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Fried-Food Consumption Does Not Increase the Risk of Stroke in the Spanish Cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC) Study

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ABSTRACT

Background: The nutritional determinants of stroke and, more specifically, the association of frying with the risk of incident stroke have rarely been studied.

Objectives: Our aim was to evaluate prospectively the association between the consumption of fried food and the risk of incident stroke in the European Prospective Investigation into Cancer and Nutrition study using the Spanish cohort.

Methods: Participants included 40,328 healthy adults (62% women) aged 29–69 y at study entry who were enrolled between 1992 and 1996. Participants were followed up until 31 December, 2017, at which time incident stroke (the main outcome) was measured. The main exposure measure was the percentage of energy obtained from fried-food consumption. Sex-specific quintiles were calculated.

Results: During a follow-up period of 23.5 y, 975 cases of stroke occurred (750 ischemic, 185 hemorrhagic, and 40 undetermined). Compared with those in the first (lowest) quintile of fried-food consumption, the multivariate HRs (95% CIs) of incident stroke in the consecutive quintiles were 1.05 (0.86, 1.30), 1.11 (0.90, 1.36), 1.05 (0.84, 1.31), and 0.91 (0.72, 1.15; *P*-trend = 0.45). There were no differences identified when subtypes of stroke were considered.

Conclusions: In this Spanish cohort, whose participants mainly used olive oil or sunflower oil when frying, the consumption of fried food was not associated with an increased risk of incident stroke. *J Nutr* 2020;00:1–8.

Keywords: stroke, fried food, types of oils, olive oil, EPIC Spanish cohort

Introduction

Frying is a common method of cooking that consists of submerging food in hot fat or oil. Frying is frequently used in Spain as well as in other Mediterranean countries for home food preparation owing to the availability of good-quality oil (1). The high temperatures reached by oil during the frying process lead to the evaporation of water. The evaporated water is then replaced by oil being absorbed into the fried food. During frying, food acquires a crispy texture, as well as a characteristic flavor, which is also considered to be appetizing. In the course of frying, food increases its energy density and accumulates toxic substances such as polymers and polar compounds (2).

The study of fried-food consumption and its effects on health has mainly been conducted in Spain and the United States. In middle-aged Spanish adults participating in the EPIC (European Prospective Investigation into Cancer and Nutrition) cohort, fried food was positively associated with general and central obesity (1), but not with ischemic heart disease (3). In the

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EPIC Spanish cohort, olive and sunflower oils were the fats most commonly used for frying. In another cohort from Spain, the SUN (Seguimiento Universidad de Navarra), high fried-food consumption was also associated with an increased risk of obesity (4), central adiposity (5), as well as hypertension (6).

The findings from the United States provided us with slightly different results. In the Nurses' Health Study and in the Health Professionals Follow-Up Study, high fried-food consumption was positively associated with an increased risk of diabetes and also moderately related to coronary artery disease (7). Again, in the Health Professionals Follow-Up Study, the consumption of fried food was associated with a higher risk of incident heart failure (8). More recently, an analysis of the Women's Health Initiative (WHI) conducted with postmenopausal American women found no association between fried-food consumption and total cardiovascular mortality, although there was a slight positive association found for some food groups (9).

Stroke is globally the second leading cause of death (10) while also being one of the main causes of disability (11). Even in some Mediterranean countries such as Spain (which has one of the lowest rates of myocardial infarction in the world), stroke still presents moderate incidence, similar to that of the United States (12). However, despite its clinical importance, the nutritional determinants of stroke, and more specifically, the influence of frying on the risk of incident stroke, have barely been studied.

To our knowledge, there have been no previous studies which directly evaluated the association between fried-food consumption and stroke. So, our aim was to evaluate prospectively the association between the consumption of fried food and the risk of incident stroke using the EPIC Spanish cohort. Both ischemic stroke as well as hemorrhagic stroke were considered. Based on previous studies conducted using the EPIC Spanish cohort (3), our hypothesis was that there would be no statistical association between fried-food consumption and incident stroke.

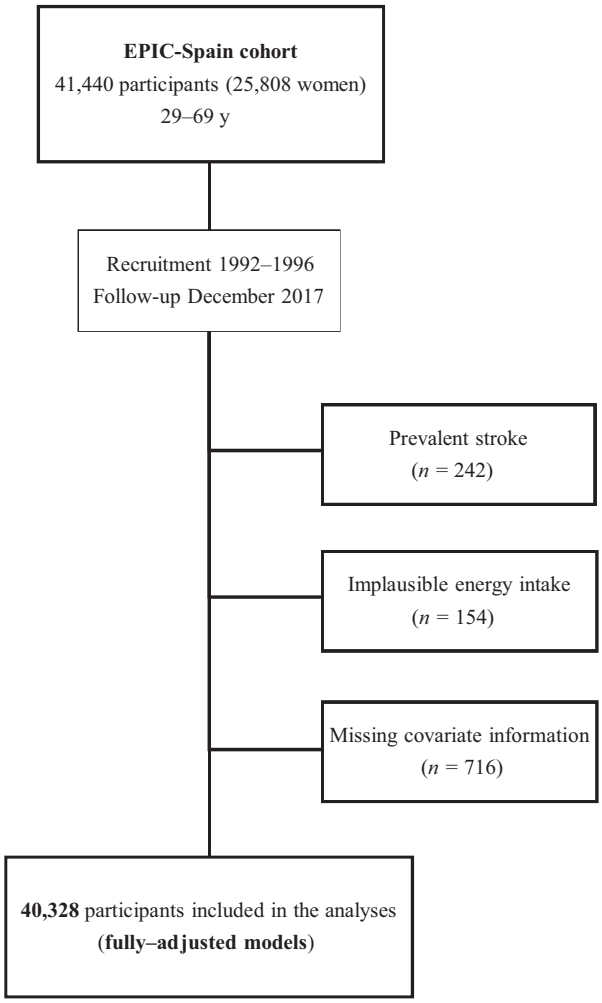

FIGURE 1 Participants' flowchart. EPIC, European Prospective Investigation into Cancer and Nutrition.

Methods

Participants

The EPIC project methods have previously been reported (13, 14). In this analysis we used the data from the EPIC Spanish cohort, which included 41,440 healthy adults from 5 Spanish regions (25,808 women) aged 29–69 y at study recruitment, which was carried out between 1992 and 1996. Three of these regions are located in northern Spain (Asturias, Gipuzkoa, and Navarra) and 2 in southern Spain, along the Mediterranean coast (Granada and Murcia). Participants were recruited in both urban and rural areas, with various educational and social backgrounds. Study participants mostly included blood donors, civil servants, and, to a lesser extent, the general population. The exposure of interest was assessed at baseline, and participants were followed up for incident events until 31 December, 2017 (Figure 1).

All participants gave written informed consent before enrollment. The study protocol was approved by the ethics committees of the International Agency for Research on Cancer (Lyon, France).

Assessment of food consumption

Data on habitual food consumption were obtained for each participant using a computerized dietary history questionnaire, which was previously validated in Spain and conducted by trained interviewers (14–18). Household measurements, standard units, as well as a collection of 35 sets of photographs (including simple foods, mixed foods, and drinks) were used to quantify the portion size of each food consumed in grams per day. These dietary history interviews lasted on average ~40 min.

Participants were asked about the food they had consumed during a typical week throughout the previous year. Food that was consumed at least twice a month was recorded. The dietary history questionnaire recorded information on ≤662 different types of food, including those consumed individually, and those consumed as part of 203 recipes and regional dishes. Of these types of food, 212 were fried and consumed at least once during a typical week. Energy and nutrient intakes were calculated using the EPIC Spanish food composition tables (compiled

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Abbreviations used: EPIC, European Prospective Investigation into Cancer and Nutrition; ICD, International Classification of Diseases; WHI, Women's Health Initiative.

and published afterwards) (19). Food consumption assessment was only performed at baseline.

Fried-food consumption

Information on cooking methods was collected as part of the dietary history questionnaire. Fried food was defined as food for which frying was the only cooking method used. Deep or pan frying were both considered, and food could also be battered, crumbed, or sautéed. To estimate the absorption of fat from frying, we used an absorption coefficient for each fried food. We also recorded the type of oil used for dressing, cooking, and frying.

Assessment of nondietary variables

Information on demographic variables, educational level, smoking, and physical activity was obtained through an interview at recruitment. Physical activity was assessed with a validated questionnaire, which included activity at work, at home, and during leisure time. Participants were also asked if they had diabetes mellitus, hypercholesterolemia, hypertension, cancer, or angina, or if they had experienced myocardial infarction or stroke. In addition, women were asked to report on their menopausal status, and the use of oral contraceptives or hormone replacement therapy. Trained observers used standardized procedures to measure weight, height, and waist circumference. BMI was calculated as weight divided by height squared (kg/m^2).

Outcome assessment

During follow-up, we ascertained incident stroke by record linkage with hospital discharge data sets [codes 430–438 of the ninth revision of the International Classification of Diseases (ICD-9)] and primary care records (codes K89, K90, and K92 from the International Classification of Primary Care and ICD-9 codes 430–438).

For mortality, cases were identified by record linkage with the centralized national data set, containing data from the regional mortality registries and available from the Spanish National Statistical Institute. ICD-9 codes 430–438 and ICD-10 codes I60–I69 were considered. A validation process was carried out to confirm and classify all identified stroke cases. The validation process was performed by a team of trained health professionals by carefully reviewing patient hospital records or, when these were not available, primary care records. Cases of stroke were classified as ischemic, hemorrhagic (cerebral or subarachnoid), or undetermined on the basis of symptoms, presence of cerebrovascular risk factors, as well as specific medical tests (computerized tomography, MRI, angiography, Doppler imaging, and/or lumbar puncture), following the 2006 guidelines from the Spanish Society of Neurology (20). Two neurologists assisted with the classification of the most difficult cases.

Statistical analysis

From the initial 41,440 participants in the cohort, we excluded the following: 242 with prevalent stroke (self-reported at baseline), 154 with implausible energy intake—defined as energy consumption >3 SDs from the mean (<788 kcal/d or >5710 kcal/d), and 716 as a result of lacking data on important covariates such as history of cerebrovascular events (n = 323), smoking (n = 22), diabetes mellitus (n = 48), hypercholesterolemia (n = 174), hypertension (n = 37), and BMI (n = 112). Thus, the analyses were carried out with 40,328 participants (Figure 1).

The density of fried-food consumption was calculated by dividing grams of fried food consumed per day by total energy intake. Participants were classified into sex-specific quintiles of density based on fried-food consumption. We used Cox regression models to obtain HRs and the corresponding 95% CIs for incident stroke. The first quintile (with the lowest consumption) was used as the reference. The P for linear trend was calculated by modeling the quintiles of the density of fried-food consumption as a continuous variable.

In the Cox models, the entry time was defined as the participants' age at recruitment and the exit time was defined as the participants' age at the point of the stroke event, death, or the end of the study follow-up (31 December, 2017), whichever came first. To prevent violations of the proportional hazards assumptions we stratified models by center. We built 3 models, with progressive adjustment for potential confounders (reported at baseline) to determine their influence on the results.

Model 1 was adjusted for age, sex, center (Asturias, Gipuzkoa, Granada, Murcia, or Navarra), and energy intake. Model 2 was in addition adjusted for alcohol consumption [no consumption, moderate consumption (defined as <40 g/d for men and <24 g/d for women), and high consumption (defined as ≥40 g/d for men and ≥24 g/d for women)], educational level (no formal education, primary, secondary, and university), smoking (never, former, <20 cigarettes/d, ≥20 cigarettes/d), physical activity at work (sedentary, standing, manual labor, heavy manual labor, does not work), physical activity at home (in metabolic equivalents; h/wk), physical activity during leisure time (in metabolic equivalents; h/wk), diabetes (yes/no), diagnosed hypertension (yes/no), diagnosed hyperlipidemia (yes/no), cancer at any site (yes/no), BMI (underweight and normal weight: <24.9; overweight: 25–29.9; and obesity: >30), waist circumference (cm), having ever used oral contraceptives (yes/no), menopause (yes/no), and use of hormone replacement therapy (yes/no). Finally, model 3 was in addition adjusted for dietary variables such as nonfried vegetables, fruits, nuts, dairy products, nonfried meat, nonfried fish, and nonfried olive oil. A sensitivity analysis was also performed excluding cases that occurred during the first 2 y of follow-up.

The associations between the most frequently consumed fried-food groups and incident stroke were depicted using restricted cubic-splines. All tests were 2-sided and $P < 0.05$ was considered statistically significant. The analyses were carried out with Stata version 13.0® (StataCorp LP). This article follows the recommendations of the STROBE—Nutritional Epidemiology initiative (21–23).

Results

Mean daily consumption of fried foods was 140 g, which represents ∼6% of the total amount of food consumed. Fried-food consumption ranged from 0 to 816 g in men, and from 0 to 658 g in women, representing 7% and 5.8% of the total caloric intake, respectively. From the total number of participants, 62% reported regularly using olive oil for frying, 24% sunflower oil, and 14% declared using other types of oils including blends of olive and sunflower oils.

Compared with participants with lower fried-food consumption, those with higher consumption were slightly younger, more educated, less sedentary, with a lower prevalence of diabetes, hypertension, and hyperlipidemia, and also had lower consumption of nonfried vegetables, fruit, nuts, milk products, nonfried meat, and nonfried fish (**Table 1**).

During a median follow-up of 23.5 y, 975 cases of stroke occurred; 750 were ischemic, 185 hemorrhagic, and 40 were classified as undetermined. For total incident stroke, no association with fried-food consumption was observed in the analysis adjusted for age, sex, centers, and energy intake (**Table 2**, Model 1). The HR for total incident stroke, comparing the highest with the lowest quintile of fried-food consumption, was 0.92 (95% CI: 0.74, 1.15). Similar results were obtained after additional adjustments for the main confounders and dietary variables (Table 2, Model 3): HR: 0.91 (95% CI: 0.72, 1.15). Statistical significance for linear trend was not reached in any of the models. Participants were also stratified according to the type of oil used for frying (olive oil or sunflower oil), and the results were similar (data not shown). Results were also similar after excluding the cases that occurred during the first 2 y of follow-up.

No statistical significance was found when considering different stroke subtypes. Comparing the highest with the

TABLE 1 Characteristics of the study participants at baseline, by sex-specific quintiles of fried-food consumption, in the EPIC-Spanish cohort (1992/1996–2017)[1]

	Quintiles of consumption of fried food					
	1 (lowest)	2	3	4	5 (highest)	*P*-trend[2]
Participants, *n*	8067	8065	8066	8065	8065	
Consumption of fried foods						
Total amount of fried-food consumption, g/d	44.3 ± 30.6	97.7 ± 42.5	138 ± 53.6	178 ± 64.4	240 ± 87.5	<0.001
Fried fish, g/d	10.7 ± 13.6	24.9 ± 21.2	35.1 ± 26.5	43.1 ± 30.2	55.4 ± 41.2	<0.001
Fried meat, g/d	8.0 ± 11.4	19.7 ± 21.0	31.0 ± 28.6	42.4 ± 34.4	56.0 ± 42.4	<0.001
Fried potatoes, g/d	9.1 ± 12.9	21.2 ± 20.3	29.5 ± 25.0	38.4 ± 30.7	54.0 ± 44.8	<0.001
Fried eggs, g/d	3.7 ± 6.6	10.0 ± 10.7	15.0 ± 13.4	20.0 ± 15.8	25.8 ± 20.3	<0.001
Sociodemographic variables						
Age, y	50.2 ± 8.4	49.2 ± 8.0	49.0 ± 7.9	48.8 ± 7.8	48.9 ± 7.9	<0.001
Educational level, %						<0.001[3]
No formal education	42.2	37.5	33.9	30.0	28.2	
Primary	31.9	36.4	39.7	43.5	45.2	
Secondary	12.5	13.9	14.6	16.1	16.6	
University	13.5	12.1	11.8	10.4	10.0	
Lifestyles						
Smoking, %						<0.001[3]
Never smoker	55.4	55.7	55.6	55.4	55.5	
Former smoker	19.3	18.6	16.9	16.6	17.1	
Smoker, ≤20 cigarettes/d	15.1	16.6	17.7	18.6	18.2	
Smoker, >20 cigarettes/d	10.2	9.1	9.8	9.4	9.3	
Physical activity at work, %						<0.001[3]
Sedentary	22.4	21.4	20.7	20.1	20.3	
Standing	64.8	65.0	64.2	64.2	62.7	
Manual labor	6.8	8.8	9.7	10.4	10.8	
Heavy manual labor	2.5	2.2	2.1	1.9	2.0	
Does not work	3.5	2.7	3.3	3.5	4.2	
Physical activity at home, METs · h/wk	68.2	69.7	70.2	69.9	67.9	0.87
Physical activity during leisure time, METs · h/wk	28.5	27.8	28.1	28.5	29.7	<0.001
BMI, kg/m^2	28.5	28.2	28.1	28.2	28.3	0.010
Waist circumference, cm	92.7	92.1	91.5	91.5	91.6	<0.001
Self-reported prevalent diseases						
Diabetes, %	7.4	5.0	4.5	3.8	3.9	<0.001
Hypertension, %	22.7	20.0	20.0	19.3	18.8	<0.001
Hyperlipidemia, %	24.6	20.7	19.5	17.5	18.4	<0.001
Cancer, %	1.0	0.9	0.7	0.9	0.9	0.68
Dietary variables						
Total energy, kcal/d	2197 ± 797	2360 ± 776	2376 ± 742	2334 ± 706	2180 ± 662	0.026
Alcohol, g/d	13.6 ± 24.9	16.7 ± 28.6	17.1 ± 28.9	17.1 ± 27.8	14.5 ± 23.7	0.029
Nonfried vegetables, g/d	267 ± 164	249 ± 147	241 ± 137	230 ± 133	217 ± 135	<0.001
Fruit, g/d	352 ± 248	332 ± 231	322 ± 233	304 ± 215	295 ± 219	<0.001
Nuts, g/d	6.4 ± 15.5	5.8 ± 14.2	4.4 ± 10.4	3.4 ± 9.3	2.2 ± 7.0	<0.001
Milk products, g/d	322 ± 197	312 ± 193	302 ± 187	286 ± 175	263 ± 166	<0.001
Nonfried meat, g/d	104 ± 65.8	105 ± 58.5	100 ± 54.0	93.2 ± 48.8	79.0 ± 44.9	<0.001
Nonfried fish, g/d	40.3 ± 39.5	32.1 ± 31.3	27.3 ± 26.4	24.8 ± 25.0	21.4 ± 22.7	<0.001
Among women						
Having ever used oral contraceptives, %	25.1	26.2	26.8	27.4	26.2	0.033
Menopause, %	2.2	2.6	2.0	2.1	2.1	0.093
Hormone replacement therapy, %	6.4	6.1	5.6	5.5	5.9	0.054

[1] $n = 40,328$. Values are percentages, means, or means ± SDs unless otherwise indicated. Range of quintiles of fried-food consumption for men in percentage of calorie intake: Q1: 0–3.6; Q2: 3.7–5.5; Q3: 5.6–7.3; Q4: 7.3–9.3; Q5: 9.4–30.5. Range of quintiles of fried-food consumption for women in percentage of calorie intake: Q1: 0–2.7; Q2: 2.7–4.5; Q3: 4.5–6.1; Q4: 6.1–8.2; Q5: 8.2–46.5. MET, metabolic equivalent.
[2] To calculate *P* for trend the quintiles were introduced in the models as a continuous variable.
[3] Chi-square.

lowest quintile of fried-food consumption, the fully adjusted HR for ischemic stroke was 0.86 (95% CI: 0.66, 1.12; *P*-trend = 0.21) and for hemorrhagic stroke was 1.05 (95% CI: 0.60, 1.86; *P*-trend = 0.79) (Table 2). A stratified analysis by diabetes status was done with similar results for incident stroke, as well as when ischemic or hemorrhagic stroke was considered (data not shown). In addition, no association was observed when specific food groups were studied (**Figure 2**).

TABLE 2 The association between consumption of fried food and stroke incidence (total, ischemic, and hemorrhagic) after follow-up in the EPIC-Spanish cohort (1992/1996–2017)[1]

	Quintiles of consumption of fried food						
	1 (lowest)	2	3	4	5 (highest)	*P*-trend	Per 100-g increase in fried-food consumption
Participants, *n*	8067	8065	8066	8065	8065		
Total incident stroke							
Events, *n*	191	192	208	201	183		
Model 1: HR (95% CI)	1 (Ref)	1.02 (0.83, 1.25)	1.10 (0.90, 1.36)	1.05 (0.84, 1.30)	0.92 (0.74, 1.15)	0.57	0.96 (0.89, 1.05)
Model 2: HR (95% CI)	1 (Ref)	1.06 (0.86, 1.29)	1.12 (0.91, 1.37)	1.06 (0.86, 1.32)	0.93 (0.75, 1.16)	0.60	0.97 (0.87, 1.05)
Model 3: HR (95% CI)	1 (Ref)	1.05 (0.86, 1.30)	1.11 (0.90, 1.36)	1.05 (0.84, 1.31)	0.91 (0.72, 1.15)	0.45	0.95 (0.87, 1.04)
Ischemic stroke							
Events, *n*	153	149	161	149	138		
Model 1: HR (95% CI)	1 (Ref)	0.98 (0.78, 1.24)	1.06 (0.84, 1.33)	0.94 (0.74, 1.20)	0.86 (0.67, 1.11)	0.24	0.93 (0.85, 1.03)
Model 2: HR (95% CI)	1 (Ref)	1.02 (0.81, 1.28)	1.07 (0.85, 1.35)	0.96 (0.76, 1.23)	0.88 (0.68, 1.13)	0.26	0.93 (0.84, 1.03)
Model 3: HR (95% CI)	1 (Ref)	1.02 (0.81, 1.29)	1.06 (0.84, 1.35)	0.95 (0.74, 1.23)	0.86 (0.66, 1.12)	0.21	0.92 (0.83, 1.02)
Hemorrhagic stroke							
Events, *n*	29	35	43	44	34		
Model 1: HR (95% CI)	1 (Ref)	1.18 (0.72, 1.95)	1.43 (0.87, 2.33)	1.41 (0.86, 2.36)	1.10 (0.65, 1.86)	0.60	1.03 (0.85, 1.25)
Model 2: HR (95% CI)	1 (Ref)	1.23 (0.75, 2.03)	1.47 (0.90, 2.40)	1.47 (0.89, 2.43)	1.12 (0.66, 1.90)	0.57	1.04 (0.86, 1.25)
Model 3: HR (95% CI)	1 (Ref)	1.25 (0.75, 2.06)	1.47 (0.90, 2.43)	1.45 (0.87, 2.42)	1.05 (0.60, 1.83)	0.79	0.99 (0.81, 1.22)

[1] $n = 40,328$. Values are HRs (95% CIs). Quintiles are sex-specific. Model 1 adjusted for age, sex, center (Asturias, Gipuzkoa, Granada, Murcia, or Navarra), and energy intake. Model 2 adjusted for the variables in model 1 and for alcohol consumption (no consumption, moderate consumption, and high consumption), educational level (no formal education, primary, secondary, and university), smoking (never, former, <20 cigarettes/d, >20 cigarettes/d), physical activity at work (sedentary, standing, manual labor, heavy manual labor, does not work), physical activity at home (metabolic equivalents · h/wk), physical activity during leisure time (metabolic equivalents · h/wk), BMI (in kg/m^2) (underweight and normal weight: <24.9; overweight: 25–29.9; and obesity: >30), waist circumference, diabetes, hypertension, hyperlipidemia, cancer, having ever used oral contraceptives, menopause, and hormone replacement therapy. Model 3 adjusted for the variables in model 2 and for nonfried vegetables, fruit, nuts, dairy products, nonfried meat, nonfried fish, and nonfried olive oil.

Discussion

In this large prospective study conducted among men and women from the EPIC Spanish cohort, we found no association between the consumption of fried food and the risk of incident stroke. When the association was analyzed by stroke subtypes, fried-food consumption remained unassociated with either ischemic or hemorrhagic stroke. The analyses included adjustments for the main risk factors as well as for some potential intermediates, such as hypertension, hyperlipidemia, and diabetes. However, a sensitivity analysis without these potential intermediates showed similar results. The current findings are in accordance with a prior study performed using the same cohort, in which no association between the consumption of fried food and the risk of ischemic heart disease was identified (3).

Frying is considered to be a detrimental cooking method owing to the fact that it increases the energy density of fried food, as well as modifying fatty acids during the cooking process. In addition, oils and food under high temperatures produce neo-formed substances. Frying increases fatty acid oxidation while releasing free fatty acids. Besides, there is also an increase in *trans* fatty acids in fried food which have been positively associated with an increased risk of hypertension. This phenomenon could be higher when oils or fats are reused (2). In addition, heat-induced harmful compounds might be generated, such as polar compounds, heterocyclic amines in protein-rich food, as well as droxymethylfurfural and acrylamide in carbohydrate-rich food (24). For example, exposure to acrylamide—which could be generated while frying potato chips, French fries, and bread at high temperatures (≥120°C)—has been positively linked to an increased risk of obesity (25).

Currently, the association between fried-food consumption and cardiovascular diseases remains controversial. The potential risk of cardiovascular disease from frying food may depend on multiple factors, including the actual composition of the food being fried, the type of oil used, how often the oil is reused, as well as the frying conditions (temperature and time) and procedures (deep or pan frying). These will ultimately determine the quality of fried food. In addition, the effects of nonprocessed fried-food consumption at home compared with industrially processed fried-food consumption generally out of the home still need further comprehensive evaluation (26).

Frying practices vary greatly depending on the location where the fried food is consumed. In the United States, for example, fried food is most often eaten outside of the home (mainly in fast-food restaurants) and it is usually industrially processed. The processing entails the use of deep frying as the cooking method (27), and the use of animal fat or corn oil as the frying medium due to their lower cost (28). Furthermore, these fats and oils are frequently reused. On the other hand, in Mediterranean countries, fried food is generally consumed at home and accompanied by healthier food options. Moreover, in Mediterranean countries olive oil is the preferred choice when frying food at home and making dressings and sauces (4, 29), and this oil is not frequently reused.

Olive oil is well known for its positive attributes, and contains components with important biological properties, including phenolic compounds, vitamin E, and other lipid-derivate molecules such as squalene, tocopherols, and triterpenes. Due to the high content of MUFAs in olive oil (80%) and its low content of PUFAs (20%), olive oil is highly resistant to oxidation (30, 31). Olive oil has been shown to have an anti-inflammatory effect as well as antiatherogenic properties, reducing oxidative stress and improving endothelial function (32–34). Moreover, in the Mediterranean diet, olive oil has

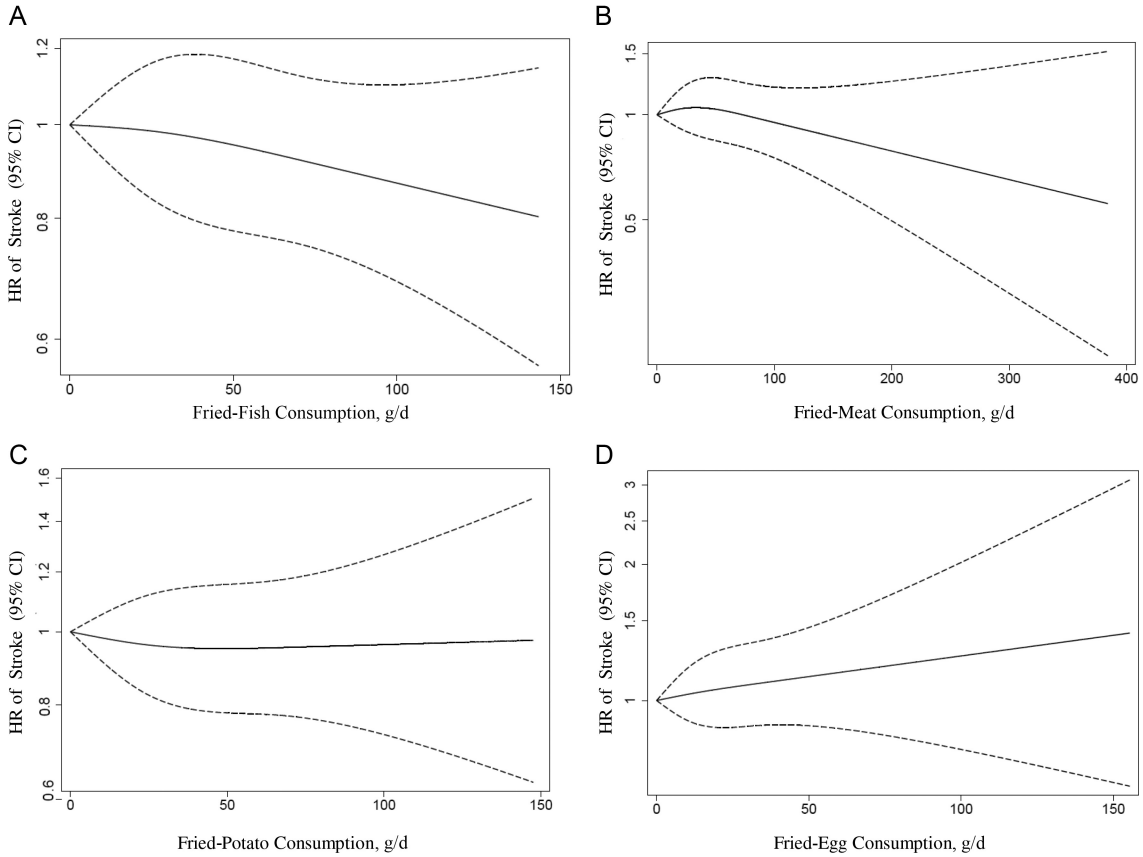

FIGURE 2 Associations between the consumption of specific food groups and the risk of incident stroke (Model 3; $n = 40{,}328$). The association of (A) fried-fish consumption, (B) fried-meat consumption, (C) fried-potato consumption, and (D) fried-egg consumption with the risk of incident stroke.

been shown to decrease blood pressure and improve lipid profile, insulin sensitivity, as well as glycemic control (34–36). It has also been found that high olive oil consumption has a protective role in stroke prevention in older adults. Phenolic compounds (mainly found in extra-virgin olive oil) seem to be responsible for this protective effect (36). However, in this study no distinction between fried and nonfried olive oil was made. Also, findings from the PREDIMED (Prevention with Mediterranean Diet) study have shown that adherence to the Mediterranean dietary pattern enriched with olive oil reduces the incidence of cardiovascular events (37). Findings from the EPIC Spanish cohort also showed a 44% reduction in cardiovascular mortality when comparing participants in the highest quartile with those in the lowest quartile of olive oil consumption (38). Again, no distinction between fried and nonfried olive oil was made. The recognized beneficial cardiovascular effect of olive oil (39) could counteract the possible harmful effects of frying.

It is also notable that the consumption of fried food in Spain is low. Subsequently, our results cannot be directly applicable to other countries with higher amounts of fried-food consumption or with other frying practices.

Other studies have reported associations between specific fried-food groups and cardiovascular disease and its risk factors. In an analysis from the WHI, consumption of fried chicken and fried fish were positively associated with total cardiovascular mortality when comparing ≥1 serving/d against nonconsumption (9). Also, in a prospective cohort study conducted in the United States among participants of REGARDS (REasons for Geographic And Racial Differences in Stroke) (40), those eating ≥2 servings of fried fish/wk (compared with <1 serving/mo) were at a significantly increased risk of cardiovascular events, including nonfatal ischemic stroke. Finally, 3 prospective cohort studies have shown that a greater consumption of potatoes, especially chips (French fries), was associated with a higher risk of type 2 diabetes, independently of BMI and other cardiovascular disease risk factors (41). Also, a meta-analysis showed the positive association of chips (French fries) with diabetes (42).

Our study has some limitations. First, diet was measured only at baseline (1992–1996), and our results are based on this baseline measurement. Second, some prevalent diseases were self-reported which could result in residual confounding (i.e., because it is frequent for hypertension to be underdiagnosed, the adjustment may not be complete, and part of the observed association may be due to a possible hypertensive status). Third, 40 cases of stroke were classified as undetermined because of the lack of appropriate neurological information. Also, the number of events of hemorrhagic stroke was small and the evidence produced could be limited. Fourth, because people regard fried food as being unhealthy, there is a potential for the underreporting of fried-food consumption and its subsequent misclassification. In addition, we lack information on the types of frying procedures (deep frying compared with pan frying) or the extent to which oil was reused. Furthermore, the questionnaire was validated for food groups, nutrients, and biomarkers (16–18), but not specifically for fried/nonfried status. However, because the classification only consists of

2 categories and the interviews were conducted by nutritionists and trained personnel, we believe that the questionnaire can be considered valid for classifying the exposure. Finally, we cannot isolate the effect of the food itself from the effect of frying; however, no statistically significant association was revealed when specific food groups were studied. This study also presents some strengths including its large sample size; the long follow-up period; the use of a validated dietary history with quantitative information on fried-food consumption; the possibility of distinguishing between types of stroke that were all validated by a team of trained health professionals by carefully reviewing patient hospital records or, if not available, primary care records or autopsies; and finally the adjustment for numerous potential confounders.

In conclusion, in this large prospective cohort study, we observed that fried-food consumption was not associated with a higher risk of stroke in this Spanish adult population. Based on the results, the public health significance of this study is that there is no evidence that fried-food consumption should be strongly limited in countries with similar cooking methods as in Spain, and where olive oil is mainly used for frying. However, this cannot be applied to other countries with different habits. It would be of great interest to replicate this study with other Mediterranean cohorts with similar culinary customs, including a low to moderate consumption of fried food as well as the use of olive oil for frying.

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