



Association Between Dietary Fiber Intake and Cardiometabolic Risk Factors in Adolescents in the United States

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Objective To determine the association between dietary fiber intake and markers of cardiometabolic risk in adolescents, with blood pressure (BP) as the primary outcome of interest and secondary outcome measures including other established markers of childhood cardiometabolic risk, such as obesity, lipids, albuminuria, estimated glomerular filtration rate (eGFR), and uric acid.

Study design Dietary fiber intake was assessed by two 24-hour dietary recall interviews, which were averaged and corrected for body weight. Logistic and linear regression models were used to analyze the cross-sectional association between dietary fiber and cardiometabolic markers. Participants aged 13-17 years in the National Health and Nutritional Examination Survey 2009-2018 who completed a 24-hour dietary recall survey were included. Exclusion criteria included pregnancy, small for gestational age status, and history of major health comorbidities.

Results In fully adjusted regression models, low dietary fiber intake was significantly associated with greater diastolic blood pressure ($\beta = -13.29$; 95% CI, -20.66 to -5.93), body mass index z-score ($\beta = -0.91$; 95% CI, -1.47 to -0.34), and uric acid ($\beta = -0.80$; 95% CI, -1.44 to -0.16).

Conclusions The association found between low dietary fiber intake and poor childhood cardiometabolic risk markers indicate a need for prospective studies using fiber intake as a dietary intervention in childhood and as a tool for prevention of many chronic conditions. (*J Pediatr* 2023;262:113616).

Dietary fibers include indigestible portions of plant products from such foods as whole grains, fruits, vegetables, and legumes. These fibers are known to interact directly with gut microbiota, which in turn produce key metabolites that impact the health of both the gut microbiome and the host. These metabolites impact the normal structure and production of intestinal mucous in the gut, which is important for keeping the bacteria in the gastrointestinal system separated from the epithelial layer of the intestinal wall.¹ A diet low in dietary fiber can lead to altered gut microbiota, which can deteriorate the mucous layer, creating a susceptibility to infections and the development of chronic inflammatory diseases.¹ Similarly, higher levels of fiber intake have been shown to have protective as well as disease-reversal effects in adult populations.^{2,3}

In recent years, dietary fiber intake has been studied in adults using the National Health and Nutrition Examination Survey (NHANES), a collection of studies and data designed to represent the health of the US population. These adult studies have shown that dietary fiber intake is associated with a decreased risk of hypertension,⁴ as well as decreased all-cause and cardiovascular mortality in older adults with hypertension.⁵ However, the effect of dietary fiber consumption and cardiometabolic health in pediatric populations has not been extensively studied. Connecting the level of dietary fiber consumption in childhood and the risk of future chronic cardiometabolic disease could be a gateway to new prevention strategies.

The aim of the present study was to determine the association between dietary fiber intake and markers of childhood cardiometabolic risk, such as blood pressure (BP), lipid levels, and proteinuria. It was hypothesized that lower dietary fiber intake will be associated with higher BP, obesity, dyslipidemia, albuminuria, and glomerular hyperfiltration.

BMI	Body mass index
BP	Blood pressure
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic blood pressure
eGFR	Estimated glomerular filtration rate
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
MEC	Mobile examination clinic
NHANES	National Health and Nutritional Examination Survey
SBP	Systolic blood pressure

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<https://doi.org/10.1016/j.jpeds.2023.113616>

Methods

This study used the NHANES, a program of studies from the Centers for Disease Control and Prevention designed to create a representative snapshot of the health of both adults and children in the US. Participants first complete a series of interviews in their homes to gather information, such as medical and social histories. This is followed by a free health examination in the NHANES mobile examination clinic (MEC), which includes laboratory data collection.⁶ The data collected from NHANES are publicly available for use and can be downloaded from the NHANES website.⁷ This study was approved as exempt by the Northwell Health Institutional Review Board.

This study examined participants aged 13-17 years enrolled in NHANES from 2009 to 2018 who completed a 24-hour dietary recall, including dietary fiber from total nutrient intake. Exclusion criteria included pregnancy, small for gestational age status, and history of major health comorbidities. This resulted in a final cohort of 3827 participants for analysis, as demonstrated in **Figure 1**.

The independent variable of interest was dietary fiber intake, assessed by two 24-hour dietary recall interviews. The initial dietary interview was conducted in the MEC, and the follow-up interview was conducted by telephone 3-10 days later. The NHANES calculated fiber intake from food and beverages according to the US Department of Agriculture Food and Nutrient Database for Dietary Studies.⁸ The values from the 2 days were averaged and adjusted for body weight. Dietary fiber intake was examined as a continuous variable, as well as divided into quartiles.

The primary outcome of interest was BP. According to the NHANES procedures, systolic BP (SBP) and diastolic BP (DBP) values were measured in the MEC via auscultation.⁸ Up to 4 measurements were taken and the SBP and DBP

values were averaged for analysis. Hypertensive BP was defined as SBP >130 mmHg or DBP >80 mmHg, and elevated BP was defined as SBP 120-129 mmHg and DBP <80 mmHg.⁹

Secondary outcome measures included other established markers of childhood cardiometabolic risk, including obesity, lipids, albuminuria, estimated glomerular filtration rate (eGFR), and uric acid. Body mass index (BMI) and BMI z-scores were calculated.¹⁰ Obesity was defined as a BMI z-score ≥ 2.0 .¹¹ Lipid laboratory data were acquired after fasting and included cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL).⁶ Dyslipidemia was defined as triglycerides ≥ 130 mg/dL, HDL cholesterol <40 mg/dL, or LDL cholesterol ≥ 160 mg/dL.¹² Urine albumin:creatinine ratio was used to determine the presence of microalbuminuria, which was defined as urine albumin:creatinine >30 mg/g.¹³ Estimated glomerular filtration rate (eGFR) was calculated using the new Schwartz formula. Hyperfiltration was defined as eGFR >140 mL/min per 1.73 m².¹⁴

Potential confounding variables for dietary fiber included age, sex, self-identified race, BMI z-score, and food insecurity. Food insecurity was defined as low or very low household food security according to the NHANES food security questionnaire. Other confounders accounted for in the regression models included total daily caloric intake, family income:poverty level ratio, passive smoke exposure, and Dietary Approaches to Stop Hypertension (DASH) diet score. Total daily caloric intake was an average of two 24-hour dietary recall interviews with the participants. Family income:poverty ratio was defined as the family's income divided by the poverty guidelines specified by the Department of Health and Human Services for that survey year. Passive smoke exposure was defined as a participant reporting at least 1 person in their household smoking inside the home according to the secondhand smoke exposure questionnaire. The DASH

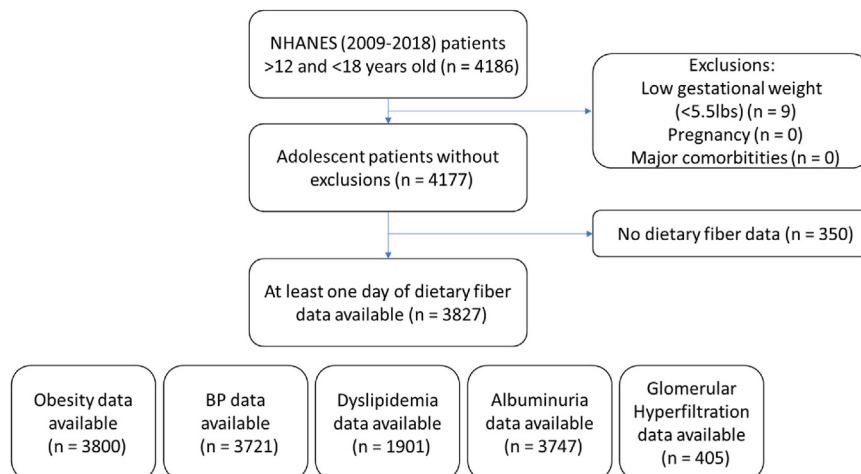


Figure 1. Flowchart of cohort selection, NHANES 2009-2018.

score took into account 9 nutrient targets, modeled after the methods described by Mellen et al.¹⁵

Data were analyzed using complex samples adjusted statistical tests in SPSS version 28 (IBM). Demographic weights were adjusted for merged analysis of 5 survey cycles. Categorical variables were described using percentage and SE, and continuous variables were described using mean and SE. *P* values <.05 were considered statistically significant. Clinical and demographic variables were entered into a linear regression model using a backward selection process to find the best fit for a model that predicted dietary fiber intake. Relationships between dietary fiber and categorical cardiometabolic variables were assessed using ORs obtained from crude and adjusted logistic regression models. Relationships between dietary fiber intake and continuous cardiometabolic variables were measured using β values obtained from crude and adjusted linear regression models. Regression models were adjusted for age and sex in model 1, and model 2 included the addition of race, total daily caloric intake, family income:poverty level ratio, food insecurity status, passive smoke exposure, and BMI z-score along with the variables of model 1. Model 3 added the DASH score in addition to the variables of model 2. However, BMI z-score was not included as a confounder in regressions for predicting obesity. Variables included in the models were chosen a priori based on a literature review.

Results

Demographic data for the study population are displayed in **Table I**. The mean age of the study participants at the time of testing was 15.0 (SE 0.025) years, with a fairly symmetric sex distribution of 50.4% male and 49.6% female. The population self-identified as 14.5% Mexican-American, 6.6% other Hispanic, 14.1% non-Hispanic Black, 55.3% non-Hispanic White, and 9.3% other races. Mean values for cardiometabolic variables of interest are also reported in **Table I**.

Table II presents demographic predictors for dietary fiber intake among the participant population. Significant associations among age, sex, BMI z-score, food insecurity, race, and dietary fiber intake were found ($R^2 = 0.247$; $P < .001$). Greater age at enrollment, female sex, higher BMI z-score, and food insecurity were all associated with lower dietary fiber intake. Non-Hispanic Black participants had significantly lower dietary fiber intake compared with non-Hispanic White participants, whereas the other race categories had significantly greater dietary fiber intake compared with non-Hispanic Whites.

Table III displays the associations found between dietary fiber intake and cardiometabolic risk markers using linear regression analysis. In model 1, lower dietary fiber was significantly associated with higher BMI z-score, higher SBP, higher DBP, higher total cholesterol, higher triglycerides, higher LDL cholesterol, lower HDL cholesterol, and higher uric acid. In model 2, lower dietary

Table I. Demographic characteristics, NHANES 2009-2018 (N = 3827)

Characteristics	Value	SE
Dietary fiber, g/kg/day, mean	0.235	0.003
Age at enrollment, y, mean	15.01	0.025
Male sex, %	50.4	1.1
BMI z-score, mean	0.703	0.025
Ratio of family income to poverty line, mean	2.621	0.063
Passive smoke exposure, %	18.2	1.5
Food insecurity, %	21.6	1.2
Total daily caloric intake, kcal/kg/day, mean	45.1	2.77
Race/ethnicity, %		
Mexican American	14.5	1.4
Other Hispanic	6.6	0.6
Non-Hispanic Black	14.1	1.2
Non-Hispanic White	55.3	2.1
Other race	9.3	0.7
SBP, mmHg, mean	108.31	0.223
DBP, mmHg, mean	59.73	0.444
Hypertensive blood pressure, %	3.2	0.3
Elevated blood pressure, %	7.9	0.6
Total cholesterol, mg/dL, mean	153.97	0.706
Triglycerides, mg/dL, mean	75.74	1.743
HDL, mg/dL, mean	51.48	0.334
LDL, mg/dL, mean	85.66	0.743
Dyslipidemia, %	31.6	1.4
Urine albumin:creatinine, mean	28.017	2.601
Microalbuminuria, %	13.3	0.8
eGFR, mL/min/1.73 m ² , mean	88.092	0.890
Uric acid, mg/dL, mean	5.057	0.027

Obesity defined as a BMI z-score ≥ 2.0 . Hypertension defined as SBP/DBP >130/80 mmHg. Elevated BP defined as SBP/DBP 120-129/<80 mmHg. Dyslipidemia defined as meeting any one of the following criteria: HDL cholesterol <40 mg/dL, LDL cholesterol ≥ 130 mg/dL, or triglycerides ≥ 130 mg/dL. Albuminuria defined as an albumin:creatinine ratio >30 mg/g.

fiber was significantly associated with higher BMI z-score, higher SBP, higher DBP, lower eGFR, and higher uric acid. In model 3, lower dietary fiber was found to be significantly associated with higher BMI z-score, higher diastolic BP, lower eGFR, and higher uric acid. No statistically significant associations were found between dietary fiber and urine albumin:creatinine. **Figure 2** displays the relationship between dietary fiber quartile and BP measurements. BP was significantly higher in the higher dietary fiber quartiles.

Table IV displays the associations found between dietary fiber intake and categorical cardiometabolic risk markers

Table II. Model predicting dietary fiber intake, $R^2 = 0.247$, NHANES 2009-2018

	β (95% CI), N = 3827	<i>P</i> value
Age at enrollment, y	-0.011 (-0.014 to -0.008)	<.001
Female sex (reference male)	-0.018 (-0.027 to -0.010)	<.001
BMI z-score	-0.056 (-0.061 to -0.050)	<.001
Food insecurity	-0.020 (-0.029 to -0.010)	<.001
Race/ethnicity		<.001
Non-Hispanic White	Reference	
Mexican American	0.043 (0.029 to 0.056)	
Other Hispanic	0.031 (0.009 to 0.053)	
Non-Hispanic Black	-0.018 (-0.028 to -0.008)	
Other race	0.018 (0.001 to 0.038)	

Table III. Relationship between dietary fiber and continuous cardiometabolic markers, NHANES 2009-2018

Markers	β (95% CI), N = 3827	P value
BMI z-score*		
Crude	-3.74 (-4.08 to -3.40)	<.001
Model 1	-3.82 (-4.17 to -3.47)	<.001
Model 2	-1.20 (-1.72 to -0.68)	<.001
Model 3	-0.91 (-1.47 to -0.34)	.002
SBP, mmHg		
Crude	-13.35 (-15.93 to -10.76)	<.001
Model 1	-13.71 (-16.32 to -11.10)	<.001
Model 2	-5.55 (-10.85 to -0.25)	.04
Model 3	-3.68 (-9.94 to 2.59)	.246
DBP, mmHg		
Crude	-10.40 (-14.52 to -6.29)	<.001
Model 1	-8.36 (-12.66 to -4.05)	<.001
Model 2	-13.43 (-20.67 to -6.20)	<.001
Model 3	-13.29 (-20.66 to -5.93)	<.001
Cholesterol, mg/dL		
Crude	-15.07 (-23.94 to -6.20)	.001
Model 1	-11.18 (-19.91 to -2.46)	.013
Model 2	-11.95 (-34.84 to 10.94)	.302
Model 3	-12.94 (-36.45 to 10.58)	.277
Triglycerides, mg/dL		
Crude	-24.36 (-45.20 to -3.52)	.023
Model 1	-25.49 (-47.27 to -3.70)	.022
Model 2	9.04 (-36.69 to 54.67)	.693
Model 3	-17.50 (-58.05 to 23.05)	.393
LDL, mg/dL		
Crude	-19.76 (-31.22 to -8.30)	<.001
Model 1	-17.93 (-29.05 to -6.81)	.002
Model 2	-4.78 (-30.34 to 20.78)	.71
Model 3	1.39 (-24.32 to 27.10)	.914
HDL, mg/dL		
Crude	12.57 (8.30 to 16.90)	<.001
Model 1	14.26 (10.07 to 18.44)	<.001
Model 2	0.68 (-9.03 to 10.38)	.89
Model 3	-0.631 (-11.27 to 10.01)	.906
Urine albumin:creatinine		
Crude	45.30 (-26.73 to -117.33)	.214
Model 1	43.43 (-27.58 to -114.44)	.227
Model 2	-57.62 (-144.50 to 29.25)	.19
Model 3	-60.86 (-157.41 to 35.68)	.213
eGFR, mL/min per 1.73 m ²		
Crude	10.45 (-2.12 to 23.02)	.102
Model 1	8.94 (-3.94 to 21.81)	.171
Model 2	37.47 (10.19 to 64.74)	.008
Model 3	42.54 (14.09 to 70.99)	.004
Uric Acid		
Crude	-1.70 (-2.07 to -1.32)	<.001
Model 1	-2.13 (-2.49 to -1.77)	<.001
Model 2	-0.83 (-1.44 to -0.22)	.008
Model 3	-0.80 (-1.44 to -0.16)	.014

Model 1 adjusted for age and sex. Model 2 adjusted for age, sex, race, BMI z-score, total daily caloric intake, family income:poverty ratio, food insecurity, and passive smoke exposure. Model 3 adjusted for age, sex, race, BMI z-score, total daily caloric intake, family income:poverty ratio, food insecurity, passive smoke exposure, and DASH score.

*Variable not adjusted for BMI z-score.

using logistic regression analysis. In model 1, lower dietary fiber was significantly associated with higher prevalence of obesity, hypertensive BP, elevated BP, dyslipidemia, and microalbuminuria. In model 2, lower dietary fiber was significantly associated with higher prevalence of obesity and lower prevalence of glomerular hyperfiltration. In model 3, lower dietary fiber was significantly associated with lower prevalence of glomerular hyperfiltration only.

Discussion

This study found a significant association between lower dietary fiber intake and higher BP in the adolescent cohort studied. Uncontrolled BP is a risk factor for coronary artery disease, stroke, peripheral artery disease, and chronic kidney disease. A systematic review of dietary patterns in adolescents found that diets low in fiber were associated with increased BP and body adiposity.¹⁶ Although the trend remained the same, the significance of the association between lower dietary fiber and SBP was lost when accounting for DASH diet accordance in model 3. This demonstrates that although fiber intake accounts for a certain degree of BP management, synergistic effects with the other components of the DASH diet, such as sodium, potassium, and magnesium, may have a greater impact. There is evidence demonstrating that a lower ratio of sodium intake to potassium intake is associated with decreased BP.¹⁷ Thus, several parts of the DASH diet target lowering BP through different nutrients. Although the mechanism by which dietary fiber affects BP is still being elucidated, there is a body of evidence associating increased dietary fiber intake with BP-lowering effects.^{2,4,5,18-20} It has been suggested that the effect on BP could be mediated through the beneficial cardiovascular effects of long-term fiber consumption, and that particular components of fiber may explain its antihypertensive effects.²¹ Further investigation in the fermentation of specific types of dietary fiber by the gut microbiome may help elucidate the beneficial effects of dietary fiber on BP.

Increased BMI z-score and increased prevalence of obesity were found to be significantly associated with decreased dietary fiber intake among the adolescents in this study. Obesity is influenced by many factors, most prominently lifestyle and diet. Obesity is also associated with decreased microbial diversity in the gut, and thus may be connected to decreased dietary fiber intake.^{1,22-25} The connection of dietary fiber, the gut microbiome, and human health markers is an active area of study.²⁶⁻²⁸ A study including 120 877 U.S. men and women found that dietary fiber intake was inversely correlated with long-term weight gain.²⁹ In addition, a 2017 study found that higher fiber intake was associated with both greater microbial diversity and lower long-term weight gain.³⁰ Of particular interest is a recent intervention study in which overweight and obese children were given oligosaccharide-inulin supplementation for 16 weeks, which resulted in significant decreases in body weight z-score, percent body fat, percent trunk fat, and serum IL-6 level.³¹ Inulin, a prebiotic dietary fiber, was used in this study to directly alter the composition of the gut microbiota, which was associated with the body composition results, thus further supporting the relationships among dietary fiber intake, BMI z-score, and obesity seen in our study.

In addition, there is evidence suggesting that the DASH diet may be effective in weight management and body composition.³² When DASH score was accounted for in model 3 in our study, the significance of the association between lower fiber intake and odds of obesity was lost. Similar

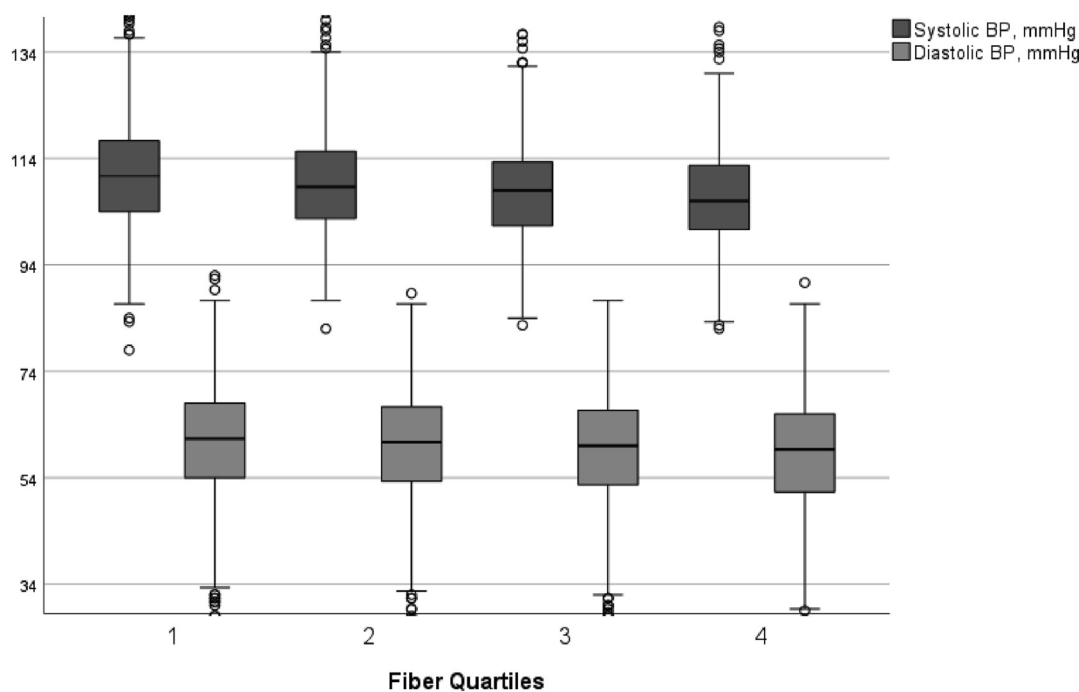


Figure 2. Relationship between dietary fiber quartiles and blood pressure, NHANES 2009-2018.

to the effect seen on SBP, this suggests that the numerous targets in the DASH diet have a greater impact on weight management than fiber alone.

Decreased dietary fiber intake also was found to be significantly associated with higher serum uric acid levels. Three other NHANES studies, 2 involving adults using data in 2009-2014⁴ and 1999-2004³³ and 1 comprising adolescents in 2005-2008,³⁴ found evidence that increased dietary fiber intake was associated with decreased uric acid levels and a decreased risk of hyperuricemia. Furthermore, Chinese study of 66 427 adults also found the same relationship as we report here.³⁵ Although the mechanism behind this finding remains unclear, it may be associated with changes in intestinal viscosity, nutrient absorption, rate of passage, production of short-chain fatty acids, and production of gut hormones.³⁶ Studies in rats have suggested that the association may be related to dietary fiber's modulation of gut microbiota and its metabolites that increase purine and uric acid catabolism, as well as excretion.^{37,38}

Although the relationship was not evident in the fully adjusted regression model, this study found that dietary fiber intake was inversely related to total cholesterol, triglyceride, and LDL cholesterol levels and directly related to HDL cholesterol levels in the crude and model 1 regressions. We also found that decreased dietary fiber was significantly associated with dyslipidemia status in the crude and model 1 regressions. This suggests that greater intake of dietary fiber in the adolescent cohort was associated with more favorable lipid status. The lipid-lowering effects of soluble dietary fiber is well established, and studies are beginning to elucidate the mechanism behind this effect.³⁹⁻⁴⁴ There are several pro-

posed mechanisms for the hypolipidemic effect of soluble dietary fiber, including lowering overall energy intake, increasing the rate of bile acid excretion, and decreasing adipokine production.⁴⁰ Moreover, many studies are exploring the effects of dietary fiber on the gut microbiome and how these effects facilitate its lipid-lowering mechanism.^{40,45,46} The SCFAs produced by anaerobic gut bacteria through soluble dietary fiber fermentation are associated with reduced cholesterol synthesis.^{40,45,47,48} Although our study only examined dietary fiber as a whole, current research is beginning to investigate how different components of soluble fiber and insoluble fiber from different foods may have differing levels of hypolipidemic effect.^{49,50} In addition, the lipid-lowering effects found in this study lost significance after the addition of demographic covariates in model 2. Further investigation is needed to understand why this occurred, but both the crude and model 1 analyses supported our hypothesis that lower dietary fiber intake would have detrimental effects on blood lipids.

Limitations of this study include the lack of longitudinal data and the bias of self-reported variables. NHANES is a cross-sectional study that does not follow participants over time. Therefore, relating future outcomes, such as a cardiometabolic condition, to adolescent dietary fiber intake is not possible with our dataset. Moreover, the dietary fiber intake variable accounted for all food items in the diet that contribute broadly to fiber. Further studies evaluating specific types of soluble and insoluble fiber and their effects on cardiometabolic outcomes in adolescents are needed. In addition, characterizing dietary fiber intake based on 24-hour dietary recall leaves room for bias in self-

Table IV. Relationship between dietary fiber and dichotomous cardiometabolic markers, NHANES 2009-2018

Markers	OR (95% CI)	P value
Obesity*		
Crude	3.02E-6 (4.28E-7 to 2.13E-5)	<.001
Model 1	2.16E-6 (2.98E-7 to 1.56E-5)	<.001
Model 2	0.03 (0.002-0.47)	.013
Model 3	0.11 (0.01-2.18)	.145
Hypertensive BP		
Crude	0.01 (0.001-0.03)	<.001
Model 1	0.005 (0.001-0.03)	<.001
Model 2	0.26 (0.01-7.60)	.427
Model 3	0.47 (0.01-15.97)	.647
Elevated BP		
Crude	0.06 (0.01-0.22)	<.001
Model 1	0.05 (0.01-0.23)	<.001
Model 2	0.273 (0.01-5.24)	.384
Model 3	0.432 (0.01-34.68)	.704
Dyslipidemia		
Crude	0.22 (0.07-0.73)	.013
Model 1	0.18 (0.06-0.59)	.005
Model 2	1.79 (0.09-35.46)	.700
Model 3	1.40 (0.05-35.73)	.838
Microalbuminuria		
Crude	3.99 (1.55-10.24)	.005
Model 1	3.87 (1.41-10.66)	.009
Model 2	0.55 (0.05-5.76)	.615
Model 3	0.53 (0.04-6.70)	.622
Glomerular hyperfiltration		
Crude	2.00 (0.29-13.59)	.475
Model 1	1.19 (0.16-9.20)	.864
Model 2	29.50 (1.49-584.77)	.027
Model 3	82.83 (2.55-2691.8)	.014

Obesity defined as a BMI z-score ≥ 2.0 . Hypertension defined as SBP/DBP of $>130/80$ mmHg. Elevated BP defined as SBP/DBP of $120-129/80$ mmHg. Dyslipidemia defined as meeting any one of the following criteria: HDL cholesterol <40 mg/dL, LDL cholesterol ≥ 130 mg/dL, or triglycerides ≥ 130 mg/dL. Albuminuria defined as an albumin:creatinine ratio >30 mg/g. Glomerular hyperfiltration defined as eGFR >140 mL/min per 1.73 m². Model 1 is adjusted for age and sex. Model 2 is adjusted for age, sex, race, BMI z-score, total daily caloric intake, family income:poverty ratio, food insecurity, and passive smoke exposure. Model 3 is adjusted for age, sex, race, BMI z-score, total daily caloric intake, family income:poverty ratio, food insecurity, passive smoke exposure, and DASH score.

*Variable not adjusted for BMI z-score.

reporting. Another limitation of this study lies in the inability to analyze common laboratory measures of inflammation, such as erythrocyte sedimentation rate, C-reactive protein, and ferritin, as values for these were not consistently available in the NHANES years examined in this study. Future studies should focus on evaluating the potential relationships of dietary fiber to these inflammatory markers.

Further studies investigating the mechanism behind the effects of dietary fiber are warranted, especially those investigating the role of particular types of fiber in modulating the gut microbiome. Longitudinal studies evaluating the effects of long-term consumption of fiber through childhood can help further elucidate its potential protective effects against chronic disease later in life. ■

CRedit Authorship Contribution Statement

Johnathon Carboni: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing –

original draft, Writing – review & editing, Visualization. **Abby Basalely:** Conceptualization, Writing – review & editing. **Pamela Singer:** Conceptualization, Writing – review & editing. **Laura Castellanos:** Conceptualization, Writing – review & editing. **Christine B. Sethna:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing, Visualization, Supervision, Project administration.

Declaration of Competing Interest

C.B.S. has served on an advisory board for Travers Therapeutics and is supported by National Institutes of Health: National Institute of Diabetes and Digestive and Kidney Diseases Grant R01 DK131091. The other authors declare no conflicts of interest.

Submitted for publication Feb 25, 2023; last revision received Jul 8, 2023; accepted Jul 12, 2023.

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