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Hypothesis-oriented food patterns and incidence of hypertension: 6-year follow-up of the SUN (Seguimiento Universidad de Navarra) prospective cohort

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Abstract

Objective: To study the association between adherence to several a priori-defined healthy food patterns and the risk of hypertension.

Design: Prospective, multipurpose, dynamic cohort study (recruitment permanently open). We followed up 10 800 men and women (all of them university graduates), who were initially free of hypertension, for a variable period (range 2–6 years, median 4·6 years). During follow-up, 640 participants reported a new medical diagnosis of hypertension. Baseline diet was assessed using a validated 136-item FFQ. Validated information about non-dietary potential confounders was also gathered. We calculated adherence to fifteen different hypothesis-oriented food patterns and assessed the association between each of them and incident hypertension using multivariable Cox models.

Setting: The SUN (Seguimiento Universidad de Navarra – University of Navarra Follow-up) Project, Spain.

Subjects: Participants recruited to the SUN cohort before October 2005 were eligible for inclusion; after excluding those with self-reported hypertension or CVD at baseline, or with extreme total energy intake, data of 10 800 were analysed.

Results: Higher adherence to the DASH (Dietary Approaches to Stop Hypertension) diet (range of the score: 0 to 5) was significantly associated with a lower risk for developing hypertension (P for trend = 0·02). The other food patterns showed no significant association with incident hypertension.

Conclusions: Our results support a long-term protection of the DASH diet against the incidence of hypertension, but we found no evidence of a similar inverse association with hypertension for any other a priori-defined healthy food pattern.

Keywords
Mediterranean diet
Blood pressure
Food patterns
Dietary scores

Approximately one billion individuals worldwide are affected by elevated values of blood pressure (BP)[1]. BP is a classical, strong and independent risk factor for CVD: a continuous and consistently progressive positive association with the risk of CVD is observed throughout the range of BP, with no evidence of a threshold. Hypertension is a well-known and modifiable determinant of myocardial infarction, heart failure, stroke and kidney disease.

Preventive strategies for lowering BP, reducing BP-related events and preventing clinical hypertension should be reasonably priced, low-risk and easily implemented. This is one of the reasons why much of the effort to reduce the population burden of hypertension focuses on implementing non-pharmacological approaches. It is well established that lifestyle modifications such as weight loss, increased physical activity, moderation of alcohol consumption, reduction in sodium intake, or a combination of these modalities, decrease BP, enhance antihypertensive drug efficacy and decrease cardiovascular risk[1]. A salient element incorporated into these interventions is dietary advice following the Dietary Approaches to Stop Hypertension (DASH) diet[2,3]. The so-called DASH diet (rich in fruits, vegetables, low-fat dairy and whole grains, but low in saturated fat and red meats) has been proved to reduce average levels of BP and to reduce the incidence of

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hypertension in short-term trials[2–5]. However, the epidemiological evidence regarding the long-term effects of a DASH-type diet on the prevention of hypertension is not completely consistent. In fact, no apparent inverse linear trend was found in a large cohort study[6]. Another study found that the DASH diet was not more effective in preventing hypertension than was high fruit and vegetable consumption alone[7]. Also, others found that general established lifestyle and dietary recommendations were similarly effective in reducing BP as adding the DASH diet to these recommendations[8]. Moreover, adherence to other healthy food patterns has sometimes been related with reductions in average BP levels or reduced risk of hypertension, but the evidence is even less consistent[9–13]. In addition, most large previous epidemiological reports about these associations are based on cross-sectional designs[9–13] and the possibility of reverse causation bias cannot be discarded. In this context, there is no universal consensus about which pattern must be recommended for the long-term prevention of hypertension. There is also a need to ascertain if some of these healthy food patterns may be equally effective in reducing the long-term risk of developing hypertension.

Diet indices or food patterns can be built a priori (as opposed to patterns derived from exploratory factor or cluster analyses) because they are hypothesis-oriented food patterns and reflect known or suspected diet and disease associations[14,15]. The approach to build these patterns consists in summarizing the diet by means of a single score that results from a function of different components, such as foods, food groups or a combination of foods and nutrients. These components are selected based on prior knowledge or scientific evidence. This approach has been thus referred to as an 'a priori approximation'[6,14–16]. Some of these indices are based on adherence to existing dietary models, such as the Mediterranean diet[17]; on adherence to existing Dietary Guidelines[18]; or on diversity in dietary intake[19].

The assessment of the association between the original and most commonly used definition for the Mediterranean Diet Score (MDS), developed by Trichopoulou *et al.*[20], and the risk of hypertension in the SUN (Seguimiento Universidad de Navarra – University of Navarra Follow-up) cohort has been the topic of a previous report by our group[21]. We found no significant association between adherence to this original MDS and the incidence of hypertension[21]. However, there are several other definitions and operational scores proposed to estimate adherence to the Mediterranean diet[17]. In addition to the MDS there are several other indices available to assess the compliance with a variety of recommended healthy dietary patterns.

The aim of the present study was to provide evidence to clarify which of the most frequently proposed healthy dietary indices is more effective for the reduction of the long-term incidence of hypertension in the SUN cohort.

Methods

Study population

The SUN project comprises an ongoing, multipurpose, prospective and dynamic cohort of university graduates conducted in Spain. The study protocol was approved by the Institutional Review Board of the University of Navarra.

The study methods have been published in detail elsewhere[22]. In short, beginning in December 1999, participants – all of them university graduates – have been periodically contacted through mailed questionnaires, which ask for comprehensive baseline characteristics of the study participants. Besides the questionnaire, they receive an invitation letter to participate. Voluntary completion of the first questionnaire is considered as informed consent. The enrolment is permanently open and each year an average of 2000–2500 new participants are newly admitted in the cohort. Follow-up is conducted through mailed questionnaires every 2 years. Non-respondents receive up to five additional mailings requesting their follow-up questionnaire.

Up to July 2008, 20 095 participants were enrolled in the SUN cohort. To warrant a minimum follow-up of 2 years, 15 829 participants recruited before October 2005 were candidates to be eligible for the present analysis because they had spent enough time in the study to be able to complete at least the 2-year follow-up questionnaire. Among them, the retention rate was 88 %. Therefore, we had follow-up information of 13 898 participants. Retention rates at 4- and 6-year follow-up were above 80 %. We excluded 1505 participants due to self-reported baseline prevalent hypertension and 1366 participants with extreme total energy intake (<2092 kJ/d or >14 644 kJ/d in women; <3347 kJ/d or >16 736 kJ/d in men)[23]. Finally, 362 participants were excluded due to prevalent CVD at baseline. Thus, the effective sample size for the analyses was 10 800 participants. Among them, 5113 had completed the 6-year follow-up, 2494 the 4-year follow-up but not the 6-year follow-up, and 3193 only the 2-year follow-up.

Exposure assessment

Habitual diet was assessed at baseline with a semi-quantitative 136-item FFQ previously validated in Spain[24]. Each item in the questionnaire included a typical portion size. Daily food consumption was estimated by multiplying the portion size by the consumption frequency for each food item. Nutrient composition of the food items was derived from Spanish food composition tables[25,26].

We tested a slightly modified definition of the original MDS proposed by Trichopoulou *et al.*[20], the Modified Mediterranean Diet Score (MMDS). This score was calculated by developing an a priori score (range: 0 to 9 points) using olive oil instead of the MUFA:SFA ratio originally used in the MDS; we also restricted the negative weighting given to the dairy products group to only whole-fat dairy. A value of 0 or 1 was assigned to each of the nine indicated components with the use of the sex-specific medians as cut-off points. For allegedly beneficial components (vegetables, legumes, fruits, cereals, fish, olive oil), participants whose consumption was below the median were assigned a value of 0, and a value of 1 otherwise. For components presumed to be detrimental (meats and meat products, whole-fat dairy products), participants whose consumption was below the median were assigned a value of 1, and a value of 0 otherwise. We also lowered the upper cut-off points of the original definition of the MDS for alcohol intake and considered only alcohol coming from red wine. A value of 1 was given to men consuming from 5 to <30 g alcohol/d and to women consuming from 2·5 to 15 g alcohol/d exclusively from red wine. Participants were categorized into a low (0–2), intermediate (3–6) or high adherence (7–9) to this MMDS.

Dietary information in our cohort was updated after 2 years of follow-up with brief questions in which participants reported whether they had increased, maintained or decreased the consumption of key food groups. With this available updated information we calculated an Updated Modified Mediterranean Diet Score (UMMDS) as follows. For changes in the consumption of fruits and vegetables, fish, alcohol or olive oil, we summed another point for each item when the participant increased his/her consumption whereas we subtracted a point for each of these items that the participant reported to have reduced his/her consumption. For any decrease in the consumption of dairy products, meats and meat products, butter or sweets we added a further point for each item; increases in the consumption of these items were computed by subtracting a point for each from the baseline score. Accordingly, this updated score (UMMDS) potentially ranged from −8 to +17.

We also looked at the association between other previously published food patterns dealing with the Mediterranean diet and the incidence of hypertension, metabolic syndrome or obesity. Thus, we calculated the Mediterranean Adequacy Index (MAI)[17,27,28], the Mediterranean Diet Quality Index (MDQI)[29], the Mediterranean Food Pattern (MFP) proposed by Sanchez-Villegas *et al.*[30] and the Mediterranean Score proposed by Panagiotakos *et al.*[31] (MSP). Further information on how to calculate these indices can be found in the Appendix and the cited references.

In order to cover a wider spectrum, we also considered several dietary patterns that were not based on the Mediterranean diet hypothesis and assessed their association with incident hypertension. Specifically, we computed the Diet Quality Index–International (DQI-I)[32]; the Recommended Food Score (RFS)[33]; the Quantitative Index for Dietary Diversity, both in terms of total energy intake (QIDD-k) and in grams of intake (QIDD-g)[19]; the Healthy Eating Index (HEI)[34]; the Alternate Healthy Eating Index (AHEI)[35]; and the Dietary Guidelines for Americans Adherence Index (DGAI)[36]. Again, detailed information on how to estimate these scores can be found in the Appendix and the cited references.

The DASH food pattern is based on recommendations originating from the DASH trial[3,5]. Similarly to the definition of the MDS, we defined a score of adherence to the DASH diet by creating an a priori 6-point score. For the DASH score, a value of 0 or 1 was assigned to each of six indicated components with the use of the results of the DASH trial and the available DASH dietary recommendations (www.dashdiet.org). Thus, daily consumption of ≥5 servings of fruit, ≥4 servings of vegetables, 2–3 servings of low-fat or non-fat dairy products, ≤1/2 serving of sweets and ≥1 serving of whole grains, and consumption of 1–3 servings of lean meat, poultry or fish, were considered as optimal and were scored with 1 point each.

In the baseline questionnaire, the following short questions concerning attitudes towards a healthy diet were included: (i) 'Do you try to eat much fruit?'; (ii) 'Do you try to eat many vegetables?'; (iii) 'Do you try to eat much fish?'; (iv) 'Do you usually snack between meals?'; (v) 'Do you try to avoid consuming butter?'; (vi) 'Do you try to reduce your fat intake?'; (vii) 'Do you try to reduce your meat consumption?'; (viii) 'Do you try to reduce your consumption of sweets?'. Another question gathered information about the frequency of eating outside the home. With the answers to these questions, we built up another score: Score of Attitudes Towards a Healthy Diet (ATHD). Attitudes towards increased fruit, vegetable or fish consumption, or reduced butter, fat, meat, snacking or frequency of eating outside the home (<1/week), each contributed 1 point to this score. Consequently, this score (ATHD) ranged from 0 to 9 points.

Ascertainment of incident hypertension

The outcome was defined by the self-report of a medical diagnosis of hypertension in any follow-up questionnaire. Self-reported diagnosed hypertension has been previously validated in a subsample of this cohort[37]. Briefly, two physicians, blinded to the information reported by participants in the questionnaires, did direct measurements of BP in the participants' home and thus confirmed self-reported hypertension or self-reported hypertension-free status in a subsample of the cohort. With the conventional measurement of BP, 82·3% (95% CI 72·8, 92·8%) of those self-reporting a diagnosis of hypertension in the questionnaires were confirmed. Among those who did not report a diagnosis of hypertension in the questionnaires, 85·4% (95% CI 72·4, 89·1%) were confirmed as non-hypertensives[37].

Assessment of other covariates

Age, sex, smoking habit, family history of hypertension, height and weight were collected in the baseline questionnaire. BMI was then calculated as the ratio between weight and the square of height (kg/m^2).

Information regarding physical activity was gathered at baseline with a specific questionnaire previously validated in Spain[38] which assessed the time spent in seventeen different activities. Each of these activities was assigned a multiple of the resting metabolic rate (MET score). For this purpose, we used information on average intensity of each activity from previously published guidelines[39].

Statistical analysis

Participants were divided into categories according to previous categorizations of these scores. In the cases in which evidence was not available, participants were divided taking into account sample sizes of each category.

Food and nutrient adjustment for total energy intake was performed with the residual method[23].

We fitted Cox regression models to assess the relative incidence of hypertension across increasing categories of the a priori-defined scores of adherence to healthy food patterns. When addressing the association between the UMMDS and the outcome, we used as exposure the updated diet after 2-year follow-up and we used as outcome only the incidence of hypertension after 4-year or 6-year follow-up (i.e. we excluded subjects who had only 2-year follow-up). In all analyses, we fitted a first Cox regression model adjusted only for age and sex. In a second model we additionally adjusted for BMI (kg/m^2), family history of hypertension, total energy intake, smoking (in three categories: never, past and current smokers) and physical activity. For the linear trend tests, we treated the exposures (scores) as continuous variables.

All *P* values are two-tailed and statistical significance was set at $P < 0{\cdot}05$. Analyses were performed with the SPSS statistical software package version 15·0 (SPSS Inc., Chicago, IL, USA).

Results

Median follow-up in this cohort was 4·6 years. During 50 304 person-years of follow-up, 640 cases of incident hypertension were observed.

Baseline characteristics of the study participants are presented in Table 1. Subjects with a higher adherence to the DASH diet were more likely to be female, older, more physically active and hypercholesterolaemic, and less likely to be current smokers. Family history of hypertension was more frequent among them. They also had a lower consumption of alcohol, a lower total fat intake and higher intakes of total energy, potassium, carbohydrate, vegetable protein and fibre. On the other hand, participants with a higher adherence to the MMDS were more likely male, older, hypercholesterolaemic and physically active. Family history of hypertension was more common among them and they were less likely to be current smokers. These subjects presented higher intakes of total energy, sodium, carbohydrate, vegetable protein, fibre and MUFA:SFA ratio and a lower total fat intake.

Hazard ratios for the incidence of hypertension according to adherence to the different patterns are shown in Table 2. A higher adherence to the DASH diet was significantly associated with a lower risk for developing hypertension in the multivariable-adjusted model. Specifically, there was a significant inverse linear trend for this association. When we additionally adjusted for alcohol consumption, the results did not change materially (Table 2). Regarding the AHEI, the comparison between extreme quintiles showed an increased risk of hypertension among those subjects with a higher adherence to this pattern. Nevertheless, there was no significant linear trend for this association. Unexpectedly, hazard ratios relating adherence to the UMMDS with the risk of hypertension showed a significant direct association (multivariable-adjusted hazard ratio = 1·34, 95 %CI 1·04, 1·73, *P* for trend = 0·002). However, none of the other healthy food patterns, including five other indices, assessing adherence to the Mediterranean diet (MMDS, MAI, MDQI, MFP and MSP) showed any significant association with the incidence of hypertension.

Discussion

These data from the SUN cohort with more than 50 000 person-years of follow-up showed that higher adherence to a DASH-type diet was associated with a reduction in the risk of hypertension in the long term. Although an updated score for the Mediterranean diet including only the subset of the cohort who completed 4-year or 6-year follow-up was unexpectedly associated with a modestly increased risk of hypertension, all other indices built to appraise adherence to the Mediterranean food pattern (MMDS, MAI, MDQI, MFP and MSP) which included all participants did not show any apparent association with the incidence of hypertension.

All assessed food patterns share some characteristics such as encouraging the consumption of high amounts of fruits and vegetables. However, they try to gather some diverse aspects of diet and thus they can be separated into two main groups: (i) those that aim to capture the healthy aspects of the Mediterranean diet (MMDS, UMMDS, MAI, MDQI, MFP and MSP); and (ii) those trying to merge existing evidence and recommendations about promoting healthy and avoiding deleterious foods and nutrients (DASH diet, DQI-I, RFS, QIDD, HEI, AHEI and DGAI).

It has long been postulated that the Mediterranean diet may be protective against CVD[40,41]. In fact, several large cohorts have found that higher adherence to the Mediterranean diet was associated with a significant reduction in total and cardiovascular mortality[20,42–44]. However, the inconsistency of these previous results with our

Table 1 Baseline characteristics* of the SUN study population according to adherence to food patterns (participants recruited during 1999–2005)

	Adherence to the DASH diet†								Adherence to the MMDS‡					
	Low (score 0)		Low–moderate (score 1)		Moderate–high (score 2)		High (score 3–6)		Low (score 0–2)		Moderate (score 3–6)		High (score 6–9)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
n	6487		3328		827		158		1824		7914		1062	
Sex (% women)	57		69		77		84		63		63		57	
Age (years)	36	11	37	11	37	12	39	12	33	9	37	11	42	12
Hypercholesterolaemia (%)	14		14		16		18		10		14		23	
Family history of hypertension (%)	37		40		38		43		35		38		42	
Smoking (%)														
Current smokers	25		23		20		15		25		24		20	
Ex-smokers	25		28		28		30		21		26		35	
BMI (kg/m^2)	23	3	23	3	23	3	23	3	2	3	23	3	24	3
Physical activity (MET × h/week)	23·5	20·9	24·9	22·2	27·1	23·1	32·1	30·2	20·9	20·4	24·5	21·4	29·2	24·8
Alcohol intake (g/d)	7	10	6	9	5	8	4	5	5	8	6	10	9	10
Na intake (g/d)	3·4	2·2	3·3	2·1	3·2	1·8	3·1	1·5	3·4	2·3	3·3	2·2	3·3	1·9
K intake (g/d)	4·3	1·2	4·9	1·6	6·2	2·1	7·3	2·1	3·6	1·0	4·8	1·5	6·0	1·6
Ca intake (g/d)	1·1	0·4	1·3	0·5	1·5	0·5	1·6	0·5	1·1	0·4	1·2	0·5	1·4	0·4
Total energy intake (kcal/d)	2347	610	2367	61	2508	622	2566	600	2124	597	2392	608	2613	541
Carbohydrate (% of energy intake)	42	7	44	8	47	8	49	7	40	7	44	7	47	7
Protein intake (% of energy intake)	18	3	18	3	18	4	18	3	18	4	18	3	18	3
Vegetable protein (g/d)	6·4	3·0	8·0	5·1	11·6	7·6	15·2	7·1	4·5	2·6	7·7	4·5	10·6	5·1
Total fat intake (% of energy intake)	38	6	36	7	33	7	31	7	40	6	37	6	33	6
MUFA (% of energy intake)	16	4	15	4	14	4	13	3	16	3	16	4	15	3
SFA (% of energy intake)	13	3	12	3	11	3	10	3	15	3	12	3	10	2
PUFA (% of energy intake)	5	2	5	2	5	2	4	1	6	2	5	2	5	1
MUFA:SFA ratio	1·3	0·3	1·3	0·4	1·4	0·4	1·4	0·4	1·1	0·2	1·3	0·3	1·5	0·4
Olive oil intake (g/d)	21	17	23	18	25	19	24	17	13	13	23	18	31	17
Fibre intake (g/d)	23	8	29	12	40	16	52	17	17	7	27	11	39	13

SUN, Seguimiento Universidad de Navarra (University of Navarra Follow-up); DASH, Dietary Approaches to Stop Hypertension; MMDS, Modified Mediterranean Diet Score; MET, metabolic equivalent.
*Mean and standard deviation unless otherwise stated.
†Based on the recommendations originating from the DASH trial, we defined a score of adherence to the DASH diet by creating an a priori 6-point score. A value of 0 or 1 was assigned to each of six indicated components with the use of the results of the DASH trial and the available DASH dietary recommendations (www.dashdiet.org). Thus, a daily consumption of ≥5 servings of fruit, ≥4 servings of vegetables, 2–3 servings of low-fat or non-fat dairy products, ≤1/2 serving of sweets and ≥1 serving of whole grains, and consumption of 1–3 servings of lean meat, poultry or fish, were considered as optimal and were scored with 1 point each.
‡The MMDS was calculated by assigning a value of 0 or 1 to each of the nine indicated components with the use of the sex-specific medians as cut-off points. For allegedly beneficial components (vegetables, legumes, fruits, cereals, fish, olive oil), participants whose consumption was below the median were assigned a value of 0, and a value of 1 otherwise. For components presumed to be detrimental (meat and meat products, whole-fat dairy products), participants whose consumption was below the median were assigned a value of 1, and a value of 0 otherwise. For alcohol, a value of 1 was given to men consuming from 5 to <30 g/d and to women consuming from 2·5 to 15 g/d exclusively from red wine.

Table 2 Hazard ratios (HR) and 95 % confidence intervals of hypertension according to adherence to a priori-defined food patterns, the SUN Study, 1999–2008

DASH score	0*	1	2	3–5	*P* for trend
n	6487	3328	827	158	
Incident cases	399	194	41	6	
Person-years	30 452	15 289	3836	727	
Age- and sex-adjusted	1·00 (ref)	0·88 (0·74, 1·05)	0·85 (0·61, 1·18)	0·54 (0·24, 1·23)	0·04
Multivariable HR (95 % CI)†	1·00 (ref)	0·89 (0·75, 1·06)	0·80 (0·57, 1·10)	0·48 (0·21, 1·08)	0·02
Multivariable HR (95 % CI)‡	1·00 (ref)	0·90 (0·75, 1·07)	0·80 (0·58, 1·11)	0·48 (0·21, 1·09)	0·02

DQI-I	0–≤45*	>45–≤55	>55–≤65	>65	*P* for trend
n	276	2040	6404	2080	
Incident cases	23	111	387	119	
Person-years	1302	9748	29 991	9263	
Age- and sex-adjusted	1·00 (ref)	0·76 (0·48, 1·19)	0·83 (0·54, 1·27)	0·84 (0·54, 1·33)	0·69
Multivariable HR (95 % CI)†	1·00 (ref)	0·87 (0·55, 1·38)	1·02 (0·66, 1·60)	1·03 (0·64, 1·64)	0·61

RFS	0–12*	13–16	17–20	>21	*P* for trend
n	3266	2805	2406	2323	
Incident cases	204	153	140	143	
Person-years	15 678	13 150	11 093	10 384	
Age- and sex-adjusted	1·00 (ref)	0·94 (0·76, 1·16)	1·03 (0·83, 1·28)	1·14 (0·92, 1·42)	0·36
Multivariable HR (95 % CI)†	1·00 (ref)	0·95 (0·77, 1·18)	1·06 (0·85, 1·33)	1·22 (0·96, 1·54)	0·18

QIDD-k (log-transformed)	≤2·34*	>2·34–≤2·61	>2·61–≤2·85	>2·85	*P* for trend
n	2700	2700	2700	2700	
Incident cases	176	144	152	168	
Person-years	12 841	12 688	12 661	12 114	
Age- and sex-adjusted	1·00 (ref)	0·85 (0·68, 1·06)	0·87 (0·70, 1·08)	0·96 (0·78, 1·19)	0·52
Multivariable HR (95 % CI)†	1·00 (ref)	0·93 (0·75, 1·17)	0·92 (0·74, 1·15)	1·04 (0·84, 1·28)	0·92

QIDD-g (log-transformed)	≤1·80*	>1·80–≤2·07	>2·07–≤2·31	>2·31	*P* for trend
n	2700	2700	2700	2700	
Incident cases	173	166	149	152	
Person-years	12 312	12 586	12 566	12 841	
Age- and sex-adjusted	1·00 (ref)	1·07 (0·87, 1·33)	0·94 (0·76, 1·18)	0·89 (0·71, 1·11)	0·41
Multivariable HR (95 % CI)†	1·00 (ref)	1·09 (0·88, 1·34)	0·95 (0·76, 1·18)	0·95 (0·76, 1·20)	0·97

HEI	≤5·0*	>5·0–≤5·7	>5·7–≤6·4	>6·4–≤7·2	>7·2	*P* for trend
n	2160	2160	2160	2160	2160	
Incident cases	115	116	138	128	143	
Person-years	10 583	10 384	10 154	9782	9402	
Age- and sex-adjusted	1·00 (ref)	0·92 (0·71, 1·19)	1·19 (0·93, 1·53)	1·08 (0·83, 1·39)	1·08 (0·83, 1·40)	0·48
Multivariable HR (95 % CI)†	1·00 (ref)	0·94 (0·73, 1·22)	1·20 (0·93, 1·54)	1·08 (0·83, 1·40)	1·17 (0·90, 1·52)	0·26

Table 2 *Continued*

AHEI	≤27·6*	>27·6–≤32·4	>32·4–≤36·8	>36·8–≤42·5	>42·5	*P* for trend
n	2160	2160	2160	2160	2160	
Incident cases	107	112	130	145	146	
Person-years	10 306	10 247	10 040	10 012	9700	
Age- and sex-adjusted	1·00 (ref)	1·04 (0·80, 1·36)	1·27 (0·98, 1·65)	1·26 (0·98, 1·62)	1·25 (0·97, 1·63)	0·37
Multivariable HR (95 % CI)†	1·00 (ref)	1·10 (0·84, 1·44)	1·35 (1·04, 1·76)	1·37 (1·06, 1·79)	1·44 (1·09, 1·91)	0·11

DGAI	≤6·5*	>6·5–≤7·5	>7·5–≤8·5	>8·5–≤9·5	>9·5	*P* for trend
n	2501	2153	2285	1733	2128	
Incident cases	150	130	136	89	135	
Person-years	12 126	10 258	10 818	7771	9331	
Age- and sex-adjusted	1·00 (ref)	0·99 (0·78, 1·25)	1·02 (0·81, 1·29)	0·92 (0·70, 1·19)	0·96 (0·75, 1·22)	0·91
Multivariable HR (95 % CI)†	1·00 (ref)	0·99 (0·78, 1·26)	1·04 (0·82, 1·32)	0·91 (0·70, 1·20)	1·04 (0·81, 1·33)	0·60

MMDS	0–2*	3–6	7–9	*P* for trend
n	1824	7914	1062	
Incident cases	91	464	85	
Person-years	8753	36937	4614	
Age- and sex-adjusted	1·00 (ref)	1·08 (0·86, 1·36)	1·11 (0·84, 1·54)	0·37
Multivariable HR (95 % CI)†	1·00 (ref)	1·07 (0·85, 1·35)	1·13 (0·83, 1·55)	0·31

UMMDS	≤3*	4–6	≥6	*P* for trend
n	2072	3464	2071	
Incident cases	103	216	195	
Person-years	11 671	19 472	11 434	
Age- and sex-adjusted	1·00 (ref)	1·18 (0·93, 1·50)	1·40 (1·10, 1·79)	0·001
Multivariable HR (95 % CI)†	1·00 (ref)	1·17 (0·91, 1·48)	1·34 (1·04, 1·73)	0·002

MAI	≤0·9*	>0·9–≤2·07	>2·07–≤2·31	>2·31	*P* for trend
n	2717	2699	2699	2485	
Incident cases	136	163	141	200	
Person-years	13 225	12 915	12 403	11 761	
Age- and sex-adjusted	1·00 (ref)	1·23 (0·98, 1·55)	0·99 (0·78, 1·25)	1·16 (0·93, 1·46)	0·49
Multivariable HR (95 % CI)†	1·00 (ref)	1·20 (0·95, 1·51)	0·97 (0·76, 1·23)	1·19 (0·95, 1·50)	0·47

Table 2 *Continued*

MDQI	≥11*	10–8	7–5	≤4	*P* for trend
n	825	4733	4252	990	
Incident cases	47	266	249	78	
Person-years	4005	22 667	19 289	4343	
Age- and sex-adjusted	1·00 (ref)	1·08 (0·79, 1·47)	1·09 (0·79, 1·50)	1·23 (0·85, 1·78)	0·28
Multivariable HR (95 % CI)†	1·00 (ref)	1·15 (0·84, 1·58)	1·16 (0·83, 1·61)	1·36 (0·93, 1·99)	0·18
MFP	**≤51·6***	**>51·6–≤57·3**	**>57·3–≤62·7**	**>62·7**	***P* for trend**
n	2700	2700	2700	2700	
Incident cases	131	138	173	198	
Person-years	12 954	12 798	12 458	12 094	
Age- and sex-adjusted	1·00 (ref)	0·95 (0·75, 1·21)	1·04 (0·83, 1·32)	1·03 (0·82, 1·30)	0·90
Multivariable HR (95 % CI)†	1·00 (ref)	0·93 (0·73, 1·18)	1·04 (0·82, 1·31)	1·05 (0·84, 1·33)	0·98
MSP	**≤29***	**30–32**	**≥33**		***P* for trend**
n	4209	3154	3437		
Incident cases	248	178	214		
Person-years	20 025	14 854	15 425		
Age- and sex-adjusted	1·00 (ref)	0·84 (0·69, 1·02)	0·94 (0·78, 1·14)		0·34
Multivariable HR (95 % CI)†	1·00 (ref)	0·86 (0·70, 1·04)	0·97 (0·80, 1·17)		0·52
ATHD	**0–2* (lowest)**	**3–4**	**5–6**	**7–9 (highest)**	***P* for trend**
n	1094	2979	4451	2276	
Incident cases	59	150	286	145	
Person-years	5272	14 168	20 584	10 280	
Age- and sex-adjusted	1·00 (ref)	0·98 (0·72, 1·32)	1·12 (0·85, 1·49)	0·97 (0·71, 1·32)	0·78
Multivariable HR (95 % CI)†	1·00 (ref)	0·95 (0·70, 1·29)	1·06 (0·79, 1·41)	0·92 (0·67, 1·26)	0·67

SUN, Seguimiento Universidad de Navarra (University of Navarra Follow-up) Study; DASH, Dietary Approaches to Stop Hypertension; DQI-I, Diet Quality Index–International; RFS, Recommended Food Score; QIDD, Quantitative Index for Dietary Diversity (in terms of total energy intake (QIDD-k) and in grams of intake (QIDD-g)); HEI,: Healthy Eating Index; AHEI, Alternate Healthy Eating Index; DGAI, Dietary Guidelines for Americans Index; MMDS, Modified Mediterranean Diet Score; UMMDS, Updated Modified Mediterranean Diet Score; MAI, Mediterranean Adequacy Index; MDQI, Mediterranean Diet Quality Index; MFP, Mediterranean Food Pattern (Sanchez-Villegas *et al.*); MSP, Mediterranean score (Panagiotakos *et al.*); ATHD, Attitudes Towards a Healthy Diet.

*Reference category.

†Adjusted for age, sex, BMI, family history of hypertension, total energy intake, physical activity, smoking and hypercholesterolaemia.

‡Additionally adjusted for alcohol intake.

findings regarding hypertension can be explained because other pathways can constitute alternative explanations of the cardioprotective effect of classical Mediterranean diets, such as those related to inflammatory status, cardiac rhythm thrombotic mechanisms, lipid levels, insulin sensitivity or endothelial function. Our results are not consistent with a previous report by Psaltoupoulou *et al.* where an index that tried to capture the nature of the traditional Mediterranean diet – the original MDS – was found to be inversely associated with average systolic and diastolic BP[45]. The cross-sectional design of the study by Psaltoupoulou *et al.*[45] together with the fact that they assessed BP average levels instead of the risk of hypertension does not allow a direct and proper comparison with our findings. On the other hand, in a previous report by another group of researchers, higher adherence to the Mediterranean diet (assessed using the MAI) was shown to be cross-sectionally associated with higher average systolic BP levels among older women[46]. Similarly to our results regarding the UMMDS, this unexpected cross-sectional finding does not support that any protection against hypertension can be expected from a higher adherence to the Mediterranean diet[21]. Our interpretation of the results regarding the Mediterranean diet and hypertension is that we found no evidence to support the hypothesis that a Mediterranean-type diet may reduce the long-term risk of hypertension, because the association was essentially null for all other indices of Mediterranean diet adherence that we tested. It is also possible that unmeasured or uncontrolled residual confounding may explain the unexpected positive association between UMMDS and hypertension. In fact, it is likely that small increases in BP, some slight weight gain or the diagnosis of some incident minor disease may have prompted decisions of participants to change their dietary habits or, because of these reasons, they may have received medical advice to improve their adherence to a Mediterranean-type diet.

The RFS has been previously associated with lower risk of CVD in women[47]. While the HEI has been associated with lower risk of CVD only in women[48,49], its variant – the AHEI – has been associated with lower risks of CVD in both women and men[35].

Adherence to a DASH-type diet has been the only dietary pattern shown to be inversely associated with the long-term incidence of hypertension in a large prospective cohort, the Iowa Women's Health Study, including 20 993 women[50]. Not surprisingly, we also found a protective association also for this pattern against the risk of hypertension. However, in the Iowa cohort, the inverse association was apparent only in the model adjusted for age and total energy intake; after adjustment for other potential confounders, there was little evidence that the long-term incidence of hypertension was independently related to the baseline DASH diet[50]. Our findings are also in agreement with the results reported by two other smaller cohorts. The first study, a German cohort of the EPIC (European Prospective Investigation into Cancer and Nutrition) project, including 8552 women followed for 2–4 years, found that participants in the third quartile of a DASH diet had significantly less hypertension incidence than those in the first quartile[6]. The other cohort study was conducted in France (SU.VI.MAX; SUpplementation en VItamines et Minéraux AntioXydants study) and included 2341 men and women followed-up for 5·4 years. They reported that the DASH pattern was inversely associated with changes in average BP, but no assessment was reported about the incidence of hypertension[7].

We are aware that our study has some limitations. First, we relied on self-reported information in the ascertainment of exposure and outcome. However, previous validation studies have shown adequate quality of this information. The FFQ that we used has been previously validated in Spain[24] and the self-report of hypertension had been previously validated in a subsample of the SUN cohort[37]. The results of the validation study suggest that self-reported hypertension can be considered a valid tool for assessing a medical diagnosis of hypertension in this highly educated cohort. Second, our sample is not representative of the general population since it is a young cohort formed entirely of university graduates. However, there is no biological reason to think that our results might not be generalizable to other population groups and this is the major support for the external validity of our findings[51]. Third, as in all observational studies, residual confounding might be an alternative potential explanation of the results found. Nevertheless, we were able to adjust for the main known risk factors for hypertension and for this reason we do not consider residual confounding as a likely important cause of the observed results. Fourth, non-differential measurement error in nutritional variables, inherent to the methodology in nutritional studies, might have occurred and we acknowledge that it may represent a difficulty for identifying associations of very low magnitude between healthy dietary patterns and the risk of hypertension. Fifth, since we have tested several dietary patterns it could be argued that multiple testing might play a role in our findings. Certainly, this issue could explain the presence of significant results it that were the case; however, it is not likely to be a major problem in our study where we found mainly non-significant results. Besides this, we have applied previously defined patterns with a clear rationale for their development. Thus, taking into account the consistency with previous studies[3,6,50] and substantial mechanistic reasons, the significant inverse linear trend found for the DASH diet is more likely to be supported by biological plausibility than to be explained just because of multiple testing.

Our findings do not support recommending the Mediterranean diet for the prevention of hypertension, but provide evidence in favour of the long-term effectiveness of the DASH diet.

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Appendix

Calculation of the dietary indices

Index	Reference	Index calculation
Diet Quality Index–International (DQI-I)	Kim *et al.* (2003)[32]	Components in four groups: Variety: overall food group variety (0–15 points); within-group variety for protein source (0–5 points) Adequacy: vegetables, fruits, cereals, fibre, protein, Fe, Ca, vitamin C (0–5 points each) Moderation: total fat, saturated fat, cholesterol, Na, empty-energy foods (0–6 points each) Overall balance: macronutrient ratio (carbohydrate:protein:fat, 0–6 points); fatty acid ratio (PUFA:MUFA:SFA, 0–4 points)
Recommended Food Score (RFS)	Kant *et al.* (2000)[33], McCullough *et al.* (2002)[47]	1 point (for each) if food items in the following categories were consumed at least once weekly: Vegetables: 15 varieties Fruit: 19 varieties Protein foods: 4 varieties Grains: 1 variety Dairy: 4 varieties
Quantitative Index for Dietary Diversity in terms of total energy intake (QIDD-k)	Katanoda *et al.* (2006)[19]	Ln QIDD-k $= \log[(1-\sum_j^n prop(j)^2)/(1-1/n)]$, where $prop(j)$ is the proportion of food group(s) j that contributes to total energy intake, n is the number of food groups and $j = 1,2,\ldots,n$. The food groups (number of food items within them) measured as a percentage of total energy intake considered were: cereals (5), nuts and seeds (2), potatoes (2), sugars and confectioneries (15), pulses (4), vegetables (9), fruits (18), fish and shellfish (7), meats (17), eggs (1), milk and other dairy products (15), oils and fats (15), seasonings and spices (3), alcoholic beverages and other beverages (14), seaweeds (0) and processed foods and others (5)
Quantitative Index for Dietary Diversity in terms of grams of intake (QIDD-g)	Katanoda *et al.* (2006)[19]	Ln QIDD-g $= \log[(1-\sum_j^n prop(j)^2)/(1-1/n)]$, where $prop(j)$ is the proportion of food group(s) j that contributes to total energy intake (g), n is the number of food groups and $j = 1,2,\ldots,n$ (the same groups as above)
Healthy Eating Index (HEI)	Kennedy *et al.* (1995)[34]	Ten components scored 0–10 points each based on the food guide pyramid and the Dietary Guidelines for Americans (1990): grains (bread, cereal, rice, pasta), vegetables, fruits, dairy products (includes yoghurt and cheese), meat group (includes meat, poultry, fish, dry beans, eggs, nuts), total fat, saturated fat, cholesterol, Na, variety
Alternate Healthy Eating Index (AHEI)	McCullough and Willett (2006)[35]	Eight components scored 0–10 points based on dietary recommendations: vegetables, fruit, nuts and soya, ratio of white to red meat, cereal fibre, *trans* fat, PUFA:SFA, alcohol. Multivitamin use scored 0–7·5 according to the length of use
Dietary Guidelines for Americans Adherence Index (DGAI)	Fogli-Cawley *et al.* (2006)[36]	Updated Guidelines for Americans (2005). Ten different indices based on energy needs. Eleven items for foods (0–1 points each): dark green vegetables, orange vegetables, legumes, other vegetables, starchy vegetables, fruits, variety, meat and beans, dairy products, all grains, discretionary energy; and nine items for healthy choices/nutrient intake: ≥50 % of grains as whole grains (0–1 point), fibre intake (0–1 point), total fat (0–1 point), saturated fat (0–1 point), *trans* fat (0–1 point), cholesterol (0–1 point), % of dairy products that are low-fat (0–0·5 point), Na (0–1 point), alcohol (0–1 point)
Mediterranean Adequacy Index (MAI)	Alberti-Fidanza and Fidanza (2004)[27]	MAI = (% energy from cereals + legumes + potatoes + vegetables + fruit fresh and dry + fish + wine + virgin olive oil)/(% energy from milk + cheese + meat + eggs + animal fats and margarines + sweet beverages + cakes and pies + cookies)
Mediterranean Diet Quality Index (MDQI)	Scali *et al.* (2001)[29]	Seven items scoring 0–2 points: saturated fat, cholesterol, meat, olive oil, fish, cereals and vegetables, and fruit
Mediterranean Food Pattern (MFP)	Sánchez-Villegas *et al.* (2002)[30]	Adherence (percentage$_i$) $= [(\sum z_i - \sum z_{min}) \times 100]/(\sum z_{max} - \sum z_{min})]$, where z_i is obtained by adding up all the z scores for the favourable Mediterranean dietary components (legumes, cereals, fruit, vegetables, alcohol, MUFA:SFA) and subtracting the z values for *trans* fat, meat and meat products and dairy products (all foods and nutrients are previously adjusted for total energy intake using the residual method)
Mediterranean Score of Panagiotakos (MSP)	Panagiotakos *et al.* (2006)[31]	Eleven items scoring 0–5 points according to their frequency of consumption: non-refined cereals (+), potatoes (+), fruits (+), vegetables (+), legumes (+), fish (+), red meat and meat products (−), whole-fat dairy products (−), olive oil in cooking (+), moderate alcohol consumption (+)