The Relationship Between Dietary Flavonoid Intake and Hypertension: A Cross-Sectional Study from NHANES

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Abstract

Background: This study aims to explore the relationship between dietary flavonoid intake and hypertension in American adults through a nationally representative sample.

Methods: A cross-sectional analysis was conducted, including 9,123 individuals from the National Health and Nutrition Examination Survey (NHANES) and the Food and Nutrient Database for Dietary Studies (FNDDS), covering data from 2007-2011 and 2017-2018. Flavonoid intake was measured using a two-day dietary recall questionnaire. Multivariate logistic regression, stratified analysis, and restricted cubic splines (RCS) were employed to assess the potential association between flavonoid consumption and hypertension, with adjustments for possible confounding variables.

Results: The study found a significant negative correlation between dietary intake of total flavonoids, flavanones, anthocyanins, and flavan-3-ols and hypertension. Statistically significant nonlinear relationships were observed for flavanones, flavan-3-ols, flavonols, and total flavonoids with hypertension, with significant p-nonlinear values of 7E-04, 0.02, 2E-04, and 0, respectively. Subgroup analysis revealed that the relationship between total flavonoid intake and hypertension is complex and influenced by glucose tolerance and hyperlipidemia. It showed different trends, with an increased risk of hypertension in individuals with impaired glucose tolerance (IGT) and a potential reduction in hypertension risk in those without hyperlipidemia.

Conclusion: This study emphasizes the potential positive role of flavonoid compounds in the prevention and management of hypertension in American adults, suggesting that moderate flavonoid intake may be more beneficial for health. These findings offer new hope and strategic support for the maintenance of cardiovascular health.

1. Introduction

Hypertension, a significant global public health issue, affects approximately 31.1% of adults worldwide, approximately 1.39 billion people[1]. This condition not only diminishes the quality of life for millions but also places a substantial burden on healthcare systems and socioeconomic structures[2]. It is well-established that hypertension is closely linked to unhealthy eating habits, including excessive alcohol consumption, high salt intake, and low potassium intake[3–5]. To effectively prevent hypertension and its progression, it is crucial to understand this relationship.

Flavonoids are a group of natural compounds, including anthocyanins, flavan-3-ols, flavanones, flavones, flavonols, and isoflavones. They are widely found in the plant kingdom and are present in entities such as fruits, vegetables, tea leaves, and red wine[6, 7]. Due to their structural diversity and diverse biological properties, these compounds have garnered scientific interest and have been substantiated to offer a range of benefits for various physiological processes, including antioxidant, anti-inflammatory, and anticarcinogenic properties[7, 8]. As research has deepened, attention has increasingly focused on the

potential connection between flavonoids and cardiovascular well-being, especially concerning their impact on hypertension[9, 10].

The main focus of this exposition is to explore the intricate relationship between dietary flavonoid intake and hypertension. For this purpose, we will utilize data from the National Health and Nutrition Examination Survey (NHANES) spanning the years 2007 through 2010 and 2017 through 2018. This scholarly endeavor aims to shed light on the potential connection between total flavonoid intake and its subcategories and the complex origins of hypertension. The ultimate goal is to improve our ability to manage hypertension through informed dietary recommendations.

2. Methods

2.1 Study Population

The participants in this study were drawn from the NHANES in the United States. An overview of the participant selection process is provided in Fig. 1. This investigation utilized data from three NHANES periods: 2007–2010 and 2017–2018, to study flavonoid intake. We analyzed a cohort of 17,299 individuals. During the sample curation, we first excluded participants under the age of 20 and then removed individuals with missing flavonoid data (n = 1107) and those without hypertension data (n = 1). As a result, our analysis focused on a group of 9,123 fully documented adults.

During the NHANES study, all participants provided written informed consent with a clear understanding of the nature and objectives of the research. This consent document received approval from the National Center for Health Statistics Ethical Review Committee, ensuring the study's ethical compliance.

2.2 Exposure and Outcomes

Information regarding total flavonoid and subcategory intake was extracted from the United States Food and Nutrition Database (FNDDS), which is linked to the NHANES database. The levels of these flavonoid compounds were determined by averaging the results of two 24-hour interviews, ensuring data reliability and accuracy. The United States Department of Agriculture database included 29 flavonoid compounds and 6 flavonoid subcategories related to NHANES 2007–2010 and 2017–2018. These categories encompassed anthocyanins, flavan-3-ols, flavanones, flavones, flavonols, and isoflavones. Additionally, the total flavonoid value was calculated. These data enabled us to estimate flavonoid intake among the U.S. population, providing crucial information for our study.

In this study, hypertension was defined as meeting any of the following criteria: systolic blood pressure (diastolic blood pressure) ≥ 140 mmHg (≥ 90 mmHg); current use of antihypertensive medication; or a prior diagnosis of hypertension by a healthcare professional[11].

2.3 Covariates

To assess the potential impact of confounding factors, we included several key covariates in our analysis. These covariates encompassed individual characteristics such as gender, age, race, marital status, the poverty-income ratio(PIR, a measure of family income relative to the poverty line, where PIR < 1 indicates income below the poverty line, and PIR > 1 indicates income above it)[12], education level, body mass index(BMI, calculated as weight (kg)/height (m^2)), alcohol consumption status, smoking status, physical activity level (measured in metabolic equivalent (MET) minutes per week, categorized as never, low, moderate, and high physical activity), total energy intake, protein intake, carbohydrate intake, sugar intake, and fat intake. These covariates were collected through standardized questionnaires. Alcohol consumption status was classified as follows:( ) never :had < 12 drinks in lifetime;( ) former: had ≥ 12 drinks in 1 year and did not drink last year, or did not drink last year but drank ≥ 12 drinks in lifetime;( ) heavy: women consuming ≥ 3 drinks per day, men consuming ≥ 4 drinks per day, or having a consecutive drinking frequency of ≥ 5;( ): moderate drinking: women consuming ≥ 2 drinks per day, men consuming ≥ 3 drinks per day, or having a consecutive drinking frequency of ≥ 2 and < 5;and( ):mild: individuals who do not meet the criteria outlined in the above categories. Smoking status was categorized as follows: never: individuals who had smoked fewer than 100 cigarettes in their lifetime;( ):former: individuals who had smoked at least 100 cigarettes in their lifetime but were currently not smoking;( ):now: individuals who had smoked at least 100 cigarettes in their lifetime and were currently smoking. Additionally, we assessed physical activity levels using self-reported data, measured in MET-minutes per week. MET-minutes were calculated based on adult physical activity guidelines, and participants were categorized as never, low, moderate, or high levels of physical activity. Definitions of high cholesterol and diabetes were based on relevant diagnostic criteria. These covariates will be used to control for confounding factors in our analysis.

2.4 Statistical Analysis

In our analysis, we utilized NHANES-recommended weights to account for planned oversampling, ensuring the accuracy of our analysis. Continuous variables are presented as the means (standard errors), while categorical variables are expressed as percentages (standard errors).We employed multiple logistic regression models to assess the association between flavonoid intake and hypertension risk. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. These models aimed to evaluate whether there was a difference in the risk of hypertension for flavonoid intake (categorized as Q2 and Q3) compared to the lowest category (Q1). We constructed several adjustment models to consider potential confounding factors: Model 1: no adjustments; Model 2: adjusted for age, sex, race, marital status, poverty-income ratio, education, BMI, smoking, alcohol consumption, and physical activity; and Model 3: in addition to Model 2, further adjusted for diabetes, high cholesterol, total energy intake, protein intake, carbohydrate intake, sugar intake, and fat intake. Furthermore, we employed restricted cubic splines (RCS) to explore the nonlinear relationship between hypertension risk and total flavonoid and subcategory intake. We also conducted interaction models to assess interactions between flavonoid intake and other variables and performed stratified analyses to investigate whether flavonoid intake had different effects or associations in different hypertension subgroups. In this study, a p-value less than

0.05 was considered statistically significant. All analyses were conducted using R software (version 4.1.2), RStudio software, and the nhanesR package.

3. Results

Table 1 provides a summary of the baseline characteristics of the participants, encompassing demographic features, lifestyle factors, dietary intake components, and disease status. Our analysis yielded several key observations. Regarding sex, the prevalence of hypertension was significantly higher in males than in females ($P < 0.001$). There is a significant positive correlation between age and hypertension ($P < 0.0001$), indicating that older individuals are more likely to develop hypertension. Regarding ethnicity, the highest prevalence of hypertension was observed in the non-Hispanic black population, while the Mexican American population had a lower prevalence of hypertension ($P < 0.0001$). Furthermore, marital status, education level, BMI, alcohol consumption habits, smoking status, physical activity levels, diabetes status, and high cholesterol status were all significantly associated with hypertension ($P < 0.0001$).

Table 1
Characteristics of the Study Population Based on the Presence of Hypertension

Variable	Total	No hypertension	With hypertension	*P*-value
Sex				< 0.001
Female (%)	48.51(0.02)	50.38(0.98)	44.76(1.07)	
Male (%)	51.49(0.02)	49.62(0.98)	55.24(1.07)	
Age, year	45.28(0.40)	40.39(0.36)	55.04(0.42)	< 0.0001
Race (%)				< 0.0001
Mexican American	7.78(0.01)	8.96(0.98)	5.43(0.73)	
Non-Hispanic Black	9.78(0.01)	8.82(0.77)	11.70(1.15)	
Non-Hispanic White	70.74(0.04)	69.97(1.74)	72.28(2.16)	
other	6.80(0.01)	7.10(0.61)	6.20(0.74)	
Other Hispanic	4.90(0.00)	5.15(0.56)	4.39(0.60)	
Marital status (%)				< 0.0001
Divorced	9.97(0.01)	8.71(0.48)	12.49(0.68)	
Living with partner	8.26(0.01)	9.31(0.56)	6.15(0.62)	
Married	54.68(0.02)	51.37(1.29)	61.28(1.31)	
Never married	20.89(0.01)	26.45(1.22)	9.76(0.91)	
Separated	2.23(0.00)	2.14(0.19)	2.40(0.33)	
Widowed	3.98(0.00)	2.01(0.20)	7.93(0.66)	
Education (%)				0.03
Completed high school	24.51(0.01)	23.61(1.28)	26.32(1.10)	
Less than high school	12.79(0.01)	12.22(0.80)	13.92(0.87)	
More than high school	62.70(0.03)	64.17(1.56)	59.76(1.36)	
Poverty Income Ratio				0.2
Poverty	12.70(0.01)	13.06(0.69)	11.99(0.82)	
No poverty	87.30(0.03)	86.94(0.69)	88.01(0.82)	

Note: Values are presented as the mean (SE) for continuous variables and as n (%) for categorical variables, with SE representing the standard error. BMI (Body Mass Index): BMI was calculated as the ratio of weight (kg) to height (m^2). IFG (impaired fasting glucose): IFG indicates impaired fasting blood glucose levels. IGT (Impaired Glucose Tolerance): IGT denotes impaired glucose tolerance.

Variable	Total	No hypertension	With hypertension	*P*-value
BMI, kg/m^2(%)				< 0.0001
Normal (18.5 to < 25)	29.45(0.01)	35.58(1.31)	17.18(0.94)	
Obese (30 or greater)	36.01(0.02)	29.14(1.08)	49.74(1.48)	
Overweight (25 to < 30)	32.87(0.01)	33.04(1.09)	32.52(1.46)	
Underweight (< 18.5)	1.68(0.00)	2.24(0.30)	0.56(0.11)	
Drinking (%)				< 0.0001
former	9.09(0.01)	7.44(0.56)	12.40(0.91)	
heavy	24.66(0.01)	27.14(1.09)	19.70(1.19)	
mild	39.10(0.02)	37.56(1.46)	42.18(1.35)	
moderate	18.69(0.01)	19.90(0.82)	16.27(0.95)	
never	8.46(0.01)	7.97(0.60)	9.46(0.63)	
Smoking (%)				< 0.0001
former	24.16(0.01)	20.52(0.97)	31.45(1.10)	
never	55.44(0.02)	57.35(1.41)	51.62(1.17)	
now	20.39(0.01)	22.13(1.09)	16.93(1.03)	
Physical activity level (%)				< 0.0001
High Activity Level	92.60(0.03)	94.35(0.51)	89.10(0.73)	
Low Activity Level	2.33(0.00)	1.51(0.21)	3.97(0.45)	
Moderate Activity Level	5.07(0.00)	4.14(0.40)	6.93(0.67)	
Diabetes (%)				< 0.0001
Diabetes	10.86(0.00)	5.58(0.52)	21.41(0.94)	
IFG	4.79(0.00)	3.61(0.35)	7.13(0.61)	
IGT	2.68(0.00)	2.07(0.30)	3.90(0.47)	
No diabetes	81.67(0.03)	88.73(0.68)	67.56(1.33)	
Hyperlipidemia (%)				< 0.0001

Note: Values are presented as the mean (SE) for continuous variables and as n (%) for categorical variables, with SE representing the standard error. BMI (Body Mass Index): BMI was calculated as the ratio of weight (kg) to height (m²). IFG (impaired fasting glucose): IFG indicates impaired fasting blood glucose levels. IGT (Impaired Glucose Tolerance): IGT denotes impaired glucose tolerance.

Variable	Total	No hypertension	With hypertension	*P*-value
No hyperlipidemia	31.95(0.01)	38.24(1.16)	19.39(1.07)	
Hyperlipidemia	68.05(0.03)	61.76(1.16)	80.61(1.07)	
energy/day, kCal	2206.87(15.30)	2239.22(19.39)	2142.18(22.54)	0.002
protein/day, g/100 kCal	85.32(0.71)	86.19(0.81)	83.56(1.02)	0.03
carbohydrate/day, g/100 kCal	259.64(1.83)	265.14(2.65)	248.63(2.80)	< 0.001
sugars/day, g/100 kCal	115.59(1.44)	118.61(1.96)	109.55(2.08)	0.004
fat/day, g/100 kCal	85.49(0.78)	86.52(1.03)	83.43(0.94)	0.03
Isoflavones(mg/d)	2.19(0.20)	2.51(0.28)	1.56(0.22)	0.01
Anthocyanidins(mg/d)	14.63(0.97)	14.76(1.07)	14.37(1.04)	0.67
Flavan_3_ols(mg/d)	190.32(8.70)	179.99(8.85)	210.99(14.45)	0.04
Flavanones(mg/d)	12.37(0.44)	12.41(0.50)	12.30(0.74)	0.9
Flavones(mg/d)	1.02(0.05)	1.04(0.06)	0.97(0.03)	0.2
Flavonols(mg/d)	20.26(0.42)	19.94(0.48)	20.92(0.52)	0.08
All of flavonoids(mg/d)	240.80(9.11)	230.65(9.56)	261.10(14.46)	0.05

Note: Values are presented as the mean (SE) for continuous variables and as n (%) for categorical variables, with SE representing the standard error. BMI (Body Mass Index): BMI was calculated as the ratio of weight (kg) to height (m^2). IFG (impaired fasting glucose): IFG indicates impaired fasting blood glucose levels. IGT (Impaired Glucose Tolerance): IGT denotes impaired glucose tolerance.

3.1 Overall association between total flavonoid and six subclass intake and hypertension

We conducted a comprehensive multinomial logistic regression analysis with the aim of scrutinizing the interplay between flavonoid intake, encompassing all flavonoids, isoflavones, anthocyanins, flavan-3-ols, flavanones, flavones, and flavonols, and the occurrence of hypertension. To control for potential confounding factors, we considered multiple models (the original model, model 1, and model 2). In the case of total flavonoid intake, the original model indicated no statistically significant association between total flavonoid intake and hypertension, with Q2 (OR: 0.98, 95% CI: 0.80–1.20, p = 0.86) and Q3 (OR: 1.03, 95% CI: 0.89–1.19, p = 0.67). After adjustment in model 1, Q3 showed a significant negative correlation (OR: 0.82, 95% CI: 0.71–0.94, p = 0.01). This compelling association continued to manifest in Model 2 (OR: 0.80, 95% CI: 0.69–0.94, p = 0.01). Regarding isoflavone intake, across all models, Q3 exhibited a

pronounced protective association, with the original model showing the strongest effect (OR: 0.72, 95% CI: 0.62–0.84, p < 0.0001). Concerning anthocyanin intake, Q3 intake exhibited a significant trend of reducing hypertension risk in both model 1 (OR: 0.69, 95% CI: 0.57–0.84, p < 0.001) and model 2 (OR: 0.70, 95% CI: 0.57–0.86, p = 0.003). Regarding flavan-3-ol intake, in both Model 1 and Model 2, Q3 demonstrated a subtle yet statistically meaningful inverse correlation (OR: 0.84, 95% CI: 0.73–0.97, p = 0.02; OR: 0.84, 95% CI: 0.71–0.99, p = 0.04). However, for flavones, flavonols, and flavanols, we did not observe statistically significant differences related to hypertension.

Table 2: Association Between Tertiles of Flavonoid Intake Levels and Hypertension

	All of flavonoids					
	crude model		Model 1		Model 2	
character	95%CI	*P*	95%CI	*P*	95%CI	*P*
Q1	ref		ref		ref	
Q2	0.98(0.80,1.20)	0.86	0.89(0.74,1.09)	0.25	0.85(0.69,1.04)	0.10
Q3	1.03(0.89,1.19)	0.67	0.82(0.71,0.94)	0.01	0.80(0.69,0.94)	0.01
p for trend		0.65		0.01		0.01
	Isoflavones					
Q1	ref		ref		ref	
Q2	0.96(0.80,1.14)	0.62	0.81(0.66,1.00)	0.05	0.81(0.65,1.00)	0.05
Q3	0.72(0.62,0.84)	<0.0001	0.80(0.66,0.96)	0.02	0.80(0.65,0.98)	0.03
p for trend		<0.0001		0.01		0.03
	Anthocyanidins					
Q1	ref		ref		ref	
Q2	0.98(0.79,1.22)	0.87	0.80(0.65,0.99)	0.04	0.81(0.65,1.02)	0.07
Q3	0.93(0.79,1.11)	0.43	0.69(0.57,0.84)	<0.001	0.70(0.57,0.86)	0.003
p for trend		0.42		<0.001		0.003
	Flavan_3_ols					
Q1	ref		ref		ref	
Q2	0.91(0.78,1.06)	0.23	0.83(0.68,1.00)	0.05	0.80(0.65,0.98)	0.03
Q3	1.05(0.91,1.20)	0.51	0.84(0.73,0.97)	0.02	0.84(0.71,0.99)	0.04
p for trend		0.47		0.03		0.04
	Flavanones					
Q1	ref		ref		ref	
Q2	1.00(0.85,1.18)	0.98	0.94(0.78,1.13)	0.49	0.94(0.78,1.14)	0.52
Q3	1.02(0.88,1.19)	0.75	0.89(0.76,1.04)	0.12	0.87(0.73,1.05)	0.13
p for trend		0.75		0.12		0.13
	Flavones					
Q1	ref		ref		ref	
Q2	1.00(0.86,1.17)	0.97	0.93(0.78,1.10)	0.36	0.94(0.79,1.12)	0.47
Q3	0.94(0.80,1.11)	0.46	0.87(0.73,1.04)	0.12	0.87(0.72,1.06)	0.15
p for trend		0.45		0.12		0.14
	Flavonols					

Q1	ref		ref		ref	
Q2	0.97(0.82,1.15)	0.71	0.91(0.75,1.11)	0.33	0.90(0.73,1.12)	0.32
Q3	1.08(0.92,1.27)	0.36	0.98(0.80,1.19)	0.80	0.95(0.77,1.17)	0.58
p for trend		0.33		0.84		0.6

Note: Data are presented in the form of odds ratios (ORs) and 95% confidence intervals (CIs). ORs are derived from average marginal predictions in logistic regression models. Crude model: Unadjusted preliminary model; Model 1: Adjusted for age, gender, race, marital status, poverty status, education level, BMI (kg/m²), alcohol use, smoking, and total physical activity metabolic equivalent; Model 2: In addition to Model 1 adjustments, further adjusted for diabetes, hyperlipidemia, energy intake, protein intake, carbohydrate intake, sugar intake, and fat intake. *P*-values are based on orthogonal polynomial contrasts calculated from adjusted prevalence estimates of hypertension across flavonoid (total or subcategories) intake categories.

3.2 Stratified analysis

In our detailed stratified analysis of the association between flavonoid intake and hypertension across various demographic and clinical variables, we obtained several noteworthy observations (Table 3). Stratifications based on age, sex, race, marital status, education, BMI, smoking, alcohol consumption, and physical activity did not reveal any significant trends between total flavonoid intake and hypertension risk. However, individuals with impaired glucose tolerance (IGT) exhibited a significantly increased risk when at Q3 levels of total flavonoid intake (OR: 4.551; 95% CI: 1.705–12.145). Notably, in the absence of hyperlipidemia, an increase in flavonoid intake was associated with a significant reduction in hypertension risk (Q3: OR: 0.567; 95% CI: 0.385–0.833). It is worth highlighting that this covariate interacted with total flavonoid intake in relation to hypertension risk.

Table 3: Weighted Stratified and Interaction Analysis of the Association between Total Flavonoid Intake and Hypertension

Covariates	Q1	Q2	Q3	p for trend	*p* for interaction
Age					0.652
<60	ref	0.932(0.708,1.227)	0.975(0.823,1.156)	0.762	
>=60	ref	0.862(0.601,1.237)	0.808(0.573,1.141)	0.239	
Sex					0.586
Male	ref	0.949(0.699,1.288)	0.884(0.706,1.107)	0.254	
Female	ref	0.919(0.725,1.166)	1.011(0.775,1.318)	0.898	
Ethnicity					0.443
Mexican American	ref	0.610(0.318, 1.170)	0.734(0.418, 1.289)	0.215	
Non-Hispanic Black	ref	1.049(0.697,1.578)	1.017(0.704,1.469)	0.902	
Other Hispanic	ref	1.155(0.590,2.261)	0.997(0.448,2.219)	0.991	
other	ref	0.729(0.384, 1.382)	0.575(0.307, 1.075)	0.07	
Non-Hispanic White	ref	1.007(0.756,1.340)	1.006(0.832,1.218)	0.948	
Marital status					0.818
Married	ref	0.922(0.697,1.222)	0.958(0.779,1.178)	0.72	
Never married	ref	1.309(0.780, 2.197)	0.893(0.571, 1.399)	0.668	
Widowed	ref	0.661(0.318, 1.371)	0.598(0.271, 1.319)	0.193	
Divorced	ref	0.950(0.610, 1.481)	0.996(0.607, 1.633)	0.995	
Separated	ref	0.426(0.181, 1.003)	1.043(0.457, 2.383)	0.964	
Living with partner	ref	0.908(0.436, 1.890)	0.903(0.509, 1.600)	0.707	
Marital status					0.399
Less than high school	ref	0.706(0.478,1.043)	0.852(0.586,1.238)	0.302	
Completed high school	ref	0.997(0.639,1.555)	1.106(0.781,1.567)	0.544	
More than high school	ref	0.983(0.717,1.350)	0.913(0.708,1.177)	0.423	
BMI (kg/m2)					0.379
Overweight (25 to <30)	ref	0.969(0.684,1.372)	1.205(0.840,1.727)	0.255	
Normal (18.5 to <25)	ref	0.859(0.548, 1.345)	0.749(0.502, 1.119)	0.144	
Obese (30 or greater)	ref	0.953(0.704,1.290)	0.859(0.655,1.128)	0.25	
Underweight (<18.5)	ref	0.696(0.108,4.503)	0.563(0.054,5.837)	0.607	

Drinking					0.179
heavy	ref	1.057(0.666, 1.680)	0.760(0.474, 1.220)	0.261	
never	ref	0.733(0.423,1.268)	1.449(0.800,2.625)	0.163	
mild	ref	1.069(0.801,1.428)	1.019(0.746,1.392)	0.948	
moderate	ref	0.810(0.550,1.191)	0.746(0.478,1.162)	0.183	
former	ref	0.876(0.492,1.561)	1.058(0.671,1.667)	0.839	
Smoking					0.224
never	ref	0.949(0.708,1.273)	0.934(0.729,1.198)	0.574	
former	ref	0.769(0.550,1.075)	0.938(0.652,1.349)	0.813	
now	ref	1.336(0.823,2.169)	0.964(0.678,1.370)	0.969	
Physical activity					0.815
High Activity Level	ref	0.904(0.739,1.106)	0.912(0.775,1.074)	0.266	
Moderate Activity Level	ref	1.162(0.419, 3.224)	1.364(0.598, 3.109)	0.429	
Low Activity Level	ref	1.001(0.282, 3.549)	1.128(0.482, 2.637)	0.78	
Diabetes					0.066
IFG	ref	0.495(0.263, 0.931)	0.554(0.252, 1.217)	0.13	
no	ref	0.941(0.727,1.216)	0.926(0.781,1.098)	0.354	
DM	ref	1.090(0.683, 1.741)	0.901(0.580, 1.399)	0.603	
IGT	ref	1.090(0.419, 2.836)	4.551(1.705,12.145)	0.002	
Hyperlipidemia					0.014
no	ref	0.759(0.452,1.275)	0.567(0.385,0.833)	0.007	
yes	ref	1.005(0.810,1.247)	1.088(0.915,1.294)	0.299	

3.3 Overall dose-response relationship between total flavonoid intake and hypertension

The outcomes of the RCS analysis, depicted in Fig. 1, unveil an absence of significant nonlinear associations between isoflavones, flavanones, and flavones with hypertension in Model 2. However, within Model 2, we identified substantial nonlinear relationships between anthocyanins, flavan-3-ols, flavonols, and total flavonoids and hypertension, manifesting a distinct U-shaped pattern (nonlinear p-values of 7E-04, 0.02, 2E-04, and 0, respectively). It is noteworthy that the minimum intake values were 48.55 mg/day for anthocyanins, 368.13 mg/day for flavan-3-ols, 13.53 mg/3 days for flavonols, and 407.63 mg/day for total flavonoids. These findings underscore the intricate and nonlinear connections between these specific flavonoid subclasses in the diet and the development of hypertension.

4. Discussion

To our knowledge, this study represents the first instance of utilizing a nationally representative sample to investigate the relationship between dietary flavonoid intake and hypertension in American adults. Hypertension, as an overarching global public health concern, has garnered extensive attention, while flavonoids, as a class of natural compounds, have exhibited latent benefits in ameliorating a spectrum of chronic maladies[13–15]. Our study aims to address gaps in previous research by exploring the potential role of flavonoids in preventing and managing hypertension. Additionally, we take into account lifestyle factors such as smoking, alcohol consumption, and physical activity, all of which have exerted a substantial impact on the prevalence of hypertension [16–18].

In the pursuit of a more comprehensive exploration into the interplay between flavonoid ingestion and hypertension, we have fashioned three distinct statistical models, each judiciously incorporating unique covariates to ensure the effective control of latent confounding factors. While each model serves a slightly different purpose, our analysis indicates that the results from Model 3 are considered the most representative due to its comprehensive control of covariates. Our research findings, in no uncertain terms, underscore the latent advantages of flavonoids in mitigating the peril of hypertension, with particular emphasis on the effulgent virtues of isoflavones and anthocyanins. This discovery suggests that increasing dietary flavonoid intake may have potential benefits in preventing hypertension. However, we also observed a potential nonlinear relationship between the intake levels of anthocyanins, flavan-3-ols, flavonols, and all flavonoid classes and the incidence of hypertension. This intimates that the volume of flavonoid consumption does not subscribe to a facile 'more is merrier' paradigm, but rather beckons for judicious modulation within the precincts of moderation. Of no less importance, our subgroup analyses reveal conspicuous correlations between flavonoids and hypertension in cohorts afflicted with IGT and those devoid of hyperlipidemia. This tantalizingly suggests that the liaison between flavonoids and hypertension may unfold its variegated nuances contingent upon the kaleidoscope of individual attributes, thereby imparting salience to the contours of personalized health stewardship and preventive strategies.

In the nascent stages of exploration, an initial revelation unveiled the latent affirmative influence of flavonoids on blood pressure, particularly their capacity to reduce it. A convergence of diverse inquiries has lent credence to the notion that integrating anthocyanins into one's dietary repertoire serves as a propitious ally in the preservation of vascular elasticity and the maintenance of normotensive hemodynamics, particularly among individuals in the prehypertensive stratum[19, 20]. Furthermore, scholarly attention has elegantly gravitated toward dietary isoflavones. A meta-analysis focused on the influence of soy on postmenopausal women's blood pressure elucidated a prominent reduction in blood pressure associated with daily soy protein consumption exceeding the threshold of 25 grams. This effect is intricately linked to the presence of isoflavonoids within the embrace of soy protein[21]. Cross-sectional research data not only illuminate the positive correlations between elevated polyphenol intake levels, notably flavanones, and dietary patterns predominantly centered around plant-based nutrition but also

harmoniously resonate with salubrious biomarkers tethered to cardiac metabolic risks[22]. It is of paramount importance to underscore that the protective mantle of flavonoids extends beyond merely ameliorating blood pressure levels. They exert a salutary influence on a spectrum of risk factors contributing to hypertension, including obesity, metabolic syndrome, and diabetes[23–27]. These empirical revelations crystallize flavonoids as promising nutritional agents, wielding a multifaceted and beneficial impact on cardiovascular well-being, thereby conferring substantive clinical and nutritional significance.

Our research findings have unveiled nuanced insights into the intricate dose-response relationship between flavonoid intake and the occurrence of hypertension. This discovery substantially enriches our understanding.

In our inquiry into the broader dose-response correlation between flavonoid consumption and hypertension, we have unearthed profound insights. The analysis elucidated a nonlinear interrelation between total flavonoid intake and the risk of hypertension. As flavonoid intake escalates, there emerges a discernible trend of diminishing hypertension risk up to a certain threshold. Beyond this inflection point, the protective effect plateaus, implying that a higher level of flavonoid intake does not confer additional benefits in terms of hypertension prevention. This nonlinear relationship accentuates the significance of optimizing flavonoid consumption in the management of hypertension risk. The molecular mechanisms underpinning the association between flavonoids and hypertension continue to be a subject of ongoing investigation. Flavonoids, secondary metabolites in various plants, exhibit structural diversity and manifest a plethora of biological activities, including antioxidative, anti-inflammatory, and antithrombotic properties[28, 29].In the context of hypertension, these bioactivities could directly influence vascular function and blood pressure regulation. Furthermore, vascular endothelial cells play a pivotal role in maintaining normal blood pressure and vascular function. Some studies suggest that flavonoids can enhance endothelial function by augmenting the synthesis of nitric oxide (NO), leading to vasodilation[30, 31].NO is a potent vasodilator that reduces vascular tension, aiding in blood pressure reduction[32]. However, the antioxidant properties of flavonoids contribute to mitigating oxidative stress-induced damage to endothelial cells, further preserving vascular health[13].The sympathetic nervous system plays a crucial role in blood pressure regulation, and flavonoids may also influence blood pressure by modulating this system. Research indicates that flavonoids can attenuate the activity of the sympathetic nervous system, reducing cardiac contractility and peripheral vascular resistance. This effect may be achieved through the modulation of neurotransmitter release or receptor signal transduction within the sympathetic nervous system[33, 34].Chronic inflammation plays a pivotal role in the onset and progression of hypertension[35].Flavonoids possess anti-inflammatory properties, and are capable of mitigating inflammatory responses by inhibiting the production of inflammatory mediators and regulating immune cell activity. This anti-inflammatory action may contribute to reducing the risk of hypertension, particularly in individuals with low-grade chronic inflammation[36, 37].Flavonoids may influence blood pressure regulation by intervening in a myriad of molecular signaling networks. This encompasses the regulation of key molecules in signaling pathways, such as cell signaling protein kinases and nuclear factor-kappa B (NF-κB). These molecules play crucial roles in biological processes such as inflammation,

oxidative stress, and cell proliferation, all of which are intricately associated with the occurrence and progression of hypertension[37–39].Further research endeavors promise to provide a more comprehensive comprehension of the relationship between flavonoids and hypertension, thereby furnishing additional strategies and pharmaceutical targets for the future prevention and treatment of hypertension. Exploration in this domain holds the potential to kindle fresh hope and opportunities for ameliorating the health status of hypertension sufferers worldwide.

Our study possesses certain strengths, as it represents an initial exploration into the correlation between flavonoid intake and hypertension within the American population aged 20 and above. This study took into consideration potential confounding variables and established the association between flavonoid intake and hypertension risk. Nevertheless, our study has limitations, as it is a cross-sectional investigation, and our findings warrant validation through clinical and longitudinal cohort studies. Due to the complexity of data collection and matching, it remains uncertain whether flavonoids and hypertension might be related through other interacting pathways. Third, it is worth noting that all participants in this study were Americans. Therefore, the observed effects of flavonoid intake on hypertension in this study may not be generalizable to Asian populations or other demographic groups.

5. Conclusions

In this study, we have, for the first time, systematically explored the relationship between dietary flavonoid intake and hypertension among American adults, utilizing a nationally representative sample. Our findings unequivocally illuminate a significant inverse association between dietary intake of total flavonoids, anthocyanins, isoflavones, and flavan-3-ols, and the risk of hypertension. This discovery underscores the potential beneficial role of flavonoid compounds in the prevention and management of hypertension. Notably, we also observed a nonlinear relationship between flavonoid intake levels and the incidence of hypertension, suggesting that a moderate intake of flavonoids may be more conducive to health. This finding aligns with the principles of dietary equilibrium, emphasizing that, in practice, a moderate and balanced intake of flavonoids may yield a more favorable impact on the prevention and management of hypertension. In summary, our study offers a novel perspective on the interplay between flavonoids and hypertension, underscoring the latent significance of dietary factors in safeguarding cardiovascular health. Further research in this domain holds promise for enhancing the well-being of hypertensive individuals worldwide, while providing robust support for future prevention and treatment strategies.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

Y.N. conceptualized and designed the study, conducted the statistical analysis and drafted the initial manuscript. A.A. contributed to data collection. L.F. reviewed and revised the paper, and assisted in writing the final version of the manuscript.

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Figures

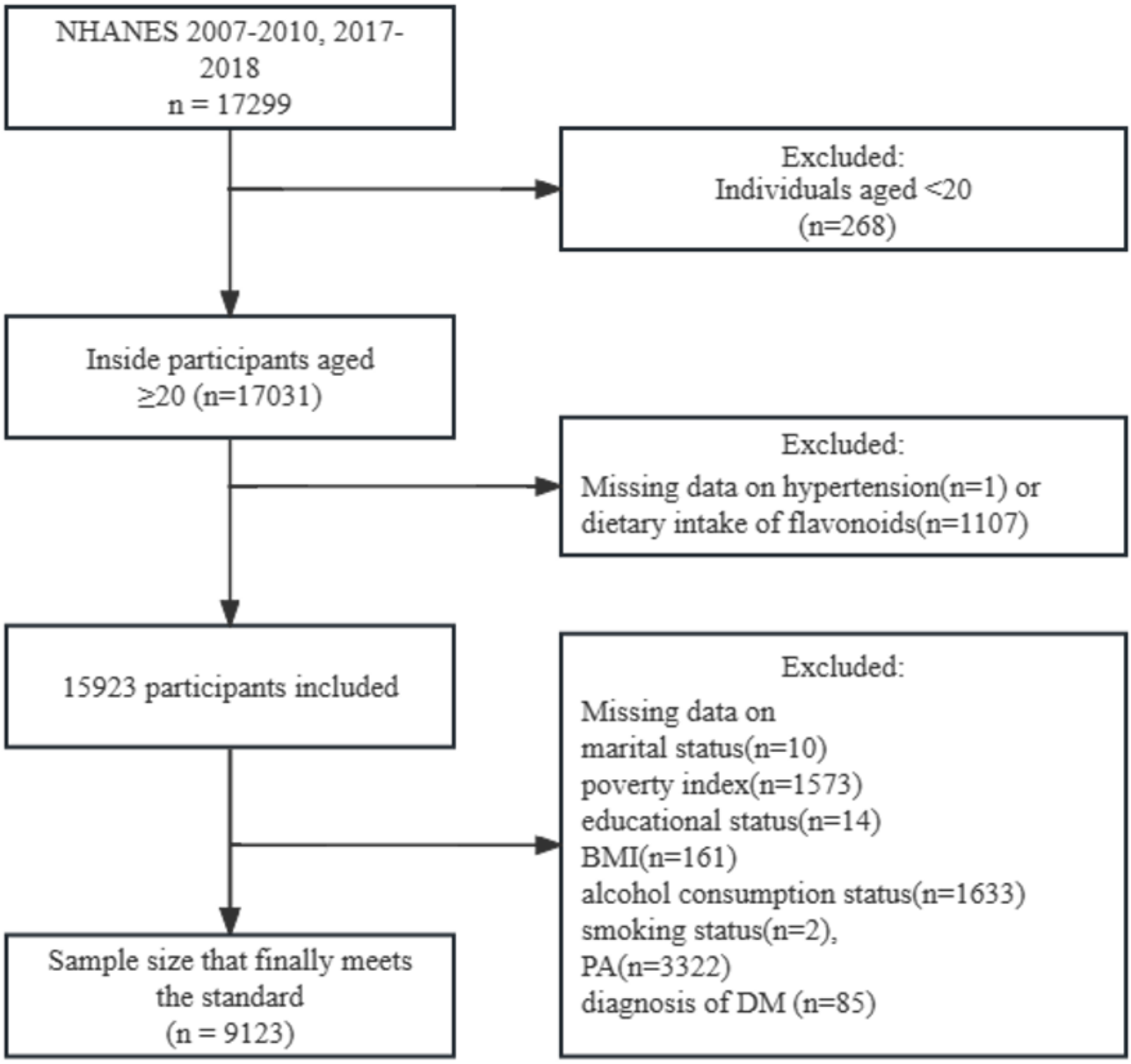

Figure 1

Flowchart of Study Population Selection

Note: BMI: body mass index; PA: physical activity, and DM refers to diabetes.

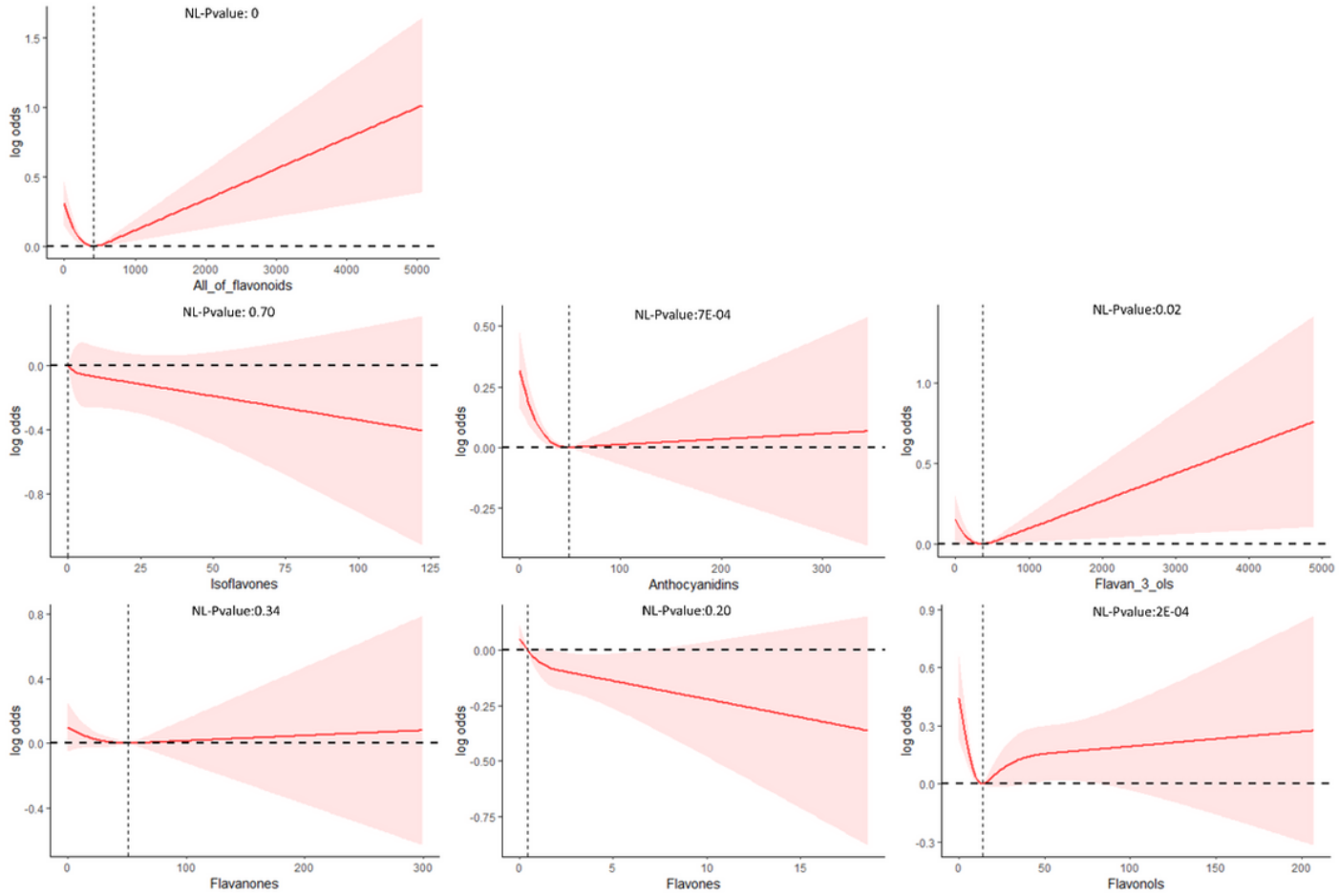

Figure 2

Dose-Response Correlation between Flavonoid Intake and Hypertension based on Model 2

Note: A *P*-value of < 0.05 for nonlinearity is considered statistically significant. We employed restricted cubic splines to explore the nonlinear trends between flavonoid intake and hypertension risk. The data in the figure are based on model 2 and are represented on a logarithmic scale (odds ratio on the y-axis) against flavonoid intake levels (mg/day).