Dietary Fatty Acids and the Risk of Hypertension in Middle-Aged and Older Women

Lu Wang, JoAnn E. Manson, John P. Forman, J. Michael Gaziano, Julie E. Buring, Howard D. Sesso

Abstract—Dietary intake of various fats may have different effects on blood pressure. We conducted a prospective cohort study to examine the association between intake of subtype and individual fatty acids (FAs) and the risk of developing hypertension among 28,100 US women aged ≥39 years and free of cardiovascular disease and cancer. Baseline intake of FAs was assessed using semiquantitative food frequency questionnaires. Incident hypertension was identified from annual follow-up questionnaires based on self-reported physician diagnosis, medication use, and blood pressure levels. A total of 13,633 women developed incident hypertension during 12.9 years of follow-up. After adjusting for demographic, lifestyle, and other dietary factors, intake of saturated FAs, monounsaturated FAs, and trans-unsaturated FAs (trans FAs) was positively associated with the risk of hypertension. The multivariable relative risks and 95% CIs of hypertension in the highest compared with the lowest quintile of intake were 1.12 (1.05 to 1.20) for saturated FAs, 1.11 (1.04 to 1.18) for monounsaturated FAs, and 1.15 (1.08 to 1.22) for trans FAs. After additional adjustment for body mass index and history of diabetes mellitus and hypercholesterolemia, these associations were attenuated and remained statistically significant only for trans FAs (relative risk in the highest quintile: 1.08; 95% CI: 1.01 to 1.15). Intake of polyunsaturated FAs, including ω3 and ω6 polyunsaturated FAs, was not significantly associated with the risk of hypertension. In conclusion, higher intake of saturated FAs, monounsaturated FAs, and trans FAs was each associated with increased risk of hypertension among middle-aged and older women, whereas only association for trans FAs remained statistically significant after adjustment for obesity-related factors. (Hypertension. 2010;56:598-604.)

Key Words: diet ■ fatty acids ■ hypertension ■ epidemiology ■ women

Dietary fat is an important modifiable risk factor for hypertension.1 Interventions that reduce total fat intake can effectively lower systolic and diastolic blood pressures (BP).2–4 Recent research further suggests that subtypes of fat with different molecular structure may have different effects on BP.5,6 Investigations using animal models have shown that diets high in saturated fats increase BP,7,8 whereas diets enriched with ω3 polyunsaturated fats protect against induced BP elevations.9–11

In previous epidemiological studies, BP has been shown positively correlated with saturated fats intake12–13 and inversely correlated with monounsaturated14 and polyunsaturated fats intake.14,15 Only a few studies have examined the prospective association between dietary fat intake16–17 or its biomarkers in blood18,19 and the risk of developing hypertension, with inconsistent results reported. In randomized trials, reduction of saturated fats intake alone did not seem to affect BP20; increase of polyunsaturated (particularly ω3) fats intake can lower BP, whereas the effect was primarily found among hypertensive but not normotensive individuals.21–23

To better understand the different roles of various dietary fats in the development of hypertension, we conducted a prospective analysis in a large cohort of middle-aged and older US women to investigate the association between baseline intake of saturated fatty acids (FAs; SFAs), mono-unsaturated FAs (MUFS), polyunsaturated FAs (PUFAs), and trans-unsaturated FAs (trans FAs) and the subsequent risk of hypertension during long-term follow-up.

Methods

Study Population

The Women’s Health Study (WHS) is a randomized, double-blind, placebo-controlled, 2×2 factorial trial evaluating the risks and benefits of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer.24–25 A third component, β-carotene, was initially included in the trial but terminated after a median treatment of 2.1 years.26 Written informed consent was obtained from all of the participants. The trial and ongoing cohort follow-up were approved by the institutional review board of Brigham and Women’s Hospital (please see http://hyper.ahajournals.org). From September 1992 to May 1995, 39,876 female US health professionals, aged ≥39 years and free from cardiovascular disease...
and cancer (except nonmelanoma skin cancer), were randomized into the WHS. Of the 39,876 women randomized, 39,310 completed a 131-item validated semiquantitative food frequency questionnaire (FFQ). For this study, we excluded 10,751 women who had hypertension at baseline, defined as having a self-reported physician diagnosis of hypertension, self-reported current systolic BP \( \geq 140 \text{ mm Hg} \) or diastolic BP \( \geq 90 \text{ mm Hg} \), or use of antihypertensive treatment. We also excluded 829 women who reported implausible total daily energy intake, 21 women who provided incomplete information on the FFQ, and 41 women who had prerandomization cardiovascular disease or cancer. After these exclusions, a baseline population of 28,100 women remained for analysis.

**Assessment of Dietary Fat Intake**

On the baseline FFQ, a commonly used unit or portion size was specified for each food item. Participants were asked how often they had consumed that amount, on average, during the previous year. Nine possible responses ranging from "never or less than once per month" to "6+ per day" were recorded. Nutrient intake was computed by multiplying the intake frequency of each unit of food by the nutrient content of the specified portion size according to food composition tables from the US Department of Agriculture.27 supplemented with information obtained from the manufacturers and published reports. The estimation of fat intake also took into account the types of fat or oil used during food preparation. The trans isomer contents of unsaturated fats were estimated based on the method proposed by Sacks and Willett.28 Intakes of SFAs, MUFAs, PUFAs, and trans FAs were each calculated as sum of the respective individual FAs. All of the FA intakes presented in the current study have adjusted for total energy intake using the residual method.29 In similar cohorts of health professionals, Pearson correlation coefficients comparing responses from the FFQ with those from four 1-week dietary records spaced over a year were 0.70 for SFAs, 0.69 for MUFAs, and 0.64 for PUFAs.30,31 FA intakes estimated from the FFQ also correlated well with FA composition of the adipose tissue (Spearman \( r = 0.51 \) for trans FAs and 0.48 for \( \alpha_6 \) PUFAs).32

**Ascertainment of Incident Hypertension**

Incident hypertension was ascertained from annual follow-up questionnaires by meeting \( \geq 1 \) of 4 criteria: (1) a new physician diagnosis of hypertension; (2) newly initiated antihypertensive treatment; (3) self-reported current systolic BP \( \geq 140 \text{ mm Hg} \); or (4) self-reported current diastolic BP \( \geq 90 \text{ mm Hg} \). Women reported the month and year of hypertension diagnosis. For incident cases missing dates of physician diagnosis or defined by other criteria, time of event was assigned by randomly selecting a date between the questionnaires with and without hypertension. Individuals who developed cardiovascular disease during follow-up, the management of which may affect BP, were censored on the date of cardiovascular disease diagnosis. In health professionals, self-reported BP correlates well with measured systolic BP \( r = 0.72 \) and diastolic BP \( r = 0.60 \),33 and the validity of self-reported hypertension is high.34 In a random sample of WHS participants, self-reported incident hypertension was confirmed in 48 (96%) of 50 women and absence of hypertension was confirmed in 45 (90%) of 50 women through telephone interviews.

**Data Analyses**

Statistical analyses were performed using SAS software (SAS Institute) version 9.1. Intake of FAs was divided into quintiles. Distribution of hypertension risk factors was compared across quintiles of FAs intake. Person-years of follow-up were calculated for each participant from randomization to the date of incident hypertension, the last day in the study, or February 29, 2007, whichever came first. After verifying the assumption of constant proportional hazard, we used Cox regression model to estimate the hazard ratio (presented as relative risk [RR]) and 95% CI of hypertension across quintiles of FAs intake, with the lowest quintile as the reference. Models first adjusted for age, race, total energy intake, and randomized treatment assignment and then additionally adjusted for lifestyle factors, including smoking, total alcohol intake, physical activity, postmenopausal status, postmenopausal hormone use, and several hypertension-related nutritional factors, including dietary intake of calcium, potassium, sodium, and fiber (multivariable model 1), and finally adjusted for obesity-related metabolic factors that may also serve as intermediate factors linking dietary FAs to hypertension development, including body mass index (BMI), history of diabetes mellitus, and history of hypercholesterolemia (multivariable model 2). Analyses were further stratified by known hypertension risk factors including age (<55 or \( \geq 55 \) years), BMI (<25 or \( \geq 25 \text{ kg/m}^2 \)), smoking status (current or noncurrent), alcohol intake (none or any), and physical activity (<600 or \( \geq 600 \text{ kcal/week} \)). We also performed several sensitivity analyses. First, we repeated all of the analyses with dietary FAs represented as the percentage of total energy intake; second, we considered incident hypertension using alternative definitions, such as self-reported elevated BP only, physician diagnosis or antihypertensive treatment only, or multiple indications. The results of sensitivity analyses were similar to main analyses (data not shown).

**Results**

Among 28,100 women free of hypertension at baseline, energy-adjusted FA intake ranged from 2.55 to 51.4 g/d for SFAs, 3.39 to 52.0 g/d for MUFAs, 2.10 to 40.5 g/d for PUFAs, and 0.01 to 12.4 g/d for trans FAs. SFA and MUFA intakes were highly correlated (Pearson \( r = 0.78 \)). PUFA intake was moderately correlated with MUFA intake (\( r = 0.55 \)) and weakly but significantly correlated with SFA intake (\( r = 0.26 \)). Trans FAs intake was moderately correlated with SFA (\( r = 0.52 \)) and MUFA (\( r = 0.63 \)) intake and weakly correlated with PUFA intake (\( r = 0.31 \)).

Table 1 shows the baseline characteristics of participants by quintiles of SFA, MUFA, and PUFA intake. For all 3 of the FA subtypes, women consuming greater amounts were heavier, more likely to be current smokers, less physically active, and had lower alcohol intake. Women consuming more SFAs and MUFAs were younger, less likely to be postmenopausal and use postmenopausal hormones, and less likely to have hypercholesterolemia, whereas they were more likely to be diabetic. Intake of all 3 of the FA subtypes was also positively associated with intake of sodium and inversely associated with intake of calcium, potassium, and fiber. Baseline systolic and diastolic BPs increased with increasing intake of all 3 of the FA subtypes. The associations of hypertension risk factors with trans FA intake were similar to the associations with SFA and MUFA intake (data not shown).

A total of 13,633 cases of incident hypertension were identified during an average of 12.9 years of follow-up, with 2,427 cases identified by elevated systolic or diastolic BP only, 61 cases identified by physician diagnosis only, 1,540 cases identified by newly initiated antihypertensive medications only, and the remaining cases identified by multiple indications. After adjusting for age, race, total energy intake, and randomized treatment, the risk of hypertension significantly increased across increasing intake of all of the FA subtypes except \( \alpha_6 \) PUFAs. Additional adjustment for lifestyle factors and nutritional factors (multivariable model 1) attenuated these associations. Intake of SFAs, MUFAs, and trans FAs remained significantly and positively associated with risk of hypertension, whereas intake of PUFA was only marginally significantly associated with risk of hypertension.
The associations for SFA, MUFA, and PUFA intake were all attenuated to null; only the positive association for SFA, MUFA, and PUFA intake were largely attenuated by dietary FAs and hypertension risk only slightly varied by baseline BMI, smoking status, alcohol consumption, and physical activity (all P values for interaction: >0.05).

The associations of major individual FA intake with risk of hypertension largely followed the associations for their respective FA subtypes (Table S1, available in the online Data Supplement at http://hyper.ahajournals.org). Among women <55 years of age, intakes of individual SFA (including 16:0 and 18:0), MUFA (including 16:1 and 18:1), PUFA (including 20:4ω6 and 22:6ω3), and trans FA (including trans 16:1, trans 18:1, and trans 18:2) were each positively associated with risk of hypertension in multivariable model 1. These associations were attenuated in multivariable model 2, with the associations for 18:1, 20:4ω6, and trans 16:1 no longer significant. Among women aged ≥55 years, intake of individual FA was generally not associated with the risk of hypertension.

**Discussion**

In this large-scale prospective cohort study of middle-aged and older women, intake of SFAs, MUFAs, and trans FA was each positively associated with risk of hypertension. The associations for SFAs and MUFAs were largely attenuated by
adjustment for potential intermediate factors, including BMI, diabetes mellitus, and hypercholesterolemia, whereas the associations for trans FAs remained significant even after these adjustments. Intake of PUFAs was generally not associated with risk of hypertension.

Various fats potentially have different effects on BP. Experimental studies found that feeding rats with SFAs resulted in impaired endothelial function and enhanced sympathetic nervous system activities, which will increase BP. In contrast, consumption of long-chain ω3 PUFAs modulated plasma phospholipid composition and cell membrane fluidity, increased the production of vasodilators, and reduced cardiac adrenergic activity, which will lower BP. The incorporation of ω6 PUFAs into cell membrane changed

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* Linear trends across increasing quintiles of FAs intake were tested using the median value of each quintile as an ordinal variable.
† Multivariable model 1 was adjusted for age (continuous), race (white or nonwhite), total energy intake (continuous), treatment (vitamin E, aspirin, β-carotene, or placebo), smoking (never, former, or current), alcohol intake (continuous), physical activity (continuous), postmenopausal status (yes, no, or uncertain), postmenopausal hormone use (never, former, or current), dietary sodium, potassium, calcium, and fiber (all in quintiles).
‡ Multivariable model 2 was adjusted for all of the covariates in multivariable model 1 plus BMI (continuous), history of diabetes mellitus (yes or no), and history of hypercholesterolemia (yes or no).
the balance between vasoconstrictors and vasodilators, and the subsequent net effects on BP have varied in different animal models. Similarly, MUFAs also modify membrane phospholipid composition and vascular reactivity, the net effects of which may either raise or lower BP. Direct effects of trans FAs on BP remain largely unclear. Because of the lack of flexible structure of their parent unsaturated FAs, trans FAs display biological features more similar to SFAs. Furthermore, because trans FAs compete with other unsaturated FAs for enzymatic desaturation, the presence of trans FAs may increase the demand for essential PUFAs.

Previous prospective studies linking FA intake with incident hypertension have yielded inconsistent results. In the Nurses’ Health Study, a cohort of 121,700 US women aged 34 to 59 years, and the Health Professionals Follow-Up Study, a cohort of 51,529 US men aged 40 to 75 years, no association was found between baseline intake of SFAs, MUFAs, PUFAs, or trans FAs assessed from FFQ and incident hypertension during a short follow-up of 4 years. Two studies investigated the association between plasma FAs, as biomarker for dietary FAs, and risk of hypertension. The Atherosclerosis Risk in Communities Study found that higher levels of SFAs and MUFAs and lower levels of PUFAs and polyunsaturated:saturated FA ratio in baseline plasma phospholipids and cholesterol ester were significantly associated with an increased 6-year incidence of hypertension. The Uppsala Longitudinal Study of Adult Men showed that the baseline plasma levels of SFA 16:0 and

![Figure. Multivariable RRs and 95% CIs of hypertension according to intake of fatty acid subtypes, stratified by baseline age (39 to <55 or 55 to 89 years). A showed results in multivariable model 1 adjusting for age, race, total energy intake, randomized treatment, smoking, alcohol intake, physical activity, postmenopausal status, postmenopausal hormone use, dietary sodium, potassium, calcium, and fiber. B showed results in multivariable model 2 additionally adjusting for BMI, history of diabetes mellitus, and history of hypercholesterolemia.](image)
18:0 were significantly higher and the plasma level of PUFA 18:2ω6 was significantly lower in men who developed sustained hypertension compared with men who remained normotensive or had white-coat hypertension. Both studies did not examine trans FAs in plasma. In randomized trials, dietary interventions that lowered saturated fat intake alone did not significantly affect BP; diets rich in MUFAs reduced BP levels but not all studies; ω3 PUFA supplementation lowered BP in hypertensive individuals but not in normotensives, and the substantial BP reductions usually occurred at relatively high doses (≥3 g/d); and ω6 PUFA (mainly 18:2ω6) supplements have not demonstrated apparent effects on BP. We are not aware of any clinical trial that tested the effect of reducing dietary trans fats on BP or risk of developing hypertension.

In our study, the positive associations of SFA, MUFA, and trans FA intakes with risk of hypertension were substantially attenuated after adjustment for BMI. This finding underscored a potential confounding effect of obesity in the dietary fat and hypertension relation. Alternatively, because dietary fat is a major source of energy that may contribute to the development of obesity, a strong impact of BMI in the FA-hypertension relation also possibly reflects that obesity and its related pathophysiological processes are important intermediate steps linking fat intake to BP change. Another intriguing finding in our study is that the associations between subtype and individual FA intake with risk of hypertension have appeared stronger among younger women versus older women. However, the test for age-related interactions only reached statistical significance for trans FAs. The lack of a clear association between intake of ω3 PUFA, ω6 PUFA, and ω6:ω3 ratio with risk of hypertension, although consistent with findings from previous studies that measured plasma FAs as biomarker for dietary FAs, was unexpected. Although in vivo and in vitro experimental studies demonstrated potential effects of PUFAs on BP control, the amount of PUFA intake in our study population is probably insufficient to strongly affect the risk of developing hypertension among initially normotensive individuals. Another possible explanation for the lack of association for PUFAs is residual confounding by unknown factors that correlate with high PUFA intake or supplement use.

Strengths of the current study include the prospective study design, large sample size, and minimal loss to follow-up. However, several limitations of this study also deserve comment. First, the assessment of dietary FA intake and ascertainment of incident hypertension are based on self-reported information in our study. Nevertheless, the validity and reproducibility of FFQ as a measure of long-term dietary intake and the accuracy of self-reported hypertension in health professionals have been demonstrated in previous validation studies. For lifestyle and clinical covariates, including BMI, a single baseline assessment is subject to misclassification considering possible change during follow-up, whereas random misclassification will typically lead to an underestimation of true association. Second, because correlations among intake of SFAs, MUFAs, and trans FAs were moderate to high in our study, we cannot completely separate their effects from each other. Third, despite comprehensive adjustment for multiple lifestyle and clinical factors, residual confounding by unmeasured or imprecisely measured hypertension risk factors may persist. Fourth, although our large sample size allowed us to assess the association between dietary FAs and risk of hypertension in various subgroups, the potential for false-positive findings implies that we should interpret any significant findings in subgroup analysis with caution. Finally, WHS participants are predominantly white female health professionals, which minimized potential confounding by race/ethnicity and socioeconomic factors but also may limit study generalizability. Yet similar associations noted in previous community-based studies suggest that our results may indeed be generalizable to other populations.

Perspectives

Current dietary guidelines for US adults recommend total fat intake between 20% and 35% of calories, saturated FAs intake <10% of calories, and trans FA consumption as low as possible. Epidemiological evidence on the relevance of such dietary recommendations to the prevention of hypertension is surprisingly limited. With total fat intake as a percentage of calories falling over recent decades, more specific recommendations on the optimal amount and type of FA intake for hypertension and cardiovascular disease prevention are needed. Our study comprehensively examined the association between intake of subtype and individual FAs and risk of hypertension. Our findings support the importance of current dietary fat recommendations for middle-aged and older women. Our findings also suggest that an adverse diet profile, along with other unhealthy lifestyle, may increase the risk of hypertension through promoting obesity. More studies are warranted to further elucidate the interrelation among dietary fat, the development of obesity, and the pathogenesis of hypertension.

Acknowledgments

We are indebted to the 39,876 participants in the WHS for their dedicated and conscientious collaboration and to the entire staff of the WHS for their assistance in designing and conducting the trial.

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Disclosures

None.

References


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First Author: Wang

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Online Supplement.

Expanded Methods Section

Study Population

The Women’s Health Study (WHS) is a randomized, double-blind, placebo-controlled, 2×2 factorial trial evaluating the risks and benefits of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer.1, 2 A third component, β-carotene, was initially included in the trial but terminated after a median treatment of 2.1 years. Written informed consent was obtained from all participants. During the course of the trial, participants received study agents and follow-up questionnaires by mail and reported the occurrence of major cardiovascular and cancer end points and risk factor information every 6 months for the first year and annually thereafter. The trial and ongoing cohort follow-up was approved by the institutional review board of Brigham and Women’s Hospital, Boston, MA. From September 1992 to May 1995, a total of 39,876 female US health professionals, aged ≥39 years and free from cardiovascular disease and cancer (except non-melanoma skin cancer), were randomized into the WHS. Of the 39,876 women randomized, 39,310 completed a 131-item validated semiquantitative food frequency questionnaire (FFQ). For this study, we excluded 10,751 women who had hypertension at baseline, defined as having a self-reported physician diagnosis of hypertension, self-reported current systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg, or use of antihypertensive treatment. Baseline systolic BP was reported as 1 of 9 ordinal categories in 10 mmHg increments from <110 to ≥180 mmHg, and diastolic BP was reported as 1 of 7 ordinal categories in 5 or 10 mmHg increments from <65 to ≥105 mmHg. We also excluded 829 women who reported implausible total daily energy intake (≤600 or ≥3,500 kcal/d), 21 women who provided incomplete information on the FFQ (>70 items left blank), and 41 women who had pre-randomization cardiovascular disease or cancer. After these exclusions, a baseline population of 28,100 women remained for analysis.

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On the baseline FFQ, a commonly used unit or portion size was specified for each food item. Participants were asked how often they had consumed that amount, on average, during the previous year. Nine possible responses ranging from “never or less than once per month” to “6+ per day” were recorded. Nutrient intake was computed by multiplying the intake frequency of each unit of food by the nutrient content of the specified portion size according to food composition tables from the US Department of Agriculture,4 supplemented with information obtained from the manufacturers and published reports. The estimation of fat intake also took into account the types of fat or oil used during food preparation. The trans isomers contents of unsaturated fats were estimated based on the method proposed by Sacks and Willett.5 Intake of SFAs, MUFAs, PUFAs, and trans FAs was each calculated as sum of the respective individual FAs. All FAs intake presented in the current study have adjusted for total energy intake using the residual method. The FFQ used in the WHS has demonstrated reasonable validity and reproducibility as a measure of long-term dietary intake. In similar cohorts of health professionals, Pearson’s correlation coefficients comparing responses from
the FFQ with those from four 1-week dietary records spaced over a year were 0.70 for SFAs, 0.69 for MUFAs, and 0.64 for PUFAs. FAs intake estimated from the FFQ also correlated well with FA composition of the adipose tissue (Spearman's r=0.51 for trans FAs and 0.48 for ω3 PUFAs). 

**Ascertainment of Incident Hypertension**

Incident hypertension was ascertained from annual follow-up questionnaires by meeting at least 1 of 4 criteria: a new physician diagnosis of hypertension; newly initiated antihypertensive treatment; self-reported current systolic BP ≥140 mmHg; or self-reported current diastolic BP ≥90 mmHg. Women reported the month and year of hypertension diagnosis. For incident cases missing dates of physician diagnosis or defined by other criteria, time of event was assigned by randomly selecting a date between the questionnaires with and without hypertension. Individuals who developed cardiovascular disease during follow-up, the management of which may affect BP, were censored on the date of cardiovascular disease diagnosis. In health professionals, self-reported BP correlates well with measured systolic BP (r=0.72) and diastolic BP (r=0.60), and the validity of self-reported hypertension is high. In a random sample of WHS participants, self-reported incident hypertension was confirmed in 48 of 50 (96%) women and absence of hypertension was confirmed in 45 of 50 (90%) women through telephone interviews.

**Other Baseline Variables**

On the baseline questionnaire, women provided self-reports of age, weight and height, smoking status, alcohol intake, physical activity, menopausal status, postmenopausal hormone use, history of diabetes and hypercholesterolemia. Body mass index (BMI) was computed as body weight (in kg) divided by square of height (in m). Total alcohol intake was calculated by summing alcohol content in consumed beer, wine, and liquor. Physical activity was assessed from self-reported frequency, intensity, and duration of walking and recreational activities, and expressed as energy expenditure in kcal/week. Diabetes was defined by self-reported physician diagnosis and confirmed by telephone interview or supplemental questionnaires. Hypercholesterolemia was defined as having a physician diagnosis, self-reported total cholesterol concentration ≥240 mg/dL, or current treatment for high cholesterol.

**Data Analyses**

Statistical analyses were performed using SAS software (SAS Institute, Cary, NC, USA) version 9.1. Intake of FAs was divided into quintiles. Distribution of hypertension risk factors was compared across quintiles of FAs intake to identify potential confounding factors. Person-years of follow-up were calculated for each participant from randomization to the date of incident hypertension, the last day in the study, or 29 February 2007, whichever came first. After verifying the assumption of constant proportional hazard over time (p>0.05), we used Cox regression model to estimate the hazard ratio (presented as relative risk, RR) and 95% confidence interval (CI) of hypertension across quintiles of FAs intake, with the lowest quintile as the reference. Models first adjusted for age (continuous), race (white, non-white), total energy intake (continuous), and randomized treatment assignment (vitamin E, aspirin,
\(\beta\)-carotene, or placebo); then additionally adjusted for lifestyle factors including smoking (never, former, current), total alcohol intake (continuous), physical activity (continuous), postmenopausal status (yes, no, uncertain), postmenopausal hormone use (never, former, current), and several hypertension-related nutritional factors including dietary intake of calcium, potassium, sodium, and fiber (all in quintiles) (multivariable model 1); and finally adjusted for obesity-related metabolic factors that may also serve as intermediate factors linking dietary FAs to hypertension development, including BMI (continuous), history of diabetes, and history of hypercholesterolemia (both yes, no) (multivariable model 2). Analyses were further stratified by known hypertension risk factors including age (<55, ≥55 years), BMI (<25, ≥25 kg/m\(^2\)), smoking status (current, non-current), alcohol intake (none, any), and physical activity (<600, ≥600 kcal/week). Multiplicative interactions were tested using Wald \(\chi^2\) tests. We also performed several sensitivity analyses. First, we repeated all analyses with dietary FAs represented as the percentage of total energy intake; second, we considered incident hypertension using alternative definitions, such as self-reported elevated BP only, physician diagnosis or antihypertensive treatment only, or multiple indications. The results of sensitivity analyses were similar to main analyses (data not shown).
References:


Table S1.
Multivariable relative risks and 95% confidence intervals of hypertension in the highest quintile compared to the lowest quintile of individual fatty acid intake, stratified by baseline age.

<table>
<thead>
<tr>
<th>Individual fatty acids</th>
<th>Aged 39 - &lt;55 years</th>
<th>Aged 55 - 89 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>P, trend</td>
</tr>
<tr>
<td></td>
<td>(5th vs 1st Quintile)</td>
<td></td>
</tr>
</tbody>
</table>

**Saturated Fatty Acids**

4:0 to 12:0†
- Multivariable model 1‡: 1.03 (0.95 - 1.11) 0.53 0.95 (0.87 - 1.04) 0.13
- Multivariable model 2§: 1.03 (0.95 - 1.11) 0.32 0.93 (0.85 - 1.02) 0.04

14:0 (myristic)
- Multivariable model 1‡: 1.02 (0.94 - 1.10) 0.58 0.94 (0.86 - 1.04) 0.19
- Multivariable model 2§: 1.00 (0.92 - 1.08) 0.87 0.90 (0.81 - 0.98) 0.02

16:0 (palmitic)
- Multivariable model 1‡: 1.24 (1.13 - 1.35) < 0.0001 1.11 (1.00 - 1.23) 0.16
- Multivariable model 2§: 1.13 (1.04 - 1.23) 0.01 1.02 (0.92 - 1.13) 0.72

18:0 (stearic)
- Multivariable model 1‡: 1.30 (1.20 - 1.42) < 0.0001 1.09 (0.98 - 1.21) 0.04
- Multivariable model 2§: 1.18 (1.08 - 1.29) 0.0002 1.00 (0.90 - 1.11) 0.85

**Monounsaturated Fatty Acids**

16:1 (palmitoleic)
- Multivariable model 1‡: 1.23 (1.13 - 1.33) < 0.0001 1.18 (1.07 - 1.30) 0.008
- Multivariable model 2§: 1.08 (1.00 - 1.18) 0.08 1.05 (0.95 - 1.15) 0.82
<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:1 (oleic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1‡</td>
<td>1.12 (1.03-1.22)</td>
<td>0.005</td>
</tr>
<tr>
<td>Multivariable model 2§</td>
<td>1.05 (0.97-1.15)</td>
<td>0.17</td>
</tr>
<tr>
<td>20:1 (eicosenoic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1‡</td>
<td>0.96 (0.90-1.03)</td>
<td>0.40</td>
</tr>
<tr>
<td>Multivariable model 2§</td>
<td>0.96 (0.90-1.03)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

**Polyunsaturated Fatty Acids**

### ω3 Polyunsaturated Fatty Acids

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:3C (α-linolenic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1‡</td>
<td>1.10 (1.02-1.18)</td>
<td>0.06</td>
</tr>
<tr>
<td>Multivariable model 2§</td>
<td>1.08 (1.00-1.16)</td>
<td>0.20</td>
</tr>
<tr>
<td>20:5C (eicosapentaenoic, EPA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1‡</td>
<td>1.03 (0.96-1.11)</td>
<td>0.92</td>
</tr>
<tr>
<td>Multivariable model 2§</td>
<td>1.05 (0.98-1.13)</td>
<td>0.43</td>
</tr>
<tr>
<td>22:6C (docosahexaenoic, DHA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1‡</td>
<td>1.08 (1.01-1.16)</td>
<td>0.09</td>
</tr>
<tr>
<td>Multivariable model 2§</td>
<td>1.08 (1.01-1.16)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

### ω6 Polyunsaturated Fatty Acids

<table>
<thead>
<tr>
<th>Fatty Acid</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:2C (linoleic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1‡</td>
<td>1.02 (0.95-1.10)</td>
<td>0.31</td>
</tr>
<tr>
<td>Multivariable model 2§</td>
<td>1.00 (0.93-1.08)</td>
<td>0.80</td>
</tr>
<tr>
<td>20:4C (arachidonic)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable model 1‡</td>
<td>1.13 (1.04-1.23)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>
**Trans unsaturated Fatty Acids**

**trans 16:1 (palmitoleic)**
- Multivariable model 1‡
  - 1.17 (1.08-1.27)  < 0.0001  1.10 (1.00-1.21)  0.10
- Multivariable model 2§
  - 1.06 (0.98-1.15)  0.18  0.99 (0.90-1.10)  0.59

**trans 18:1 (oleic)**
- Multivariable model 1‡
  - 1.26 (1.16-1.37)  < 0.0001  0.96 (0.87-1.06)  0.46
- Multivariable model 2§
  - 1.18 (1.09-1.28)  0.0002  0.92 (0.84-1.02)  0.17

**trans 18:2 (linoleic)**
- Multivariable model 1‡
  - 1.27 (1.17-1.38)  < 0.0001  1.02 (0.93-1.12)  0.67
- Multivariable model 2§
  - 1.18 (1.09-1.28)  < 0.0001  0.98 (0.89-1.07)  0.54

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* Linear trends across increasing quintiles of FAs intake were tested using the median value of each quintile as an ordinal variable.

† Short- to medium- chain saturated fatty acids, including 4:0 (butyric acid), 6:0 (caproic acid), 8:0 (caprylic acid), 10:0 (capric acid), and 12:0 (lauric acid), were combined due to the low percentage in total fat intake and similar food sources.

‡ Multivariable model 1 adjusted for age (continuous), race (white, non-white), total energy intake (continuous), treatment (vitamin E, aspirin, β-carotene, or placebo), smoking (never, former, current), alcohol intake (continuous), physical activity (continuous), postmenopausal status (yes, no, uncertain), postmenopausal hormone use (never, former, current), multivitamin use (never, former, current), dietary sodium, potassium, calcium, and fiber (all in quintiles).

§ Multivariable model 2 adjusted for all covariates in multivariable model 1 and additionally adjusted for BMI (continuous), history of diabetes (yes, no), history of hypercholesterolemia (yes, no).