30.5–121.25. Range for uPDI-UnPF: 29.75–107.0.

degraded food matrix (e.g., fiber reduction and the loss of certain protective compounds), together with contaminants created during food processing or derived from packaging. These different factors, often related to food processing in both animal and plant foods, may not be harmful individually, or when the level of consumption of unhealthy plant foods is balanced with healthy plant foods. In our study, an association between ultra-processed plant-based food consumption (uPDI-UPF score) and CVD risk was observed, but the association was even more pronounced for ultra-processed animal-based products (animal-sourced UPF). The detrimental impact of excessive red meat and processed meat consumption on cardiovascular health has been consistently reported in the literature, with several studies demonstrating a strong association between their intake and an increased risk of CVD.[39]

The originality of our work lies in the use of an overall score (PDI-food processing) along with indicators (proportion of plant-based and animal-based foods, ultra-processed or not), allowing a fuller assessment of diet and its quality. The prospective design of this study, the detailed and updated dietary intake assessments, and the fine classification of foods in the NOVA categories, with a cultural adaptation, further ensure sound results. The repeated 24-h dietary records (comprising some 3500 different food items) provide a more accurate measure of dietary intake than food frequency questionnaires, for example. The statistical power of the NutriNet-Santé cohort also facilitates the description of associations with a wide range of plant-based dietary patterns (healthy/unhealthy and UnPF/UPF) that are not always common in the general population, given that plant-based diets are not the primary dietary choice in Westernized populations.

Certain limitations are acknowledged. First, the participants of the NutriNet-Santé cohort are volunteers, and therefore may be more health-conscious and interested in nutrition-related topics, and have a healthier diet than the general population. However, the consumption of ultra-processed foods was similar to that in the general population (ENNS), representing

30–35% of total energy intake.[40] The mean date of dietary data collection in our study was December 31, 2010. Since then, both the availability and consumption of ultra-processed foods (UPF) have markedly increased in France. This temporal context suggests that the associations observed in our analyses may in fact underestimate the current impact of UPF consumption on cardiometabolic health. Therefore, if the same study were conducted even more recently, stronger associations might be expected. Misclassification of food (e.g., in NOVA categories), cannot be entirely ruled out. However, the level of detail in the NutriNet-Santé nomenclature, coupled with the availability of the information for home-made or industrial products and their brands limited potential errors. For example, we were able to separate healthy foods such as whole grain products, or yogurts, into different NOVA categories according to their level of food processing (e.g., plain yogurt with no additives vs. artificially flavored and texturized 'fruit' yogurt or freshly baked whole bread from the bakery vs. packaged industrial pre-sliced brown bread with additives). Our study suggested indeed that both food quality and processing are important and need to be considered to adequately measure diet exposure in epidemiological studies. Our follow-up period may not have fully captured long-term dietary habit changes and although residual confounding cannot be entirely ruled out, adjustments for a wide range of confounders and sensitivity analyses (including the exclusion of the first two years of follow-up, and the fact that some participants may follow some specific diet on medical advice) suggest our findings are robust. Also, the results from the sensitivity analyses performed for modifications in the construction of the PDI-food processing scores reported only minor changes, indicating a good internal validity of these scores. This was an observational study and prone to measurement error. No causal conclusion can therefore be drawn despite the adjustments.

Conclusion and implications

Our results highlight the importance of simultaneously considering balance between plant-based and animal-based foods, their nutritional quality and processing level of foods when evaluating their association with the risk of developing a cardiovascular disease. Future research could usefully explore the impact on health of different categories of ultra-processed foods, particularly plant-based substitutes (e.g., meat and dairy alternatives). Public health recommendations should therefore emphasize not only a reduced meat and animal product consumption, but also an increase in minimally processed and nutritionally healthy plant-based foods, while limiting the consumption of ultra-processed foods, to improve cardiovascular health.

Contributors

The authors' responsibilities were as follows: SH, MT, LFK and EK-G were responsible for developing the design and protocol of the NutriNet-Santé study and led the underlying process of data acquisition.

BA, EKG, MT, JB initiated and conceptualized the study. CP and BA were involved in data management: they had access to raw data and verified it. CP performed statistical analyses. CP and BA drafted the manuscript. CP, BA, EKG, JB, SW, BS and MT contributed to the statistical analyses and interpretation of data. All authors were involved in interpreting the results, critically reviewed the manuscript for important intellectual content and approved the final version to be published. BA and CP had had final responsibility for the decision to submit for publication and are the guarantors.

Data sharing statement

Data described in the article, code book, and analytic code will be made available upon request pending application and approval. Researchers from public institutions can submit a collaboration request including information on the institution and a brief description of the project to collaboration@etude-nutrinet-sante.fr. All requests will be reviewed by the steering committee of the NutriNet-Santé study. If the collaboration is accepted, a data access agreement will be necessary and appropriate authorizations from the competent administrative authorities may be needed. In accordance with existing regulations, no personal data will be accessible.

Declaration of interests

All theauthors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2025.101470.

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