Association of fried food consumption with all cause, cardiovascular, and cancer mortality: prospective cohort study

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ABSTRACT

OBJECTIVE
To examine the prospective association of total and individual fried food consumption with all cause and cause specific mortality in women in the United States.

DESIGN
Prospective cohort study.

SETTING
Women's Health Initiative conducted in 40 clinical centers in the US.

PARTICIPANTS
106 966 postmenopausal women aged 50-79 at study entry who were enrolled between September 1993 and 1998 in the Women's Health Initiative and followed until February 2017.

MAIN OUTCOME MEASURES
All cause mortality, cardiovascular mortality, and cancer mortality.

RESULTS
31 558 deaths occurred during 1 914 691 person years of follow-up. For total fried food consumption, when comparing at least one serving per day with no consumption, the multivariable adjusted hazard ratio was 1.08 (95% confidence interval 1.01 to 1.16) for all cause mortality and 1.08 (0.96 to 1.22) for cardiovascular mortality. When comparing at least one serving per week of fried chicken with no consumption, the hazard ratio was 1.13 (1.07 to 1.19) for all cause mortality and 1.12 (1.02 to 1.23) for cardiovascular mortality. For fried fish/shellfish, the corresponding hazard ratios were 1.07 (1.03 to 1.12) for all cause mortality and 1.13 (1.04 to 1.22) for cardiovascular mortality. Total or individual fried food consumption was not generally associated with cancer mortality.

CONCLUSIONS
Frequent consumption of fried foods, especially fried chicken and fried fish/shellfish, was associated with a higher risk of all cause and cardiovascular mortality in women in the US.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Around 25-36% of North American adults consume foods, usually fried, from fast food restaurants every day

Scientific evidence about the effect of fried foods on mortality is sparse and controversial

WHAT THIS STUDY ADDS

Fried food consumption, especially fried chicken and fried fish/shellfish, was observed to be associated with a higher risk of all cause and cardiovascular mortality among postmenopausal women in the United States

Introduction

Fried foods are widely consumed in the United States and worldwide. Frying is a complex cooking process that modifies the composition of foods and the frying medium through oxidation, polymerization, and hydrogenation.[1] During frying, foods can lose water and absorb fat, and the frying oils deteriorate, especially when reused.[1] Moreover, frying makes food crunchy and more appetizing, which can lead to excess intake.[2]

Several cohort studies in US populations showed that higher consumption of fried foods was associated with an increased risk of type 2 diabetes[3] and cardiovascular diseases,[3 4] which are among the leading causes of death. However, a study in a Mediterranean population found no association between fried food consumption and coronary heart disease.[1] Little is known about the relation between fried food consumption and mortality.[1 5] It is important to understand the associations between fried foods and health outcomes because 25-36% of North American adults consume foods, usually fried, from fast food restaurants every day.[3 6 7] Thus, we used data from a large, prospective cohort to examine the association of total and specific fried food consumption with all cause, cardiovascular, and cancer mortality in US women.

Methods

Study population
The Women's Health Initiative has been previously described in detail.[8] Briefly, between 1993 and 1998, postmenopausal women aged 50-79 at study entry were recruited through 40 clinical centers. Most clinics used a tracking system to calculate the response rate to their mailings and other recruitment efforts, but the types of system and information tracked varied widely across centers. No study wide system was implemented because the clinics wanted to maintain as much local flexibility as possible. Therefore, the response rate (that is, the number of women making contact for initial screening) varied across clinics and sources of mailing lists from less than 2% to about 20% for initial mailings; however, total mailing numbers and response rates to mailings are not available across clinics. A total of 373 092 women completed the initial screening form. Of these women, 68 132 (18%) underwent the subsequent screening visits to be randomized into the clinical trial, and 93 676 (25%) were enrolled in the observational study. The clinical trial consisted of four components: a dietary modification trial, two hormonal treatment trials, and a calcium and vitamin D clinical trial. The clinical trial and observational study were closed in 2004-05 and the participants

were invited to continue being followed in the Women's Health Initiative extension study, which has follow-up data to February 2017. Written informed consent was obtained from each participant. Institutional review board approval was obtained from all participating institutions.

In this study, we included participants in the observational study component and clinical trial components, with the exception of the dietary modification trial. This is because participants in the dietary modification trial were randomized to evaluate the effects of a low fat diet,[9] which could affect their habitual consumption of fried foods. Of the eligible participants, 108 308 women (90 009 (96%) in the observational study; 18 299 (95%) in the clinical trial) had valid food frequency questionnaire data, which were defined as reported energy intake between 600 and 5000 kcal/day (1 kcal=4.18 kJ=0.00418 MJ). We excluded 104 women who had missing data on information about postmenopausal hormone therapy use. We also excluded 1238 women who died within three years after the baseline visit, to rule out the possibility that the participants changed their diet because of their preterminal or terminal illness. Therefore, 106 966 women (88 881 in the observational study; 18 085 in the clinical trial) were included in the present analysis.

Dietary assessment

We used a standardized written protocol, centralized training of staff, and quality assurance visits by the clinical coordinating center to ensure uniform administration of data collection. Diet was measured at baseline in the Women's Health Initiative using a self administered food frequency questionnaire developed and validated with characteristics described for the study,[10] adapted from the health habits and lifestyle questionnaire.[11] The three sections of the Women's Health Initiative's food frequency questionnaire included 122 composite and single food line items asking about frequency of consumption and portion size, and 19 adjustment questions related to type of fat intake. There were also four summary questions asking about the usual intake of fruits and vegetables and added fats for comparison with information gathered from the line items. The questionnaire was designed to record food intake relevant to multiethnic and geographically diverse population groups. The questionnaire has been shown to produce reliable estimates (correlation coefficient $r_{\text{all nutrients}}$=0.76) that are comparable to those for eight days of dietary intake compiled from four 24 hour dietary recalls and four days of food records (r=0.37, 0.62, 0.41, 0.36 for energy, percentage of energy from fat, carbohydrate, and protein, respectively).[10] The nutrient database used to analyze the questionnaire is derived from the nutrition data systems for research,[12] which provides nutrient information for more than 140 nutrients and compounds, including energy, saturated fat, and sodium.

Total fried food consumption was the total consumption of the following three items: fried chicken, fried fish/shellfish, and other fried foods. Fried chicken was described as "fried chicken" on the questionnaire. Fried fish/shellfish was described as "fried fish, fish sandwich, and fried shellfish (shrimp and oysters)" on the questionnaire. Other questionnaire items on fried foods included "French fries, fried potatoes, fried rice, fried cassava and fritters," "snacks such as potato chips, corn chips, tortilla chips, pork skins, Ritz and cheese crackers," "fried plantains," "taco and tostada," "flauta and crispy rolled taco," and "Indian fried bread" on the questionnaire. We assumed that all these categories consisted primarily of deep fried foods.[13] There were exceptions, such as "Ritz and cheese crackers" as part of the snacks category. However, the contribution of these single items within their general category is likely to be small.[13] The primary exposure of this study was total fried food consumption, and the secondary exposures were individual types of fried foods.

Ascertainment of death

Deaths were ascertained by reviewing death certificates, medical records, autopsy reports, and by linkage to the national death index.[14] Death certificates and hospital records were obtained and adjudicated by adjudicators who were unaware of study components or randomization assignment. Deaths in the clinical trial component of the Women's Health Initiative were centrally adjudicated, as were major causes of cardiovascular death and the five main cancer outcomes. Other deaths were adjudicated locally.[14] Records from the most relevant hospital admission preceding death and from the time of death, autopsy records, and the death certificate were used by adjudicators to determine the causes of death. For many deaths occurring out of hospital, documentation was limited to the death certificate and records of the most recent admission to hospital before death. In these instances, the immediate and underlying cause of death was determined from the death certificate.[14] Ascertainment of outcomes was complete as of 28 February 2017. Mortality endpoints for this study included all cause (primary outcome), cardiovascular, and cancer mortality.

Other covariate assessments

The following information was collected at baseline through self reporting: demographic characteristics (age, race/ethnicity, education, annual income), lifestyle (smoking status, physical activity, alcohol intake, coffee intake, total energy intake, overall diet quality), medical history (cardiovascular disease, cancer, diabetes), and drug use and past hormone use (unopposed estrogen use, estrogen plus progesterone use). Overall diet quality was indicated by alternative healthy eating index 2010 score.[15] This score was based on the intake levels of 11 components: vegetables, fruits, whole grains, sugar-sweetened beverages and fruit juice, nuts and legumes, red and processed meat, trans fat, long chain (n-3) fats (eicosapentaenoic and docosahexaenoic acid), polyunsaturated fatty

acids, sodium, and alcohol. Recreational moderate to vigorous intensity physical activity, including walking, was assessed by questionnaire, and metabolic equivalent task hours per week of physical activity for each participant was calculated, as described in detail elsewhere.[8][16] Weight and height at baseline were measured during clinic visits using standard methods. We calculated body mass index as weight (in kilograms) divided by height (in meters squared).[2]

Statistical analysis

Comparisons of covariates among different groups were performed using analysis of variance for continuous variables and χ^2 test for categorical variables. We used Cox proportional hazards models to estimate age adjusted and multivariable adjusted hazard ratios and 95% confidence intervals for mortality associated with total fried food consumption and its components. Person years were calculated from the baseline food frequency questionnaire until death, the last national death index search date, or the end of the previously described Women's Health Initiative extension study 2 on 28 February 2017. Model 1 adjusted for the following variables: age at baseline, race or ethnicity, education, annual income, observational study or clinical trial, unopposed estrogen use, estrogen plus progesterone use, smoking status, physical activity, coffee intake, total energy intake, alternative healthy eating index 2010 score, baseline diabetes, cardiovascular disease, and cancer. For each of the three fried food items, mutual adjustment for other fried food items was also added. Model 2 additionally adjusted for body mass index, which was a potential mediator of the study association reported in the literature.[1]

We evaluated whether the associations would vary according to the following variables: age (<65 v ≥65), race or ethnicity (white v non-white), smoking status (never smoked v ever smoked), physical activity (<10 v ≥10 metabolic equivalent task hours per week), unopposed estrogen use (never used v ever used), estrogen plus progesterone use (never used v ever used), oil used for frying at home (no fat added, olive or canola oil, others (other oils, butter, margarine, etc) or mixed use of oils), and obesity status (body mass index <30 v ≥30). For sensitivity analysis, we repeated the analyses by excluding women in the trials, adding types of oil used for home frying into the model, and adding trans fatty acid intake into the model.

All statistical tests were based on a priori hypotheses and therefore there was no adjustment for multiple testing. All statistical analyses were conducted using SAS (version 9.4; SAS Institute). All tests were two sided with statistical significance set at P<0.05.

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design, or implementation of the study. No patients were asked to advise on interpretation or writing up of results. This study used deidentified information collected in a national health study. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results

During 1 914 691 person years of follow-up (individual level mean follow-up duration 17.9 years), 31 558 deaths occurred, consisting of 9320 deaths from cardiovascular disease, 8358 deaths from cancer, and 13 880 deaths from other causes. Table 1 shows that women with more frequent total fried food consumption were more likely to be younger, non-white, with less education, and on lower income. They were more likely to be participants from the Women's Health Initiative clinical trials, be current smokers, have lower physical activity levels, drink more coffee, have a higher total energy intake, and have a lower diet quality. They were also more likely to have diabetes but less likely to have cardiovascular disease at baseline, and more likely to have a higher body mass index. Women with higher total fried food consumption were more likely to consume calories from dietary total fat rather than carbohydrate or total protein. They tended to consume fewer vegetables, fruits, and whole grains, and more sugar-sweetened beverages, nuts and legumes, red and processed meat, trans fat, polyunsaturated fatty acid, and sodium. There was a moderate correlation between two of the three fried food items: fried chicken and fried fish/shellfish; r=0.40, P<0.001.

More frequent total fried food consumption was associated with a higher risk of all cause mortality (table 2): multivariable adjusted hazard ratio 1.01 (95% confidence interval 0.98 to 1.05) for less than one serving per week, 1.03 (0.99 to 1.07) for one to two servings per week, 1.03 (0.99 to 1.08) for three to six servings per week, and 1.08 (1.01 to 1.16) for at least one serving per day (P=0.02 for trend) compared with no consumption. For the specific fried food items, fried chicken consumption was associated with a higher risk of all cause mortality: 1.06 (1.03 to 1.09) for less than two servings per month, 1.12 (1.07 to 1.17) for two to three servings per month, and 1.13 (1.07 to 1.19) for at least one serving per week (P<0.001 for trend) compared with no consumption (table 3). Fried fish/shellfish consumption of at least one serving per week was associated with a higher risk of all cause mortality (1.07; 1.03 to 1.12). Other fried food consumption was not associated with all cause mortality. These associations persisted after additional adjustment for body mass index.

Total fried food consumption of at least one serving per day was associated with a modestly higher but not significant risk of cardiovascular mortality: hazard ratio 1.08 (95% confidence interval 0.96 to 1.22; table 2). Fried chicken consumption was associated with a higher risk of cardiovascular mortality: 1.08 (1.02 to 1.14) for less than two servings per month, 1.17 (1.08 to 1.25) for two to three servings per month, and 1.12 (1.02 to 1.23) for at least one serving per week (P<0.001 for trend) compared with no consumption (table 4). Fried fish/shellfish consumption of at least

Table 1 | Demographic characteristics according to frequency of baseline total fried food consumption. Data are percentages or mean (standard deviation) unless indicated otherwise

Variables	Frequency of total fried food consumption					P
	None (n=15 166)	<1 serving/week (n=38 482)	1-2 servings/week (n=33 210)	3-6 servings/week (n=15 480)	≥1 serving/day (n=4628)	
Age at baseline (years)	64.9 (7.3)	64.3 (7.3)	63.1 (7.3)	62.4 (7.2)	61.3 (7.3)	<0.001
Race/ethnicity:						
White	90.5	87.9	82.2	77.1	68.5	<0.001
Black	4.4	5.5	8.5	11.3	17.2	
Hispanic	2.4	3.0	4.2	5.7	7.7	
Others	2.5	3.3	5.0	5.8	6.5	
Missing	0.3	0.3	0.2	0.2	0.2	
Education:						
High school or less	24.6	28.8	34.2	38.8	44.9	<0.001
Some college	25.2	27.0	27.2	26.9	25.4	
College	12.8	11.7	10.7	9.9	8.8	
Postgraduate	36.7	31.8	27.2	23.4	19.9	
Missing	0.7	0.8	0.8	0.9	1.0	
Annual income:						
<20 000	13.6	14.5	15.5	18.2	21.6	<0.001
20 000-49 999	38.1	40.7	42.7	42.4	43.1	
>50 000	40.5	38.0	35.0	32.4	28.1	
Missing	7.9	6.8	6.8	6.9	7.3	
WHI component:						
Clinical trial	13.7	15.7	17.9	19.8	20.6	<0.001
Observational study	86.3	84.3	82.2	80.2	79.4	
Unopposed estrogen use:						
Never used	67.1	64.5	64.0	65.9	66.8	<0.001
Past user	13.0	13.7	13.6	13.1	12.8	
Current user	20.0	21.8	22.4	21.0	20.4	
Estrogen+progesterone use:						
Never used	73.4	72.7	74.4	76.1	78.9	<0.001
Past user	8.6	9.1	8.7	8.7	6.7	
Current user	18.0	18.2	16.9	15.3	14.5	
Smoking status:						
Never	48.9	50.2	50.6	49.6	47.8	<0.001
Past	45.7	42.7	40.4	39.7	40.3	
Current	4.0	5.6	7.6	9.5	10.8	
Missing	1.3	1.4	1.4	1.3	1.2	
Physical activity (MET-h/week):						
<10	36.3	45.2	53.5	59.8	64.7	<0.001
≥10	61.9	52.8	44.2	38.0	33.1	
Missing	1.9	2.0	2.3	2.2	2.3	
Alcohol intake:						
Non-drinker	42.0	38.8	39.6	42.7	48.3	<0.001
Moderate	45.1	47.8	46.9	43.5	39.6	
Heavy	12.9	12.4	13.4	13.7	12.1	
Coffee intake (medium serving/day)	2.1 (1.7)	2.0 (1.7)	2.1 (1.8)	2.2 (1.9)	2.4 (2.2)	<0.001
Total energy intake (kcal/day)*	1377.1 (470.6)	1401.4 (485.6)	1593.7 (551.0)	1906.2 (644.3)	2470.4 (834.7)	<0.001
AHEI 2010 score	55.7 (10.6)	51.1 (10.5)	47.1 (10.2)	44.4 (10.3)	42.7 (10.4)	<0.001
Baseline diabetes	4.5	4.9	5.8	7.3	9.7	<0.001
Baseline cardiovascular disease	7.0	6.3	6.3	5.8	6.1	<0.001
Baseline cancer	1.5	1.5	1.5	1.6	1.3	0.73
Body mass index:						
<25.0	49.6	43.3	35.3	29.2	23.9	<0.001
25.0-29.9	31.9	34.4	34.8	34.0	30.6	
≥30	17.3	21.2	29.0	35.8	44.3	
Missing	1.2	1.1	1.0	1.0	1.3	
Dietary carbohydrate (%E)	58.7 (9.6)	54.5 (9.1)	50.2 (8.6)	47.2 (8.3)	45.0 (8.0)	<0.001
Dietary total fat (%E)	23.6 (7.5)	27.9 (7.5)	32.5 (7.4)	36.0 (7.3)	39.0 (7.0)	<0.001
Dietary total protein (%E)	17.8 (3.6)	17.1 (3.3)	16.7 (3.1)	16.2 (3.0)	15.7 (3.1)	<0.001
Vegetables (servings/day)	2.9 (1.5)	2.5 (1.4)	2.3 (1.3)	2.3 (1.3)	2.5 (1.4)	<0.001
Fruits (servings/day)	3.1 (1.9)	2.5 (1.8)	2.1 (1.7)	1.9 (1.6)	1.7 (1.6)	<0.001
Whole grains (g/day)	41.0 (31.9)	35.0 (28.0)	32.9 (27.5)	32.8 (27.9)	35.0 (30.0)	<0.001
SSBs (servings/day)	0.7 (0.8)	0.8 (0.8)	0.9 (0.9)	1.0 (1.0)	1.2 (1.4)	<0.001
Nuts and legumes (servings/day)	0.2 (0.3)	0.2 (0.3)	0.2 (0.3)	0.3 (0.3)	0.4 (0.4)	<0.001
Red and processed meat (servings/day)	0.7 (0.7)	0.9 (0.8)	1.3 (0.9)	1.7 (1.2)	2.3 (1.6)	<0.001
Trans fat (%E)	1.4 (0.9)	1.8 (1.0)	2.3 (1.0)	2.7 (1.1)	3.0 (1.0)	<0.001
EPA+DHA (mg/day)	141.2 (151.2)	115.6 (117.9)	118.7 (106.2)	136.1 (126.7)	175.8 (200.1)	<0.001

Table 1 | Continued

Variables	Frequency of total fried food consumption					
	None (n=15 166)	<1 serving/week (n=38 482)	1-2 servings/week (n=33 210)	3-6 servings/week (n=15 480)	≥1 serving/day (n=4628)	P
PUFA (%E)	5.2 (1.9)	5.9 (2.0)	6.7 (2.0)	7.5 (2.0)	8.3 (2.1)	<0.001
Sodium (g/day)	2.4 (1.0)	2.4 (0.9)	2.7 (1.0)	3.2 (1.2)	4.1 (1.6)	<0.001
Alcohol (drinks/day)	0.4(0.8)	0.4(0.8)	0.4(0.8)	0.4(0.9)	0.4(1.0)	0.14

AHEI=alternative healthy eating index; DHA=docosahexaenoic acid; EPA=eicosapentaenoic acid; MET=metabolic equivalent; PUFA=polyunsaturated fatty acid; SD=standard deviation; SSB=sugar-sweetened beverage; WHI=Women's Health Initiative, %E=percentage of energy.
*1 kcal=4.18 kJ=0.00418 MJ.

one serving per week was associated with a higher risk for cardiovascular mortality: 1.13 (1.04 to 1.22; table 4). Other fried foods were generally not associated with cardiovascular mortality. These associations persisted after additional adjustment for body mass index.

Neither total nor specific fried food consumption was associated with cancer mortality (table 2 and table 5). However, for fried fish/shellfish consumption of less than two servings per month, the hazard ratio was 0.92 (95% confidence interval 0.87 to 0.97), and for other fried food consumption of less than two servings per month, the hazard ratio was 1.09 (1.02 to 1.17) compared with no consumption (table 5). These associations persisted after adjusting for body mass index.

The results of sensitivity analyses were similar when women in the clinical trial were excluded, oils used for frying were added into the model, or trans fatty acid intake was added into the model (eTables 2-3). The association of total or specific fried food consumption with all cause mortality did not vary by race or ethnicity, physical activity, or oil used for frying (P values ≥0.06). The association of total or specific fried food consumption with all cause mortality generally tended to be more obvious among women younger than 65, those who ever smoked, those who never used unopposed estrogen or estrogen plus progesterone, and those without obesity (eTable 4). The association of total or specific fried food consumption with cardiovascular mortality did not vary by race or ethnicity, smoking status, physical activity, unopposed

estrogen use, estrogen plus progesterone use, oil used for frying, or obesity status (P values ≥0.07). The association of fried chicken or fried fish/shellfish consumption with cardiovascular mortality was more obvious among women younger than 65 (eTable 5). Generally, the association of total or specific fried food consumption with cancer mortality did not vary by age, race/ethnicity, smoking status, physical activity, unopposed estrogen use, or oil used for frying (P values ≥0.08); in addition, the association did not vary by obesity status or estrogen plus progesterone use after stratification (eTable 6).

Discussion

In this large prospective cohort study, we comprehensively examined the associations of total and specific fried foods with all cause, cardiovascular, and cancer mortality. We found a significantly positive association of fried food consumption, especially fried chicken and fried fish/shellfish, with risk of all cause and cardiovascular mortality. These associations were slightly attenuated, but remained significant, after additional adjustment for a variety of factors that were related to mortality, including age, race/ethnicity, socioeconomic status, hormone use, lifestyle factors, health status, and body mass index.

Results in relation to other studies

Previous studies on fried food consumption and mortality are scarce[15] and their findings have been

Table 2 | Association of total fried food consumption with all cause and cause specific mortality among 106 966 postmenopausal women. Data are hazard ratios (95% confidence intervals) unless indicated otherwise

Mortality	Frequency of total fried food consumption					P for trend
	None	<1 serving/week	1-2 servings/week	3-6 servings/week	≥1 serving/day	
All cause mortality:						
No of deaths/participants	4693/15 166	11 755/38 482	9529/33 210	4283/15 480	1298/4628	—
Age adjusted model	1.00 (ref)	1.06 (1.02 to 1.09)	1.13 (1.10 to 1.17)	1.20 (1.15 to 1.25)	1.36 (1.28 to 1.44)	<0.001
Multivariable model 1	1.00 (ref)	1.01 (0.98 to 1.05)	1.03 (0.99 to 1.07)	1.03 (0.99 to 1.08)	1.08 (1.01 to 1.16)	0.02
Multivariable model 2	1.00 (ref)	1.01 (0.98 to 1.05)	1.02 (0.99 to 1.06)	1.03 (0.98 to 1.07)	1.07 (1.01 to 1.15)	0.06
Cardiovascular mortality:						
No of deaths/participants	1416/15 166	3456/38 482	2842/33 210	1221/15 480	385/4628	—
Age adjusted model	1.00 (ref)	1.04 (0.98 to 1.11)	1.16 (1.09 to 1.24)	1.19 (1.10 to 1.29)	1.43 (1.27 to 1.60)	<0.001
Multivariable model 1	1.00 (ref)	1.00 (0.94 to 1.06)	1.03 (0.97 to 1.10)	1.00 (0.92 to 1.09)	1.08 (0.96 to 1.22)	0.29
Multivariable model 2	1.00 (ref)	0.99 (0.93 to 1.06)	1.02 (0.95 to 1.09)	0.99 (0.91 to 1.07)	1.06 (0.94 to 1.20)	0.57
Cancer mortality:						
No of deaths/participants	1180/15 166	3071/38 482	2568/33 210	1203/15 480	336/4628	—
Age adjusted model	1.00 (ref)	1.06 (0.99 to 1.14)	1.11 (1.03 to 1.18)	1.16 (1.07 to 1.26)	1.16 (1.02 to 1.31)	<0.001
Multivariable model 1	1.00 (ref)	1.03 (0.96 to 1.10)	1.02 (0.95 to 1.09)	1.01 (0.93 to 1.10)	0.95 (0.83 to 1.08)	0.61
Multivariable model 2	1.00 (ref)	1.03 (0.96 to 1.10)	1.01 (0.94 to 1.08)	1.00 (0.92 to 1.09)	0.93 (0.82 to 1.06)	0.41

Multivariable model 1=age at baseline, race/ethnicity, education, annual income, whether they were from the observational study or the clinical trial, unopposed estrogen use, estrogen+progesterone use, smoking status, physical activity, coffee intake, total energy intake, diet quality score, baseline diabetes status, baseline cardiovascular status, and baseline cancer status; multivariable model 2=multivariable model 1+body mass index; ref=reference.

Table 3 | Association of individual fried food consumption with all cause mortality among 106 966 postmenopausal women. Data are hazard ratios (95% confidence intervals) unless indicated otherwise

Fried food items	Frequency of consumption				P for trend
	None	<2 servings/month	2-3 servings/month	≥1 serving/week	
Fried chicken:					
No of deaths/participants	19 788/68 709	6642/21 980	3188/10 268	1940/6009	—
Age adjusted model	1.00 (ref)	1.14 (1.11 to 1.17)	1.26 (1.22 to 1.31)	1.38 (1.31 to 1.44)	<0.001
Multivariable model 1	1.00 (ref)	1.06 (1.03 to 1.09)	1.12 (1.07 to 1.17)	1.13 (1.07 to 1.19)	<0.001
Multivariable model 2	1.00 (ref)	1.06 (1.03 to 1.09)	1.11 (1.07 to 1.16)	1.12 (1.06 to 1.18)	<0.001
Fried fish/shellfish:					
No of deaths/participants	17 549/60 169	7292/24 958	4017/13 489	2700/8350	—
Age adjusted model	1.00 (ref)	1.04 (1.01 to 1.07)	1.11 (1.07 to 1.15)	1.22 (1.17 to 1.27)	<0.001
Multivariable model 1	1.00 (ref)	0.97 (0.94 to 0.99)	0.99 (0.96 to 1.03)	1.07 (1.03 to 1.12)	0.07
Multivariable model 2	1.00 (ref)	0.97 (0.94 to 0.99)	0.99 (0.95 to 1.03)	1.07 (1.02 to 1.12)	0.10
Other fried foods:					
No of deaths/participants	6613/20 484	7166/22 699	5669/19 468	12 110/44 315	—
Age adjusted model	1.00 (ref)	1.04 (1.01 to 1.08)	1.04 (1.01 to 1.08)	1.10 (1.07 to 1.14)	<0.001
Multivariable model 1	1.00 (ref)	1.01 (0.98 to 1.05)	0.98 (0.95 to 1.03)	0.98 (0.95 to 1.01)	0.06
Multivariable model 2	1.00 (ref)	1.01 (0.98 to 1.05)	0.98 (0.95 to 1.02)	0.98 (0.95 to 1.01)	0.05

Multivariable model 1=age at baseline, race/ethnicity, education, annual income, whether they were from the observational study or the clinical trial, unopposed estrogen use, estrogen+progesterone use, smoking status, physical activity, coffee intake, total energy intake, diet quality score, baseline diabetes status, baseline cardiovascular status, and baseline cancer status; multivariable model 2=multivariable model 1+body mass index; ref=reference.

inconsistent. Similar to our findings, a previous study in the US found that fried food consumption was associated with the risk of incident type 2 diabetes and cardiovascular disease.[3] Additionally, the observed associations of fried chicken consumption and fried fish/shellfish consumption with cardiovascular mortality were consistent with previous studies. These studies found fried food consumption was associated with a higher risk of heart failure,[4 17] acute myocardial infarction,[18-20] total ischemic heart disease,[21] and death.[22 23] We are aware that a previous study in Spain, a Mediterranean country, reported that fried food consumption was not associated with all cause mortality.[1] Frying practice and medium vary by cooking tradition and the location where fried foods are consumed. For example, in the US, fried foods are eaten more often away from home (eg, in fast food restaurants) than at home; away from home, fried foods are usually deep fried[24] in corn oil, which is the most common frying medium.[25] In Mediterranean countries, however, fried foods are consumed at home as frequently as away from home, with pan frying and deep frying commonly used,[26] and mostly with olive oil for home frying.[27 28] The types of oil used for frying in Spain (mainly olive oil and sunflower oil) could partially explain the difference observed between our study and the study in Spain. Some studies showed that olive oil consumption was associated with a decreased risk of overall and cardiovascular mortality.[29 30]

Thus it is important to examine the associations of fried foods with mortality in different settings because the results of studies from one setting are not necessarily applicable to another. No previous study has examined the association of fried food consumption with cancer mortality.

Table 4 | Association of individual fried food consumption with cardiovascular mortality among 106 966 postmenopausal women. Data are hazard ratios (95% confidence intervals) unless indicated otherwise

Fried food items	Frequency of consumption				P for trend
	None	<2 servings/month	2-3 servings/month	≥1 serving/week	
Fried chicken:					
No of deaths/participants	5721/68 709	2005/21 980	986/10 268	608/6009	—
Age adjusted model	1.00 (ref)	1.19 (1.13 to 1.26)	1.37 (1.28 to 1.47)	1.51 (1.39 to 1.64)	<0.001
Multivariable model 1	1.00 (ref)	1.08 (1.02 to 1.14)	1.17 (1.08 to 1.25)	1.12 (1.02 to 1.23)	<0.001
Multivariable model 2	1.00 (ref)	1.07 (1.02 to 1.13)	1.15 (1.07 to 1.24)	1.11 (1.01 to 1.21)	<0.001
Fried fish/shellfish:					
No of deaths/participants	5067/60 169	2209/24 958	1173/13 489	871/8350	—
Age adjusted model	1.00 (ref)	1.09 (1.04 to 1.15)	1.14 (1.07 to 1.21)	1.37 (1.27 to 1.47)	<0.001
Multivariable model 1	1.00 (ref)	1.00 (0.95 to 1.06)	0.98 (0.92 to 1.05)	1.13 (1.04 to 1.22)	0.05
Multivariable model 2	1.00 (ref)	1.00 (0.95 to 1.05)	0.97 (0.91 to 1.04)	1.12 (1.04 to 1.22)	0.09
Other fried foods:					
No of deaths/participants	2041/20 484	2136/22 699	1656/19 468	3487/44 315	—
Age adjusted model	1.00 (ref)	1.02 (0.96 to 1.08)	1.02 (0.95 to 1.08)	1.09 (1.03 to 1.15)	0.002
Multivariable model 1	1.00 (ref)	0.99 (0.93 to 1.05)	0.96 (0.89 to 1.02)	0.95 (0.90 to 1.01)	0.09
Multivariable model 2	1.00 (ref)	0.98 (0.93 to 1.05)	0.95 (0.89 to 1.02)	0.95 (0.89 to 1.01)	0.06

Multivariable model 1=age at baseline, race/ethnicity, education, annual income, whether they were from the observational study or the clinical trial, unopposed estrogen use, estrogen+progesterone use, smoking status, physical activity, coffee intake, total energy intake, diet quality score, baseline diabetes status, baseline cardiovascular status, and baseline cancer status; multivariable model 2=multivariable model 1+body mass index; ref=reference.

Table 5 | Association of individual fried food consumption with cancer mortality among 106 966 postmenopausal women. Data are hazard ratios (95% confidence intervals) unless indicated otherwise

Fried food items	Frequency of consumption				
	None	<2 servings/month	2-3 servings/month	≥1 serving/week	P for trend
Fried chicken:					
No of deaths/participants	5345/68 709	1721/21 980	794/10 268	498/6009	—
Age adjusted model	1.00 (ref)	1.06 (1.01 to 1.12)	1.08 (1.01 to 1.17)	1.20 (1.10 to 1.32)	<0.001
Multivariable model 1	1.00 (ref)	1.02 (0.96 to 1.08)	0.98 (0.91 to 1.07)	1.03 (0.93 to 1.14)	0.84
Multivariable model 2	1.00 (ref)	1.01 (0.95 to 1.07)	0.98 (0.90 to 1.06)	1.03 (0.93 to 1.14)	0.99
Fried fish/shellfish:					
No of deaths/participants	4735/60 169	1837/24 958	1082/13 489	704/8350	—
Age adjusted model	1.00 (ref)	0.95 (0.90 to 1.01)	1.07 (0.99 to 1.14)	1.13 (1.05 to 1.23)	0.004
Multivariable model 1	1.00 (ref)	0.92 (0.87 to 0.97)	0.99 (0.92 to 1.06)	1.05 (0.97 to 1.15)	0.70
Multivariable model 2	1.00 (ref)	0.92 (0.87 to 0.97)	0.99 (0.92 to 1.06)	1.05 (0.96 to 1.14)	0.80
Other fried foods:					
No of deaths/participants	1588/20 484	1859/22 699	1528/19 468	3373/44 315	—
Age adjusted model	1.00 (ref)	1.10 (1.03 to 1.18)	1.09 (1.02 to 1.17)	1.13 (1.06 to 1.20)	<0.001
Multivariable model 1	1.00 (ref)	1.09 (1.02 to 1.17)	1.05 (0.98 to 1.13)	1.04 (0.97 to 1.11)	0.94
Multivariable model 2	1.00 (ref)	1.09 (1.02 to 1.17)	1.05 (0.98 to 1.13)	1.03 (0.97 to 1.11)	0.95

Multivariable model 1=age at baseline, race/ethnicity, education, annual income, whether they were from the observational study or the clinical trial, unopposed estrogen use, estrogen+progesterone use, smoking status, physical activity, coffee intake, total energy intake, diet quality score, baseline diabetes status, baseline cardiovascular status, and baseline cancer status; multivariable model 2=multivariable model 1+body mass index; ref=reference.

Possible explanations of findings

There are several possible explanations for the associations of fried foods with cardiovascular and all cause mortality, although the detailed mechanisms are not well understood. The food could lose water and absorb fats during frying,[31 32] which would increase the energy density of food. Frying could also lead to excess energy intake by making food more aromatic and appealing in texture, thus improving food palatability.[2 33] Additionally, frying deteriorates oils through the process of oxidation and hydrogenation, leading to a loss of unsaturated fatty acids such as linoleic acid and an increase in the corresponding trans fatty acids such as trans linoleic acid.[1 34]

In our study, the associations persisted after adjustment for total energy intake and additional adjustment for trans fatty acid intake, suggesting that the associations could not be fully explained by increased energy intake or trans fatty acid. Another possibility is the higher levels of dietary advanced glycation end products as a result of frying,[35 36] which could have an important role in the development of cardiovascular disease, mainly through induction of oxidative stress and inflammation.[37-39] Previous studies have shown that higher levels of dietary advanced glycation end products were associated with higher risk of all cause and cardiovascular mortality.[40 41] Moreover, frying at a high temperature can lead to acrylamide formation in some foods, such as French fries and potato chips. Dietary acrylamide has been associated with higher risk of all cause, cardiovascular, and cancer mortality.[39 42] One possible explanation for the lack of association between fried foods and cancer mortality in our study could be that the dietary intake of acrylamide from fried foods might not be high enough to have an effect on cancer mortality; it could also be because of the different types of cancers. Further investigation is needed to examine the associations of fried foods with different cancer

sites. In addition, reused cooking fat could inhibit the activity of paraoxonase, an enzyme that inhibits the activity of low density lipoprotein cholesterol,[43] which is involved in the pathogenesis of atherosclerosis.[44] Finally, some of the fried foods such as fried chicken or fried fish could be ultra-processed foods that are usually high in added sodium, which could partially contribute to the higher risk of mortality related to these foods.[45]

Further studies are warranted to fully understand the mechanisms for the associations of fried foods with all cause and cardiovascular mortality. For example, studies could compare the same foods fried with different frying oils, fried with the same oil at different temperatures, or cooked using different methods such as grilling. These comparisons could help determine the role of different oils, the extent of oil degradation, and the changes in the food itself in the associations of fried foods with all cause and cardiovascular mortality. It is also important to explore the associations of fried foods with different cancer types to better understand the associations of fried foods and cancer mortality.

Strengths and limitations of study

Our study had several strengths, including the large sample size, the prospective study design which could establish the temporal direction of the associations, and the long term follow-up. Although the Women's Health Initiative was not designed to be a nationally representative sample of US women, the geographical, socioeconomic, and racial or ethnic diversity of the participants could improve the generalizability of the findings to other populations with similar characteristics. We also had detailed data on confounders that could potentially alter the association of fried food consumption with mortality, thus we could explore the role of fried food consumption thoroughly.

We acknowledge that there are several limitations. Firstly, we do not know the degree of browning,

duration, temperature, and method (deep or pan) used for frying or how often oils were reused. We have information on the oils that were used for frying at home, but we do not know the proportion of fried foods consumed at home or away from home. Therefore, the information provided is limited and it is not possible to determine whether and how the associations between fried foods and mortality differ by the type of oil used for frying. Secondly, we cannot separate the effect of a specific food from the effect of frying for any fried food. For example, we cannot separate the effect of frying from the potentially protective effects of fish/shellfish, which could in part explain the reduced risk of cancer mortality in those consuming some fish versus no fried fish. Thirdly, on the food frequency questionnaire, some fried foods were grouped together as one item. For example, fried potatoes and French fries were not separated from fried rice, fried cassava, and fritters. Therefore, we could not separate the associations of each of these items with mortality in the present study. Previous studies on fried potato consumption and mortality have yielded inconsistent results.[1 5 46] Finally, as in other observational studies, even though we have adjusted for a wide variety of covariates that relate to mortality, residual confounding by unidentified confounders is still possible.

Conclusions and public health implications

We have identified a risk factor for cardiovascular mortality that is readily modifiable by lifestyle and cooking choices. Reducing the consumption of fried foods, especially fried chicken and fried fish/shellfish, could have a clinically meaningful effect across the public health spectrum. In conclusion, in this large prospective cohort study, we observed that fried food consumption, especially fried chicken and fried fish/shellfish, was associated with a higher risk of all cause and cardiovascular mortality among postmenopausal women in the US. Further studies are warranted to elucidate the underlying mechanisms.

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Web appendix: Supplementary material