Individual and Combined Effects of Dietary Factors on Risk of Incident Hypertension

Prospective Analysis From the NutriNet-Santé Cohort

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Abstract—Dietary intake is pointed as one of the major determinants in hypertension development. Data in the area are mostly obtained from cross-sectional studies. We aimed to investigate the prospective association between (1) individual nutritional factors and (2) adherence to the Dietary Approach to Stop Hypertension and the risk of incident hypertension in a large cohort study. We prospectively examined the incidence of hypertension among 80 426 French adults participating in the NutriNet-Santé cohort study. Self-reported sociodemographic, lifestyle health questionnaires and dietary consumption assessed by three 24-hour records were completed at baseline and yearly thereafter. Associations between quartiles (Q) of nutrients and food groups and adherence to Dietary Approach to Stop Hypertension diet and hypertension risk were assessed by multivariable Cox proportional hazards models. During a mean follow-up of 3.4±2.1 years, 2413 cases of incident hypertension were documented. Dietary intakes of sodium (Q4 versus Q1): hazard ratio (HR)=1.17 (95% confidence interval [CI], 1.02–1.35), potassium: HR=0.82 (95% CI, 0.72–0.94), animal protein: HR=1.26 (95% CI, 1.11–1.43), vegetable protein: HR=0.85 (95% CI, 0.75–0.95), fiber: HR=0.81 (95% CI, 0.71–0.93), magnesium: HR=0.77 (95% CI, 0.67–0.89), fruit and vegetables: HR=0.85 (95% CI, 0.74–0.97), whole grain: HR=0.84(95% CI, 0.76–0.93), nuts: HR=0.72 (95% CI, 0.63–0.83), and red and processed meat: HR=1.25 (95% CI, 1.11–0.42) were associated with risk of hypertension. Besides, adherence to the Dietary Approach to Stop Hypertension was strongly inversely associated with incident hypertension: (Q4 versus Q1) HR=0.66 (95% CI, 0.58–0.75). Our results confirmed the association of several nutritional factors intake and incident hypertension and highlighted that adopting a global healthy diet could strongly contribute to the prevention of hypertension. **(*Hypertension*. 2017;70:712-720. DOI: 10.1161/HYPERTENSIONAHA.117.09622.)** • **Online Data Supplement**

Key Words: blood pressure ■ diet ■ epidemiology ■ hypertension ■ meat

Hypertension is the most prevalent chronic disease affecting >30% of adults aged ≥25 years worldwide.[1] Its prevalence is still rising, making it the most important contributor to the global burden of disease and to global mortality.[2] In that context, preventive strategies from a public health perspective are urgently needed, and primary nutritional prevention has been advanced to fight the hypertension epidemic. Effect of several nutrients (eg, salt, potassium, fiber, etc) or foods (eg, fruits, vegetables, etc) on blood pressure (BP) is well established[3–6] but remains unclear for others, in particular, magnesium, calcium, dairy products, and nuts.[7,8] Moreover, epidemiological data on the relationships between nutrition and hypertension are numerous but often result from cross-sectional analyses rather than prospective analyses, and the latter have been conducted in specific populations presumably similar in socioeconomic status and health consciousness.[9,10] Although research on the effect of different nutrients on BP is important to understand potential biological mechanisms underlying the associations, these studies are constrained by the correlation of dietary intakes disregarding their potential interaction and synergistic effect and the inability to detect small effects of individual dietary/nutritional components.[11,12] In that context, the Dietary Approach to Stop Hypertension (DASH)[13] is a healthy diet rich in fruits, vegetables, whole grains, nuts, and low-fat dairy and reduced in saturated and total fat, red and processed meat, sweet products beverages, which has been shown, using a clinical randomized trial design, to improve BP level in both normotensive and hypertensive individuals. However, findings of epidemiological observational studies investigating the role of adherence to a DASH-type diet on the primary prevention of hypertension are inconsistent. In western countries, no apparent reduced risk was found in 2 large cohort studies,[14,15] whereas a positive association was reported in 2 others.[16,17] There is, therefore, still a need to ascertain the effect of healthy diet on hypertension risk as adopting a healthy diet is usually recommended by guidelines worldwide with the aim of preventing and improving the risk of hypertension.[18,19]

Received April 24, 2017; first decision May 11, 2017; revision accepted July 11, 2017.

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The online-only Data Supplement is available with this article at http://hyper.ahajournals.org/lookup/suppl/doi:10.1161/HYPERTENSIONAHA.117.09622/-/DC1.

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The aim of the present study was to investigate and compare the associations between (1) individual nutritional factors and (2) adherence to the DASH and the risk of incident hypertension in a large cohort of French adults with an accurate assessment of nutritional intake.

Population and Methods

Study Design

The NutriNet-Santé cohort study is an ongoing French web-based study, launched in May 2009 to investigate the relationship between nutrition and chronic diseases. Details concerning study protocol, design, and methods have been detailed elsewhere.[20] Briefly, the NutriNet-Santé study was implemented in the general population, targeting Internet-user volunteers aged ≥18 years recruited by a vast multimedia campaign. Using a dedicated secured website, participants were asked to complete self-administered questionnaires at baseline and every year thereafter, providing information on sociodemographics, lifestyles, health status, and dietary behaviors. All participants provided an informed consent form. The International Research Board of the French Institute for Health and Medical Research (0000388FWA00005831) and the Comité National de l'Informatique et des Libertés (CNIL number: 908450 and number: 909216) approved the NutriNet-Santé study.

Data Collection and Treatment

Dietary Intake Assessment

At inclusion, participants completed three 24-hour dietary records (24HR) randomly allocated during a 2-week period, including 2 week days and 1 weekend day. This collection method is known to provide more accurate estimates of individuals' intakes than food frequency questionnaire.[21] Participants reported all foods and beverages consumed at each eating occasion. Nutrient intakes were estimated using the NutriNet-Santé food composition table, which includes >3000 food items.[22] Portion sizes were either estimated with the help of photographs, derived from a validated picture booklet[23] presenting 3 different portions sizes, or quantity consumed was directly entered by participants. Daily dietary intake was calculated as the weighted average from the three 24HR (a weighting coefficient was used to take into account intraindividual variability of weekdays and weekend days). Several validation studies, in particular against biomarkers, were performed on subgroups to assess the quality of nutritional data collected.[22] Alcohol intake (grams of ethanol per day) was calculated from an alcohol use frequency questionnaire or from the 24HR when no consumption in the frequency questionnaire was reported.

We also computed a 40-points DASH score developed by Fung et al,[24] assessing adherence to a DASH-style diet. The DASH score includes 8 dietary components, the consumption of which should be elevated (fruits, vegetables, nuts and legumes, low-fat dairy, and whole grains) or limited (sodium, sweetened beverages, and red and processed meats). For each component, participants' subscores (ranging from 1 to 5) were based on sex-specific quintiles. The final DASH score ranging from 8 to 40 was then obtained by adding the subscores of each component.

Demographic, Anthropometric, and Lifestyle Data Collection

Baseline questionnaires provided data on educational level, smoking status, self-reported weight and height (which permit to calculate the body mass index by dividing weight, in kilograms, by height, in square meters). Physical activity was assessed using the French version of the short form of the International Physical Activity Questionnaire, in French language.[25]

Case Ascertainment

At inclusion, participants filled self-administered health questionnaire providing their personal and familial history of hypertension and medication use allowing exclusion of prevalent cases. Incident cases were identified through annual follow-up questionnaires in 2413 participants who reported a new diagnosis of hypertension and use of relevant BP medication. In the cohort, case ascertainments were based for 73% on self-reported diagnosis of hypertension and adequate vasoactive treatment, for 7% on self-reported diagnosis of hypertension only, and for 20% on adequate vasoactive treatment report without having declared other pathology requiring such treatment.

Study Sample

Of the 140 001 volunteers included between May 2009 and October 2015, we selected those with 3 validated 24HR: 16 570 participants were not included because they were identified as energy under-reporters based on the method developed by Black[26] and 26 998 because they provided <3 valid 24HR. Second, participants with prevalent hypertension, cancer, diabetes mellitus, and cardiovascular disease and women who were pregnant at baseline (n=11 731) were excluded, as well as participants with missing or invalid data on health status, anthropometric measurements, or physical activity (n=4276), leaving 80 426 participants for the analyses Figure.

Statistical Analysis

The participants' characteristics were compared across DASH score quartile. Tests for linear trend were performed for continuous variable and Mantel–Haenszel χ^2 tests for categorical variables. We estimated the risk of hypertension with Cox proportional hazards models. We provided hazards ratios and 95% confidence intervals across quartiles of nutritional factor consumption (the first as reference) except for whole grains, legumes, nuts, and soda for which hazards ratios express the relative risk in consumers' tertiles of intakes relative to participants reporting no consumption. Age was used as primary time-dependent variable. Participants contributed person-time until age at diagnosis of hypertension, death, or last completed health follow-up questionnaire, whichever occurred first. The assumptions of proportionality were checked through examination of the log–log (survival) versus log–time plots. The first model was adjusted for age (time scale) and sex. The multivariable model was further adjusted for educational level, total energy intake, and known factors related to hypertension: body mass index, smoking status and alcohol consumption, physical activity, and familial history of hypertension. These models were computed for potential hypertension-related nutrients, major food groups, and both dietary indexes reflecting DASH-type diet.

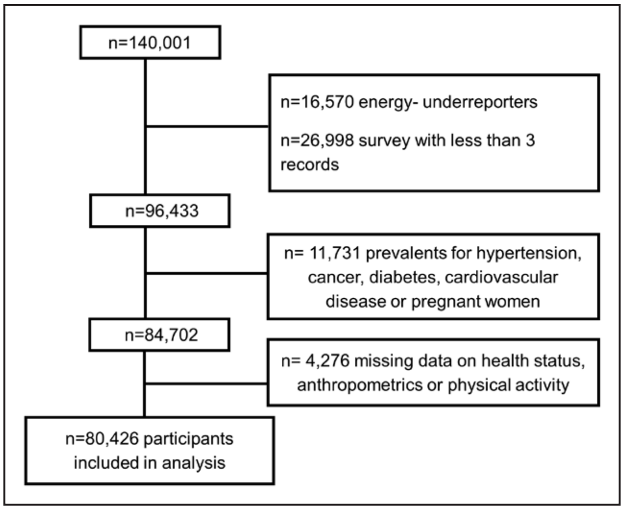

Figure. Flow chart.

Two additional models were performed in adding first all nutrients and second all food groups, which were significantly associated with hypertension risk in the fully previous model.

All tests were 2-sided; *P*<0.05 was considered statistically significant. Statistical analyses were performed using SAS software version 9.2 (SAS Institute, Cary, NC).

Results

We analyzed data from 80426 participants of whom 2413 reported a new diagnosis of hypertension. Mean follow-up was 3.4±2.1 years.

Table 1 summarizes participants' characteristics and dietary data at baseline and according to DASH score quartiles. Age; education level; physical activity; and dietary intake of plant proteins, potassium, magnesium, calcium, fruits and vegetables, whole grains, legumes, low-fat dairy products, and nuts were increased across DASH score quartiles, whereas body mass index; tobacco use; alcohol and soda consumption; and intake of animal proteins, fats, and sodium decreased.

Tables 2 and 3 report multivariable-adjusted hazards ratios across dietary factors. In the fully adjusted models, risk of incident hypertension, comparing the fourth to the first quartile, was significantly increased by 17% for sodium intake, 22% for sodium/potassium ratio, 26% for animal protein, and 25% for red and processed meat consumption. Besides, risk of incident hypertension was significantly reduced by 18% for dietary potassium, 15% for plant proteins, 19% for dietary fiber, 23% for magnesium, 15% for fruits and vegetables, 16% for wholegrain, and 28% for nuts consumption.

The relationships remained significant for sodium, potassium, magnesium, and animal and vegetable proteins, when adding simultaneously sodium, potassium, magnesium, animal and plant proteins, and fibers in the same model and similarly for red and processed meat, whole grains, and nuts intake when adding simultaneously in the same model (data not tabulated). There were no significant association between the risk of hypertension and intake of lipids (total and subtypes of fatty acids), phosphorus, calcium, vitamin D, and consumption of low-fat dairy products, starchy refined foods, or soda. Association between risk of hypertension and overall diet using DASH score is reported in Table 4. In the fully adjusted model, participants with a DASH score in the fourth quartile had a 34% lower risk than those in the first quartile.

Discussion

In a large cohort of healthy French adults, using accurate dietary data, our results confirmed some previously documented associations between incidence of hypertension and several nutrient and food groups such as sodium, potassium, fruits and vegetables, and fibers; but also showed associations that are less consistently reported in the scientific literature like the strong protective role of magnesium and nuts consumption or the magnitude of harmful role of animal protein consumption. Moreover, to the best of our knowledge, our study was the first to investigate the overall diet, nutrients, and foods on hypertension in the same sample, making it possible to balance their respective role.

Nutrients and Foods

Sodium and Potassium

We confirmed the widely described inverse association between sodium consumption and risk of hypertension.[3,4] However, this association was found only for high consumption. Indeed, we found a greater risk only for participants in the fourth quartile, with an average sodium consumption of 3901 mg/d without accounting for the salt added to table. Average consumption in the first quartile was 1669 mg/d. This is consistent with the recent results from the PURE study (Prospective Urban Rural Epidemiology)[27] that reported a nonuniform relation between sodium excretion and BP, challenging the current guidelines to limit sodium intake to ≤2400 mg/d to prevent hypertension.[18,19] In line with our results as regards sodium/potassium ratio, the authors of the PURE study found that potassium excretion counterbalanced the adverse effect of high sodium excretion on BP and suggested that diets rich in potassium might be more effective than an aggressive salt reduction to prevent hypertension. Consistent with previous observational studies[5,27–29] and meta-analysis,[30] we also observed an inverse relationship between potassium intake and risk of hypertension.

Fiber, Whole Grain

Association between high dietary fibers and lower risk of hypertension has been reported in observational studies in both men and women but did not remain significant after multiple adjustments for confounding factors in women.[9,10] The potential protective effect on BP has been linked to their ability to increase insulin sensitivity[31] and improve endothelial function.[32] Although our results were consistent with a protective role of fiber intake on BP, we cannot determine whether this can be ascribed specifically to the dietary fibers or to other components of foods highly correlated to fiber intake like potassium and magnesium. Indeed, the association did not remain significant when adding these nutrients in the same model. A synergistic effect of these nutrients is also possible because fibers have been shown to improve mineral absorption, in particular magnesium, in the gastrointestinal system.[33,34]

Magnesium and Nuts

The largest decreases in risk of hypertension were observed for magnesium intake consistently with other observational

Table 1. Baseline Characteristics of 80 426 Participants and According to Adherence to DASH Diet (Quartiles of DASH Score)

Characteristics	All	Q1	Q2	Q3	Q4	*P* Trend
DASH score	23.9±4.9	17.6±2.3	22.1±0.8	25.4±1.1	30.3±2.1	…
n	80 426	19 967	17 489	23 647	19 323	…
% Men	20.1	21.5	20.3	19.5	19.2	<0.0001
Age, y	41.9±14.0	36±12.5	41±13.6	43.9±13.9	46.4±13.9	<0.0001
BMI, kg/m^2	23.3±4.1	23.8±4.7	23.6±4.2	23.3±4	22.7±3.6	<0.0001
Alcohol intake, g/d	7.5±10.7	8.3±12.5	7.8±10.9	7.5±10.4	6.3±8.8	<0.0001
Smoking status, %						<0.0001
Never smoker	51.4	48.7	51.5	51.7	53.6	
Former smoker	31.8	25.8	30.9	33.9	36.1	
Current smoker	16.8	25.6	17.6	14.4	10.3	
Physical activity, %						<0.0001
Low	24.2	31.3	26.0	22.5	17.4	
Medium	43.3	41.5	43.5	44.1	44.1	
High	32.5	27.3	30.6	33.4	38.5	
Education level, %						<0.0001
Primary	2.2	2.3	2.3	2.3	2.1	
High school	31.2	36.7	32.0	29.6	26.8	
University or equivalent	66.6	61.1	65.7	68.2	71.1	
Total energy intake, kcal/d		1906±501	1834±479	1817±466	1840±458	<0.0001
Nutrients						
Proteins, %EI*	17.3±4.0	17.2±4.4	17.4±4	17.5±3.9	17±3.9	0.009
Fats, %EI*	39.3±6.7	40.8±6.1	39.6±6.4	38.7±6.6	38.2±7.2	<0.0001
Total carbohydrates, %EI*	43.1±7.1	41.7±6.9	42.7±6.9	43.5±6.9	44.4±7.2	<0.0001
Fiber, g/d	19.6±7.5	14.8±4.9	17.4±5.5	20.1±6.2	25.8±8.4	<0.0001
Sodium, mg/d	2681±920	2907±958	2737±917	2633.4±891	2454±857	<0.0001
Potassium, mg/d	2968±837	2623±726	2802±757	3019±771	3409±884	<0.0001
Magnesium, mg/d	335±116	285±89	308±96	338±105	407.9±131	<0.0001
Phosphorus, mg/d	1264±360	1201±345	1221±342	1264±344	1366±384	<0.0001
Calcium, mg/d	926±316	839±310.3	898±304	945±306	1015±317	<0.0001
Vitamin D, mg/d	2.9±2.4	2.5±2.1	2.6±2.3	2.7±2.4	2.9±2.6	<0.0001
Food						<0.0001
Fruits and vegetables, g/d	467±243	291±161	406±182	506±203	658±255	
Starchy, g/d	244±109	241±104	239±105	241±107	256±118	
Whole grains, g/d	34.6±49.6	10.5±23.5	20.9±34.9	36.5±46.4	69.5±62.7	
Legumes, g/d	12.4±27.6	6±17.1	9.2±22.1	12.4±26.7	21.8±37.6	
Low-fat dairy, g/d	191±152	165±141	189±149	201±153	207±160	
Nuts, g/d	5.0±12.5	1.3±4.8	2.6±7.6	4.5±10.7	11.6±19.3	
Soda, mL/d	48.8±111.9	120.5±171.2	43.2±92.4	23.6±63.7	10.5±39.2	

BMI indicates body mass index; DASH, Dietary Approach to Stop Hypertension; EI, energy intake; and Q, quartile.
*Total energy intake without alcohol.

studies[35,36] and for nuts consumption. The latter relationship remained similar even after additional adjustment for sodium intake (Table S1 in the online-only Data Supplement). This beneficial effect has been previously pointed in an ancillary analysis of the PREDIMED study (Primary Prevention of Cardiovascular Disease With a Mediterranean Diet) testing the effect of a diet supplemented with nuts on BP.[37] This effect may be attributed to magnesium and to poly unsaturated fatty acid content of nuts. Finally, nuts consumption was low in our sample, which probably reflects consumption in the general population, and could be more promoted in nutritional policies.

Proteins

A meta-analysis of 40 randomized controlled trials reported that dietary protein intake had a significant but small beneficial effect on BP: (systolic: −0.21; 95 confidence interval, −0.32 to −0.09 and diastolic: −0.18; 95 confidence intervals −0.29 to −0.06).[38]

Table 2. HRs of Hypertension According to Quartiles of Nutrients Intake

Nutrients	Quantity per Quartile, Mean±SD	HRs (95% CI)*	*P* Trend†	HRs (95% CI)‡	*P* Trend†
Sodium	mg/d		0.0009		0.0045
Q1	1669±293	1 (ref)		1 (ref)	
Q2	2303±145	0.93 (0.82–1.04)		0.94 (0.83–1.06)	
Q3	2843±176	1.00 (0.89–1.12)		1.00 (0.88–1.13)	
Q4	3910±740	1.16 (1.04–1.31)		1.17 (1.02–1.35)	
Potassium	mg/d		0.01		0.02
Q1	2016±300	1 (ref)		1 (ref)	
Q2	2645±139	0.87 (0.77–0.98)		0.87 (0.76–0.98)	
Q3	3142±156	0.85 (0.76–0.96)		0.86 (0.75–0.98)	
Q4	4068±650	0.81 (0.72–0.92)		0.82 (0.72–0.94)	
Sodium/ potassium ratio			<0.0001		0.009
Q1	0.6±0.1	1 (ref)		1 (ref)	
Q2	0.8±0	1.05 (0.95–1.17)		1.04 (0.93–1.15)	
Q3	1±0	1.09 (0.97–1.23)		1.05 (0.93–1.18)	
Q4	1.4±0.2	1.31 (1.17–1.47)		1.22 (1.08–1.37)	
Proteins	%EI*		<0.0001		0.2
Q1	13±1.4	1 (ref)		1 (ref)	
Q2	15.8±0.6	1.21 (1.06–1.38)		1.13 (0.99–1.29)	
Q3	17.9±0.7	1.26 (1.11–1.43)		1.11 (0.97–1.26)	
Q4	22.5±3.9	1.46 (1.29–1.65)		1.15 (1.00–1.31)	
Animal protein	%EI§		<0.0001		0.003
Q1	7±2	1 (ref)		1 (ref)	
Q2	10.3±0.7	1.29 (1.13–1.46)		1.17 (1.03–1.34)	
Q3	12.6±0.7	1.31 (1.16–1.49)		1.11 (0.98–1.26)	
Q4	17.3±4.1	1.65 (1.46–1.86)		1.26 (1.11–1.43)	
Plant protein	%EI§		<0.0001		0.005
Q1	4±0.5	1 (ref)		1 (ref)	
Q2	4.9±0.2	0.96 (0.85–1.08)		1.02 (0.90–1.15)	
Q3	5.7±0.3	0.83 (0.74–0.93)		0.91 (0.81–1.02)	
Q4	7.4±1.4	0.72 (0.64–0.81)		0.85 (0.75–0.95)	
Total carbohydrates	%EI§		0.05		0.9
Q1	34.3±4	1 (ref)		1 (ref)	
Q2	41±1.3	0.95 (0.85–1.06)		0.96 (0.86–1.08)	
Q3	45.3±1.3	0.91 (0.82–1.02)		1.00 (0.90–1.13)	
Q4	51.9±3.9	0.86 (0.76–0.96)		0.89 (0.78–1.01)	
Fat	%EI§		0.7		0.6
Q1	30.7±3.8	1 (ref)		1 (ref)	
Q2	37.4±1.3	1.05 (0.94–1.18)		1.04 (0.93–1.16)	
Q3	41.5±1.2	1.03 (0.92–1.15)		0.99 (0.88–1.11)	
Q4	47.5±3.2	1.00 (0.89–1.12)		0.96 (0.85–1.08)	

(*Continued*)

Table 2. Continued

Nutrients	Quantity per Quartile, Mean±SD	HRs (95% CI)*	*P* Trend†	HRs (95% CI)‡	*P* Trend†
SFA	%EI§		0.9		0.9
Q1	10.9±2	1 (ref)		1 (ref)	
Q2	14.8±0.8	1.03 (0.92–1.14)		1.01 (0.90–1.12)	
Q3	17.2±0.7	1.02 (0.91–1.14)		0.99 (0.88–1.11)	
Q4	20.8±1.9	1.05 (0.94–1.18)		1.01 (0.89–1.13)	
MUFA	%EI§		0.4		0.6
Q1	10.7±1.6	1 (ref)		1 (ref)	
Q2	13.6±0.6	1.07 (0.96–1.19)		1.05 (0.94–1.17)	
Q3	15.6±0.7	1.05 (0.94–1.18)		1.02 (0.91–1.14)	
Q4	19.4±2.5	0.99 (0.88–1.11)		0.97 (0.87–1.09)	
PUFA	%EI§		0.1		0.2
Q1	3.6±0.5	1 (ref)		1 (ref)	
Q2	4.7±0.3	1.09 (0.97–1.22)		1.05 (0.94–1.18)	
Q3	5.8±0.3	1.06 (0.95–1.19)		1.02 (0.91–1.15)	
Q4	8.3±2.1	0.97 (0.86–1.08)		0.94 (0.84–1.06)	
Fiber	g/d		<0.0001		0.009
Q1	12±2	1 (ref)		1 (ref)	
Q2	16±1	0.89 (0.79–1.01)		0.93 (0.82–1.05)	
Q3	21±1	0.79 (0.70–0.89)		0.84 (0.74–0.95)	
Q4	30±7	0.71 (0.63–0.80)		0.81 (0.71–0.93)	
Magnesium			<0.0001		0.001
Q1	216±31	1 (ref)		1 (ref)	
Q2	286±17	0.97 (0.86–1.09)		0.96 (0.85–1.09)	
Q3	350±21	0.89 (0.79–1.00)		0.87 (0.77–0.99)	
Q4	490±108	0.76 (0.68–0.86)		0.77 (0.67–0.89)	
Phosphorus			0.5		0.7
Q1	869±122	1 (ref)		1 (ref)	
Q2	1123±56	0.95 (0.84–1.07)		0.94 (0.83–1.06)	
Q3	1328±66	1.03 (0.92–1.16)		0.98 (0.86–1.11)	
Q4	1735±306	0.99 (0.88–1.11)		0.94 (0.81–1.09)	
Calcium			0.7		0.9
Q1	569±103	1 (ref)		1 (ref)	
Q2	798±53	1.06 (0.94–1.19)		1.05 (0.93–1.18)	
Q3	990±61	1.03 (0.92–1.16)		1.02 (0.90–1.15)	
Q4	1345±242	1.00 (0.89–1.13)		1.01 (0.89–1.15)	
Vitamin D					
Q1	0.9±0.3	1 (ref)	0.1	1 (ref)	0.2
Q2	1.6±0.2	1.04 (0.93–1.18)		1.04 (0.92–1.17)	
Q3	2.5±0.3	1.00 (0.89–1.13)		1.00 (0.88–1.13)	
Q4	5.7±2.9	1.13 (1.01–1.26)		1.11 (0.99–1.25)	

BMI indicates body mass index; CI, confidence interval; EI, energy intake; HR, hazard ratio; MUFA, mono unsaturated fatty acid; PUFA, poly unsaturated fatty acid; Q, quartile; and SFA, saturated fatty acid.

*Model 1: adjusted for age (as primary time dependent variable) and sex.

†Trends were tested using quartiles of intakes as ordinal variable.

‡Model 2: model 1 additionally adjusted for smoking (never, former, and current), alcohol consumption (continuous), BMI (continuous), physical activity, educational level, total energy intake, and family history of hypertension.

§Total energy intake without alcohol.

Table 3. HRs of Hypertension According to Quartiles of Food Groups' Intake

Food Groups	Quantity per Quartile, Mean±SD	HRs (95% CI)*	*P* Trend†	HRs (95% CI)‡	*P* Trend†
Fruits and vegetables	g/d		0.0004		0.03
Q1	199±72	1 (ref)		1 (ref)	
Q2	370±40	0.91 (0.81–1.04)		1.00 (0.88–1.13)	
Q3	515±46	0.84 (0.75–0.95)		0.95 (0.84–1.07)	
Q4	786±206	0.78 (0.69–0.88)		0.85 (0.74–0.97)	
Low-fat dairy	g/d		0.3		0.5
Q1	36±24	1 (ref)		1 (ref)	
Q2	117±23	1.00 (0.90–1.12)		0.99 (0.89–1.11)	
Q3	207±32	0.92 (0.82–1.03)		0.93 (0.83–1.04)	
Q4	403±123	1.00 (0.89–1.12)		1.00 (0.89–1.13)	
Starchy			0.03		0.2
Q1	123±37	1 (ref)		1 (ref)	
Q2	200±17	0.94 (0.84–1.06)		0.96 (0.86–1.08)	
Q3	264±21	0.98 (0.88–1.10)		1.00 (0.90–1.13)	
Q4	389±86	0.85 (0.75–0.96)		0.89 (0.78–1.02)	
Whole grains			<0.0001		0.01
No consumption	0±0	1 (ref)		1 (ref)	
T1	9±4	0.92 (0.80–1.05)		0.97 (0.85–1.12)	
T2	31±10	0.89 (0.80–0.98)		0.92 (0.83–1.02)	
T3	102±55	0.77 (0.69–0.85)		0.84 (0.76–0.93)	
Legumes			0.07		0.2
No consumption	0±0	1 (ref)		1 (ref)	
T1	9±4	0.97 (0.85–1.12)		0.98 (0.86–1.13)	
T2	29±7	1.01 (0.89–1.15)		1.05 (0.93–1.19)	
T3	79±38	0.84 (0.73–0.96)		0.87 (0.76–1.00)	
Nuts			<0.0001		<0.0001
No consumption	0±0	1 (ref)		1 (ref)	
T1	2±1	0.90 (0.79–1.02)		0.97 (0.85–1.10)	
T2	8±2	0.83 (0.73–0.94)		0.91 (0.80–1.03)	
T3	30±22	0.63 (0.55–0.72)		0.72 (0.63–0.83)	
Red and processed meat			<0.0001		0.002
Q1	7±8	1 (ref)		1 (ref)	
Q2	40±9	1.14 (1.01–1.29)		1.08 (0.95–1.22)	
Q3	73±11	1.27 (1.13–1.43)		1.17 (1.03–1.32)	
Q4	136±42	1.47 (1.30–1.65)		1.25 (1.11–1.42)	
Soda			0.08		0.2
No consumption	0±0	1 (ref)		1 (ref)	
T1	36±16	1.06 (0.93–1.20)		1.06 (0.93–1.20)	
T2	96±21	1.16 (1.01–1.33)		1.14 (0.99–1.31)	
T3	285±185	1.16 (0.99–1.36)		1.12 (0.95–1.31)	

BMI indicates body mass index; CI, confidence interval; HRs, hazard ratios; Q, quartile; and T, tertile.
*Model 1: adjusted for age (as primary time dependent variable) and sex.
†Trends were tested using quartiles of intake as ordinal variable.
‡Model 2: model 1 additionally adjusted for smoking (never, former, and current), alcohol consumption (continuous), BMI (continuous), physical activity, educational level, total energy intake, and family history of hypertension.

Proteins may play a role on BP through their contents in arginine and tryptophan, 2 amino acids involved in NO production, which is known to have anti-inflammatory, antithrombotic, vasorelaxant, and antihypertrophic properties on endothelium.[39] Noteworthy, a recent study reported that long-term intake of animal products (meat and poultry but also seafood) was associated

Table 4. HRs of Hypertension According to Adherence to DASH Diet

Quartile of DASH Score	HRs (95% CI)*	*P* Trend†	HR (95% CI)‡	*P* Trend†
Q1	1 (ref)	<0.0001	1 (ref)	<0.0001
Q2	0.86 (0.76–0.97)		0.93 (0.82–1.05)	
Q3	0.72 (0.64-0.08)		0.81 (0.73–0.92)	
Q4	0.53 (0.47–0.60)		0.66 (0.58–0.75)	

CI indicates confidence interval; DASH, Dietary Approach to Stop Hypertension; HR, hazard ratio; and Q, quartile.

*Model 1: adjusted for age (as primary time dependent variable) and sex.

†Trends were tested using quartiles of intake as ordinal variable.

‡Model 2: model 1 additionally adjusted for smoking (never, former, and current), alcohol consumption (continuous), BMI (continuous), physical activity, educational level, total energy intake, and family history of hypertension.

with increased risk of hypertension.[40] According to the authors, this noxious effect would result from the process of cooking, producing advanced glycoxidation end products and heterocyclic amines, which increase oxidative stress and inflammation counteracting the potential beneficial effect. These dual mechanisms could explain the inconsistent findings of protein effect in the literature regardless the protein's origins. Ours findings were in agreement with these explanations as we found no significant association with risk of hypertension and global protein consumption but a significant increased risk with animal protein and a decreased risk with vegetable proteins.

Calcium, Vitamin D, and Dairy Products

Unlike results of a recent meta-analysis of prospective cohort studies[8] and of the DASH trial showing that the BP-lowering effect of dairy consumption combined with a diet rich in fruit and vegetables was more important compared with a diet rich in fruits and vegetables alone,[13] we did not observe association between incidence of hypertension and vitamin D, neither calcium or low-fat dairy intakes.

Global Diet

Individual nutrient or food approach does not allow to account for synergic effects. When considering the diet as a whole, a 44% decrease in risk of incident hypertension was observed among participants with a high adherence to the DASH-type diet. This is consistent with the findings of the Spanish SUN cohort study (Seguimiento Universidad de Navarra).[16] Our results highlighted that global healthy diet had more important influence on hypertension risk than individual nutritional factor. It is probable that undetectable associations when studying individual nutritional components are cumulated and emerged when considering the diet in a holistic manner.

Limitations and Strengths of Our Study

The major strengths of our study were the large size of participants issued from the general population, its prospective design, and the quality and completeness of dietary data assessing with repeated 24HR validated against biomarkers.[22] Moreover, the study collected a wide range of data, which allowed to take into account all potential confounding factors. Nevertheless, there were some limitations. First because hypertension was self-reported, misclassification bias remained possible; however, almost all participants who reported a new case of hypertension have also reported an adequate vasoactive treatment. Second, the data collection method remains not perfect. In the NutriNet-Santé study, validation studies reported that quality of the collected data was acceptable or high for anthropometrics data and comparable with that in conventional research for nutritional factors. Third, this sample of volunteers is not representative of the French general population, leading to limitations in terms of external validity. Indeed, women and well-educated individuals were over-represented compared with national data in the NutriNet-Santé cohort study, and it has been shown that participants of the cohort exhibit healthier dietary habits.[22]

Perspectives

Our results suggest that if an increased consumption of potassium, magnesium, whole grains, vegetable proteins, and nuts and a decreased consumption of sodium, animal proteins, and red and processed meat are major nutritional factors to prevent hypertension, adopting an overall healthy diet has strongest protective role on hypertension. Preventing hypertension through the improvement of dietary intake could have major public health benefits.

Acknowledgments

We thank all volunteers who participated in the NutriNet-Santé study and all the health professionals and staff at the coordinating centre.

Sources of Funding

The NutriNet-Santé study is supported and has received grants by the following institutions: Fondation cœurs et Artères, Ministère de la Santé, Institut de Veille Sanitaire, Institut National de la Prévention et de l'Education pour la Santé, Fondation pour la Recherche Médicale, Institut de Recherche en Santé Publique, Institut National de la Santé et de la Recherche Médicale, Institut National de la Recherche Agronomique, Conservatoire National des Arts et Métiers, and Université Paris 13.

Disclosures

None.

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Novelty and Significance

What Is New?

- This study reports the association between nutrition and hypertension incidence in a large sample of general population through an accurate assessment of nutritional intake.

What Is Relevant?

- Besides several major nutritional factors associated with incidence of hypertension, adopting an overall healthy diet has the strongest protective role on hypertension.

Summary

Preventing hypertension through the improvement of dietary could have major public health benefits.

Hypertension
JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Hypertension. 2017;70:712-720; originally published online July 31, 2017;
doi: 10.1161/HYPERTENSIONAHA.117.09622
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0194-911X. Online ISSN: 1524-4563

TITLE

Individual and combined effects of dietary factors on risk of incident hypertension: prospective analysis from the NutriNet-Santé cohort.

Short title: Nutrition and incident hypertension

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Association between nuts intakes and hypertension corrected for sodium intakes

Table S1: Hazards Ratios of hypertension according to quartiles of Nuts intakes additionally corrected for sodium intakes

Nuts intakes	Nuts quantity per quartile (mean±SD)	HRs (95% CI)*	p-trend‡	HRs (95% CI)†	p-trend‡
No consomption	0±0	1 (ref)		1 (ref)	
T1	2± 1	0.90 (0.79-1.02)		0.97 (0.85-1.10)	
T2	8±2	0.83 (0.73-0.94)	<.0001	0.91 (0.80-1.03)	<.0001
T3	30±22	0.63 (0.55-0.72)		0.72 (0.63-0.83)	

*model 1 : adjusted for age (as primary time dependent variable) and sex

†model 2: model1 additionally adjusted for smoking (never, former, current), alcohol consumption (continuous), BMI (continuous), physical activity, educational level, total energy intake, and family history of hypertension and sodium intakes

‡trends were tested using quartiles intakes as ordinal variable

Abbreviation: HRs, Hazard Ratios; 95% CI, 95%Confidence Intervals;