



# Diets higher in animal and plant protein are associated with lower adiposity and do not impair kidney function in US adults<sup>1,2</sup>

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## ABSTRACT

**Background:** Higher-protein diets are associated with decreased adiposity and greater HDL cholesterol than lower protein diets. Whether these benefits can be attributed to a specific protein source (i.e., nondairy animal, dairy, or plant) is unknown, and concerns remain regarding the impact of higher-protein diets on kidney function.

**Objective:** The objective of this study was to evaluate trends of protein source on markers of cardiometabolic disease risk and kidney function in US adults.

**Design:** Total, nondairy animal, dairy, and plant protein intake were estimated with the use of 24-h recall data from NHANES 2007–2010 ( $n = 11,111$ ;  $\geq 19$  y). Associations between source-specific protein intake and health outcomes were determined with the use of models that adjusted for sex, race and ethnicity, age, physical activity, poverty-to-income ratio, individual intake (grams per kilogram) for each of the other 2 protein sources, body mass index (BMI) (except for weight-related variables), and macronutrient (carbohydrate, fiber, and total and saturated fat) intake.

**Results:** Mean  $\pm$  SE total protein intake was  $82.3 \pm 0.8$  g/d (animal:  $37.4 \pm 0.5$  g/d; plant:  $24.7 \pm 0.3$  g/d; and dairy:  $13.4 \pm 0.3$  g/d). Both BMI and waist circumference were inversely associated [regression coefficient (95% CI)] with animal [ $-0.199$  ( $-0.265$ ,  $-0.134$ ),  $P < 0.0001$ ;  $-0.505$  ( $-0.641$ ,  $-0.370$ ),  $P < 0.0001$ ] and plant [ $-0.346$  ( $-0.455$ ,  $-0.237$ ),  $P < 0.0001$ ;  $-0.826$  ( $-1.114$ ,  $-0.538$ ),  $P < 0.0001$ ] protein intake. Blood urea nitrogen concentrations increased across deciles for animal [0.313 (0.248, 0.379),  $P < 0.0001$ ; decile 1–10:  $11.6 \pm 0.2$  to  $14.9 \pm 0.3$  mg/dL] and dairy [0.195 (0.139, 0.251),  $P < 0.0001$ ; decile 1–10:  $12.7 \pm 0.2$  to  $13.9 \pm 0.2$  mg/dL] but not plant protein intake. Glomerular filtration rate and blood creatinine were not associated with intake of any protein source.

**Conclusions:** Diets higher in plant and animal protein, independent of other dietary factors, are associated with cardiometabolic benefits, particularly improved central adiposity, with no apparent impairment of kidney function. *Am J Clin Nutr* doi: 10.3945/ajcn.116.133819.

**Keywords:** higher-protein diet, kidney function, cardiometabolic risk, NHANES, protein source, central adiposity

## INTRODUCTION

Americans generally consume protein at amounts higher than the Recommended Dietary Allowance (RDA<sup>6</sup>; 0.8 g/kg body weight), but well within the Acceptable Macronutrient Distribution Range

for protein (10–35% of total calories) (1–3). The primary source of dietary protein in the American adult diet is nondairy animal sources (chicken and beef), followed by plant (yeast breads and rolls or buns) and dairy (milk) sources (4). Recent cross-sectional data suggest that Americans who habitually consume dietary protein at amounts higher than the RDA have lower cardiometabolic disease risk (2). In that study of  $\sim 24,000$  adults, individuals who consumed higher-protein diets had a lower BMI and waist circumference (WC) and an increased HDL cholesterol concentration compared with individuals who consumed protein at amounts consistent with the RDA (2). A cross-sectional analysis of Iranian nationals found similar associations between higher-protein diets and measures of central adiposity in women and HDL cholesterol in both sexes (5). Contributions by specific protein source were not reported in either study. As such, studies that stratify the effects of dietary protein on cardiometabolic disease risk by protein source (i.e., nondairy animal, plant, and dairy) are necessary to distinguish the effects that are likely to be attributable to protein, per se, compared with the concomitant nutritional components in whole foods.

Despite increasing evidence suggesting that higher-protein diets may confer cardiometabolic benefits, there is a persisting concern that maintaining a higher protein intake may contribute to acute and long-term declines in kidney function (6, 7). The Kidney Disease Outcomes Quality Initiative Nutrition Guidelines (8) recommend a low-protein diet (0.6 g protein/kg) for nondialyzed individuals with chronic kidney disease (CKD); within this population, low protein intake (0.3–0.6 g/kg) has been shown to reduce renal death and delay the onset of dialysis

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<sup>6</sup> Abbreviations used: BUN, blood urea nitrogen; CAD, coronary artery disease; CKD, chronic kidney disease; GFR, glomerular filtration rate; RDA, Recommended Dietary Allowance; WC, waist circumference.

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(RR: 0.68; 95% CI: 0.55, 0.84) compared with higher protein intake ( $\geq 0.8$  g/kg) (9). In adults with no history of CKD, increases in glomerular filtration rate (GFR), blood urea nitrogen (BUN), and calcium excretion are normal adaptive responses to shorter- and longer-term (1–104 wk) higher protein intake (10). To our knowledge, conclusive evidence of the relation between transient changes in kidney function and long-term renal decline in individuals with normal kidney function does not exist, particularly as it relates to protein source.

The objective of this study was to evaluate decile trends of protein source on markers of cardiometabolic disease risk and kidney function in a representative sample of free-living US adults. We hypothesized that the beneficial relations between protein and cardiometabolic disease risk outcomes, including BMI, WC, and HDL cholesterol, would be consistent with our previous report (2), regardless of source, and that higher-protein diets would not be associated with impaired kidney function.

## METHODS

### Study overview and participants

The NHANES is a large ongoing dietary survey of a nationally representative sample of the noninstitutionalized US population. The data are collected and released by the National Center for Health Statistics of the CDC every 2 y. Data from NHANES 2007–2008 and 2009–2010 were combined for this analysis, which included 11,111 adults (aged  $\geq 19$  y) who completed a 24-h dietary recall, excluding pregnant or lactating women, individuals with a BMI (in  $\text{kg}/\text{m}^2$ )  $\leq 18.5$ , and those with incomplete dietary records or missing data. All participants or proxies provided written informed consent, and the Research Ethics Review Board at the National Center for Health Statistics approved the survey protocol. A detailed description of the survey design and the data collection procedures are reported elsewhere (11).

### Protein intake

USDA food composition databases, including the Food and Nutrient Database for Dietary Studies, versions 4.1 and 5.0, and the linked USDA Nutrient Database for Standard Reference, releases 22 and 24, were used to determine the protein amount and type from foods consumed by NHANES participants (12, 13), as described previously (4). In addition, the USDA list of 150 total food categories was used to define food sources by protein type (14). More than 90% of all protein was categorized as nondairy animal, dairy, or plant, with only 8% of protein intake not able to be categorized (primarily in the mixed-food category). All references to animal protein within the text, figure, and tables denote nondairy animal protein, unless stated otherwise.

### Outcome variables

Body weight, BMI, WC, blood pressure (diastolic and systolic), glycated hemoglobin, HDL cholesterol, BUN, blood creatinine, GFR [Chronic Kidney Disease Epidemiology Collaboration creatinine equation (15)], fasting triglycerides, LDL cholesterol, glucose, and insulin were obtained from examination (16) and laboratory files (17). HOMA-IR was calculated as the product of plasma insulin (picomoles per liter) and glucose (millimoles per liter) divided by 22.5 (18).

## Statistical analysis

Data were analyzed with the use of SAS 9.2 and SUDAAN release 11.0 (Research Triangle Institute). Appropriate weighting factors were used to adjust for oversampling of selected groups, survey nonresponses of some individuals, and for the day of the week the interview was conducted (19). Means and percentages  $\pm$  SEs of total, animal, dairy, and plant protein were determined by using PROC DESCRIPT in SUDAAN with the use of data from the first 24-h recall. Deciles of total, animal, dairy, and plant protein intake were developed by estimating individual usual intake with the use of the National Cancer Institute method (20), as reported previously (4). Least-squares means and SEs of biochemical outcome variables were determined for subjects in each decile of total, animal, dairy, and plant protein intake (grams per kilogram body weight) with use of PROC REGRESS in SUDAAN after adjustment for covariates. In model 1, outcome variables were adjusted for sex, race and ethnicity, age, physical activity (categorized as sedentary, moderate, or vigorous on the basis of responses to questions on activity), poverty-to-income ratio, individual intake (grams per kilogram) for each of the other 2 protein sources (e.g., regression analysis for animal protein was adjusted for individual intake of dairy and plant protein), and BMI (except for weight related variables). In model 2, outcome variables were adjusted for all model 1 variables, in addition to carbohydrate, fiber, total fat, and saturated fat intake (i.e., macronutrients). Trends across deciles of habitual dietary protein intake were computed for the covariate-adjusted biochemical variables. Subjects with missing data for a variable of interest were eliminated from that particular analysis. Significance was set at a Bonferroni-adjusted  $\alpha$  of  $P < 0.0008$  [ $P < 0.05$  divided by 60 (4 protein source groups and 15 sets of variables analyzed)].

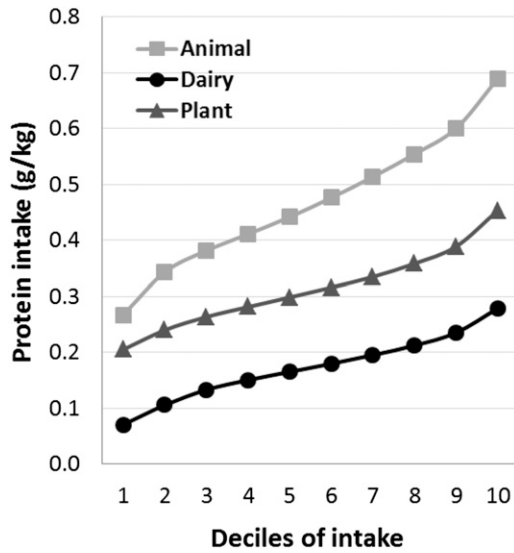
## RESULTS

### Protein intake

Mean  $\pm$  SE total protein intake was  $82.3 \pm 0.8$  g/d, of which  $37.4 \pm 0.5$  g/d (range:  $2.9 \pm 0.1$  to  $98.0 \pm 1.7$  g/d) was animal protein,  $13.4 \pm 0.3$  g/d (range:  $0.03 \pm 0.003$  to  $41.7 \pm 0.9$  g/d) was dairy protein, and  $24.7 \pm 0.3$  g/d (range:  $7.6 \pm 0.2$  to  $52.1 \pm 0.6$  g/d) was plant protein. Approximately 6.8  $\pm$  0.2 g/d protein could not be attributed to animal, dairy, or plant food sources. Protein intake (grams per kilogram) of each source more than doubled from deciles 1 to 10 (**Figure 1**).

### Population demographics

The percentage of women consuming animal, plant, or dairy protein decreased across increasing intake deciles. With increasing deciles of animal protein intake, the percentage of the Hispanic and non-Hispanic black populations increased, whereas the percentage of the non-Hispanic white population decreased. With increasing deciles of dairy protein intake, the percentage of the non-Hispanic white population increased, whereas both percentages of the Hispanic and non-Hispanic black populations decreased. In the case of increasing plant protein deciles, the percentage of the Hispanic population increased, the percentage of the non-Hispanic black population decreased, and the percentage of the non-Hispanic white population remained unchanged (**Table 1**).



**FIGURE 1** Deciles of total and source-specific (nondairy animal, dairy, and plant) protein intake in adults aged  $\geq 19$  y: NHANES 2007–2010 ( $n = 11,111$ )

**Weight-related markers**

Body weight, BMI, and WC were inversely associated with habitual intake of total, animal, dairy, and plant protein when adjusted for model 1 covariates (Table 2). The associations remained significant for total, animal, and plant protein, but not dairy, in model 2.

**Cardiometabolic disease risk factors**

Deciles of animal protein intake were positively associated with glucose in model 1. This association remained significant in

model 2. Deciles of plant protein intake were positively associated with diastolic blood pressure in model 1, but not in model 2. In both models 1 and 2, there were no significant associations between deciles of total or dairy protein and any cardiometabolic disease risk factor (Table 3).

**Markers of kidney function**

In model 1, deciles of plant protein intake were positively associated with GFR and inversely associated with BUN and creatinine; these variables were no longer significant after model 2 adjustments. In both models 1 and 2, there was a positive association between total, animal, and dairy protein intake and BUN (Table 4). Total protein intake was associated with creatinine in model 1, but not model 2, and had no relation with GFR in either model. Deciles of animal and dairy protein intake were not associated with creatinine or GFR (Table 4).

**DISCUSSION**

The current cross-sectional study demonstrated the following: 1) animal and plant protein, but not dairy protein, are inversely associated with WC, BMI, and body weight; 2) with the exception of a positive relation between animal protein and blood glucose, plant, dairy, and animal protein are not associated with any marker of increased cardiometabolic disease risk; 3) animal, dairy, and plant protein are not associated with GFR or creatinine concentrations, but animal and dairy protein are positively associated with BUN. These findings are consistent with our previous work demonstrating a beneficial relation between protein intake and weight-related outcomes (2), but further suggest the relative contribution of specific protein sources. Perhaps most importantly, our analysis shows that habitual

**TABLE 1** Demographics of US adults according to protein type intake: NHANES 2007–2010<sup>1</sup>

	Deciles of individual protein intake, g/kg			Decile trend	
	1	5	10	$\beta$ (95% CI)	P
<b>Population with animal protein intake</b>					
Female, %	93.0 $\pm$ 0.9	65.8 $\pm$ 2.1	3.4 $\pm$ 0.7	-11.095 (-11.359, -10.831)*	<0.0001
Age, y	49.3 $\pm$ 0.9	49.8 $\pm$ 0.7	37.9 $\pm$ 0.5	-1.121 (-1.243, -0.999)*	<0.0001
<b>Ethnicity, %</b>					
Hispanic	10.6 $\pm$ 1.4	13.3 $\pm$ 1.7	20.2 $\pm$ 2.6	0.770 (0.522, 1.018)*	<0.0001
Non-Hispanic white	75.3 $\pm$ 2.7	70.0 $\pm$ 2.7	61.0 $\pm$ 3.4	-1.212 (-1.539, -0.885)*	<0.0001
Non-Hispanic black	8.9 $\pm$ 1.2	12.0 $\pm$ 1.6	12.1 $\pm$ 1.2	0.212 (0.007, 0.417)*	0.0429
<b>Population with dairy protein intake</b>					
Female, %	48.5 $\pm$ 1.7	52.1 $\pm$ 1.9	45.3 $\pm$ 1.9	-0.611 (-1.029, -0.193)*	0.0056
Age, y	44.5 $\pm$ 0.7	46.7 $\pm$ 0.8	44.6 $\pm$ 0.7	-0.197 (-0.325, -0.069)*	0.0037
<b>Ethnicity, %</b>					
Hispanic	18.9 $\pm$ 2.7	12.4 $\pm$ 2.1	11.2 $\pm$ 1.7	-0.515 (-0.936, -0.093)*	0.0183
Non-Hispanic white	51.5 $\pm$ 3.9	73.1 $\pm$ 3.0	80.4 $\pm$ 2.1	2.819 (2.236, 3.403)*	<0.0001
Non-Hispanic black	20.3 $\pm$ 2.2	10.4 $\pm$ 1.4	4.4 $\pm$ 0.6	-1.739 (-2.217, -1.262)*	<0.0001
<b>Population with plant protein intake</b>					
Female, %	67.3 $\pm$ 1.8	51.0 $\pm$ 2.3	34.7 $\pm$ 1.9	-3.321 (-3.682, -2.959)*	<0.0001
Age, y	43.8 $\pm$ 0.6	48.9 $\pm$ 0.5	42.6 $\pm$ 0.7	-0.192 (-0.351, -0.034)*	0.0189
<b>Ethnicity, %</b>					
Hispanic	12.5 $\pm$ 2.1	11.5 $\pm$ 1.9	17.7 $\pm$ 2.5	0.491 (0.151, 0.831)*	0.0061
Non-Hispanic white	62.0 $\pm$ 3.6	71.4 $\pm$ 2.9	68.2 $\pm$ 3.3	0.404 (-0.221, 1.029)	0.1974
Non-Hispanic black	22.0 $\pm$ 2.5	10.6 $\pm$ 1.4	6.9 $\pm$ 0.9	-1.416 (-1.853, -0.978)*	<0.0001

<sup>1</sup>Values are means  $\pm$  SEs unless otherwise indicated.  $n = 11,111$ . \*Significant regression coefficient,  $P < 0.05$ . Adapted from reference 4 with permission.

**TABLE 2**Association of individual usual protein-type intake deciles with body weight, BMI, and waist circumference in US adults: NHANES 2007–2010<sup>1</sup>

	Decile of individual usual protein intake, g/kg			Model 1 decile trend <sup>2</sup>		Model 2 decile trend <sup>3</sup>	
	1	5	10	$\beta$ (95% CI)	$P^4$	$\beta$ (95% CI)	$P^4$
Body weight, kg ( $n = 9966$ )							
Total	97.3 $\pm$ 1.1	82.3 $\pm$ 0.7	67.6 $\pm$ 0.7	-2.896 (-3.107, -2.684)*	<0.0001	-1.516 (-1.750, -1.283)*	<0.0001
Animal	84.3 $\pm$ 0.8	82.3 $\pm$ 0.9	76.7 $\pm$ 0.8	-0.707 (-0.908, -0.505)*	<0.0001	-0.629 (-0.837, -0.422)*	<0.0001
Dairy	81.9 $\pm$ 0.9	84.0 $\pm$ 0.9	77.7 $\pm$ 0.6	-0.578 (-0.749, -0.407)*	<0.0001	-0.284 (-0.482, -0.087)	0.0062
Plant	94.9 $\pm$ 1.3	84.0 $\pm$ 1.0	71.0 $\pm$ 0.4	-2.431 (-2.694, -2.167)*	<0.0001	-1.018 (-1.378, -0.659)*	<0.0001
BMI, kg/m <sup>2</sup> ( $n = 9966$ )							
Total	33.9 $\pm$ 0.4	28.8 $\pm$ 0.3	24.2 $\pm$ 0.2	-0.956 (-1.018, -0.894)*	<0.0001	-0.497 (-0.577, -0.417)*	<0.0001
Animal	29.5 $\pm$ 0.3	28.9 $\pm$ 0.3	27.2 $\pm$ 0.3	-0.231 (-0.296, -0.167)*	<0.0001	-0.199 (-0.265, -0.134)*	<0.0001
Dairy	28.6 $\pm$ 0.3	29.2 $\pm$ 0.3	27.3 $\pm$ 0.2	-0.210 (-0.269, -0.152)*	<0.0001	-0.113 (-0.185, -0.042)	0.0030
Plant	32.9 $\pm$ 0.4	29.2 $\pm$ 0.3	25.3 $\pm$ 0.2	-0.800 (-0.884, -0.716)*	<0.0001	-0.346 (-0.455, -0.237)*	<0.0001
Waist circumference, cm ( $n = 9679$ )							
Total	108.9 $\pm$ 0.9	98.7 $\pm$ 0.5	86.3 $\pm$ 0.6	-2.251 (-2.405, -2.096)*	<0.0001	-1.193 (-1.357, -1.029)*	<0.0001
Animal	99.5 $\pm$ 0.5	98.7 $\pm$ 0.7	93.7 $\pm$ 0.6	-0.541 (-0.668, -0.414)*	<0.0001	-0.505 (-0.641, -0.370)*	<0.0001
Dairy	97.9 $\pm$ 0.7	99.3 $\pm$ 0.7	94.8 $\pm$ 0.5	-0.434 (-0.576, -0.291)*	<0.0001	-0.235 (-0.397, -0.073)	0.0059
Plant	107.5 $\pm$ 1.1	99.4 $\pm$ 0.7	88.9 $\pm$ 0.4	-1.929 (-2.141, -1.718)*	<0.0001	-0.826 (-1.114, -0.538)*	<0.0001

<sup>1</sup>Values are least-squares means  $\pm$  SEs. \*Significant regression coefficient.<sup>2</sup>Data were analyzed with the use of ANOVA and adjusted for age, sex, ethnicity, physical activity, poverty-to-income ratio, and individual usual intake (g/kg) for each of the other 2 protein types (animal, dairy, and plant).<sup>3</sup>Data were adjusted in addition for carbohydrate, total fat, saturated fat, and fiber intake.<sup>4</sup>Significance was set at a Bonferroni-corrected  $P$  value of <0.0008 (0.05/60).

consumption of higher-protein diets is not associated with impaired kidney function in adults with no history of renal disease.

Source-specific associations were examined with the use of statistical models to limit residual nutritional confounders inherent in foods containing the other 2 protein sources (model 1) and independent of other macronutrients within the food itself and the complete diet (model 2). Animal, dairy, and plant protein were inversely associated with weight-related indicators when considered within their food matrix; however, when adjustments were made for carbohydrate, fiber, total fat, and saturated fat, only animal and plant protein intake were related to WC, BMI, and body weight. Sample size, corrections for multiple comparisons, the relatively small contribution of dairy (16%) to total protein intake, and less variation in intake across deciles likely are responsible for the lack of an association with dairy protein (4). Nevertheless, animal and plant protein intake were associated with lower body weight and central adiposity, findings that may be attributed to the metabolic efficiency (energy produced relative to energy cost of metabolism) of protein (21, 22). Metabolic efficiency calculations indicate that protein is the least efficient of the metabolic pathways, suggesting that because more energy is needed to use protein as a fuel, compared with carbohydrate and fat, higher-protein diets may lower body weight (21).

Interestingly, animal protein was positively associated with blood glucose with both statistical models, suggesting that animal protein itself, more than the other nutrients in the foods and total diet, may alter glycemic regulation. Although our study does not allow us to distinguish the specific animal protein foods responsible for this effect, meta-analyses have found that consuming high amounts of red and processed meat increases the risk of type 2 diabetes and cardiovascular disease-related and all-cause mortality (23–32). Less evidence exists to evaluate the relation between white meat (poultry and fish) and cardiovascular disease

mortality; however, results predominantly indicate null or slightly inverse associations (23, 32, 33). Furthermore, consumption of 1–4 servings fish/wk provides protection from coronary artery disease (CAD) mortality and stroke (34, 35). The wide variation in types of animal protein suggests that investigating specific foods may be more informative than grouped sources. However, a study investigating the relation between protein intake (lowest quintile: 12.4%  $\pm$  1.7% compared with highest quintile: 22.8%  $\pm$  3.4% of total intake) and CAD incidence in US adults found that CAD risk was not associated with total, vegetable, or animal protein intake, including dairy, nor was it associated with any major dietary food source of protein (36). Additional prospective cohort studies have differentiated by source and indicate that animal (nondairy and dairy) and plant protein neither positively nor negatively affect long-term CAD risk (37, 38).

Protein source associations, or lack thereof, with HDL cholesterol and diastolic blood pressure were unexpected. Our previous finding of an association between total protein intake and HDL cholesterol was not replicated by the current analysis. This discrepancy may be due to the smaller sample size ( $n = 11,111$  compared with  $n = 23,876$ ) or slight differences in statistical model adjustments (i.e., adjustment for saturated fat intake) between studies. In addition, plant protein was associated with increased diastolic blood pressure in model 1; however, this relation was no longer significant after further adjustment for carbohydrate, fiber, total fat, and saturated fat. This suggests that other nutrients in foods containing plant protein may be driving the relation. The primary food sources of plant protein are yeast breads and rolls or buns—comprising  $\sim$ 18% of all plant protein consumed—which commonly contribute meaningful amounts of sodium to the diet (4).

Our analysis of protein source and kidney function yielded positive associations between animal and dairy protein intake and BUN. These associations are expected, given that urea is

**TABLE 3**

Association of individual usual protein-type intake deciles with cardiometabolic risk factors in US adults: NHANES 2007–2010<sup>1</sup>

	Decile of individual usual protein intake, g/kg			Model 1 decile trend <sup>2</sup>		Model 2 decile trend <sup>3</sup>	
	1	5	10	$\beta$ (95% CI)	<i>P</i> <sup>4</sup>	$\beta$ (95% CI)	<i>P</i> <sup>4</sup>
<b>Diastolic blood pressure, mm Hg (n = 9633)</b>							
Total	70.0 ± 0.5	70.1 ± 0.8	70.2 ± 0.7	0.115 (0.000, 0.229)	0.0505	-0.054 (-0.253, 0.146)	0.5880
Animal	70.4 ± 0.5	70.3 ± 0.6	71.1 ± 0.7	0.148 (-0.016, 0.311)	0.0751	0.038 (-0.130, 0.206)	0.6486
Dairy	71.4 ± 0.6	70.3 ± 0.6	70.2 ± 0.5	-0.071 (-0.183, 0.040)	0.1999	-0.120 (-0.268, 0.028)	0.1072
Plant	70.0 ± 0.5	70.8 ± 0.5	71.2 ± 0.6	0.175 (0.102, 0.247)*	<0.0001	0.249 (0.082, 0.416)	0.0048
<b>Systolic blood pressure, mm Hg (n = 9672)</b>							
Total	120.8 ± 0.6	121.5 ± 0.7	122.6 ± 0.7	0.126 (-0.036, 0.287)	0.1232	0.102 (-0.133, 0.337)	0.3826
Animal	121.0 ± 0.4	121.4 ± 0.6	122.9 ± 0.5	0.082 (-0.102, 0.266)	0.3695	0.035 (-0.168, 0.238)	0.7270
Dairy	121.7 ± 0.5	121.9 ± 0.7	121.1 ± 0.8	0.024 (-0.132, 0.180)	0.7600	-0.055 (-0.256, 0.146)	0.5812
Plant	121.6 ± 0.6	121.9 ± 0.7	121.4 ± 0.8	-0.061 (-0.199, 0.078)	0.3786	-0.064 (-0.307, 0.180)	0.5979
<b>Glucose, mg/dL (n = 4345)</b>							
Total	104.1 ± 1.5	103.9 ± 1.0	107.8 ± 1.4	0.507 (0.114, 0.901)	0.0132	0.535 (0.145, 0.924)	0.0087
Animal	102.3 ± 0.9	104.2 ± 1.1	107.7 ± 1.5	0.730 (0.416, 1.044)*	<0.0001	0.571 (0.320, 0.822)*	0.0001
Dairy	104.6 ± 1.6	104.4 ± 1.0	109.1 ± 1.9	-0.016 (-0.366, 0.334)	0.9272	-0.064 (-0.405, 0.277)	0.7039
Plant	106.2 ± 1.6	102.3 ± 0.8	105.6 ± 1.6	0.003 (-0.356, 0.362)	0.9869	0.217 (-0.278, 0.712)	0.3786
<b>Glycated hemoglobin, % (n = 9532)</b>							
Total	5.54 ± 0.02	5.61 ± 0.03	5.65 ± 0.03	0.008 (0.001, 0.016)	0.0295	0.006 (-0.003, 0.015)	0.1597
Animal	5.52 ± 0.02	5.63 ± 0.04	5.64 ± 0.04	0.012 (0.002, 0.021)	0.0143	0.009 (0.001, 0.017)	0.0306
Dairy	5.59 ± 0.04	5.58 ± 0.04	5.67 ± 0.03	0.000 (-0.009, 0.009)	0.9546	-0.002 (-0.012, 0.008)	0.7391
Plant	5.57 ± 0.03	5.57 ± 0.03	5.60 ± 0.02	0.003 (-0.005, 0.011)	0.4093	0.008 (-0.002, 0.019)	0.1224
<b>Insulin, μU/mL (n = 4286)</b>							
Total	10.6 ± 0.5	12.4 ± 0.4	13.2 ± 0.6	0.221 (0.020, 0.423)	0.0326	0.241 (-0.022, 0.503)	0.0708
Animal	11.5 ± 0.4	13.2 ± 0.4	13.6 ± 0.7	0.174 (0.013, 0.334)	0.0346	0.154 (-0.010, 0.319)	0.0652
Dairy	13.0 ± 0.5	12.7 ± 0.6	13.3 ± 0.5	0.003 (-0.122, 0.129)	0.9559	-0.050 (-0.195, 0.095)	0.4886
Plant	12.5 ± 0.5	12.6 ± 0.4	12.4 ± 0.6	0.002 (-0.136, 0.139)	0.9794	-0.054 (-0.217, 0.108)	0.5014
<b>HOMA-IR (n = 4286)</b>							
Total	2.77 ± 0.15	3.32 ± 0.13	3.74 ± 0.21	0.098 (0.022, 0.174)	0.0132	0.112 (0.017, 0.207)	0.0227
Animal	2.98 ± 0.13	3.54 ± 0.14	3.86 ± 0.28	0.084 (0.030, 0.138)	0.0036	0.076 (0.024, 0.128)	0.0058
Dairy	3.56 ± 0.17	3.38 ± 0.18	3.88 ± 0.24	0.004 (-0.045, 0.052)	0.8829	-0.011 (-0.066, 0.044)	0.6778
Plant	3.37 ± 0.16	3.32 ± 0.14	3.41 ± 0.16	0.013 (-0.037, 0.063)	0.6066	0.010 (-0.062, 0.081)	0.7857
<b>LDL cholesterol, mg/dL (n = 4235)</b>							
Total	116.6 ± 2.9	118.8 ± 1.8	116.3 ± 2.6	0.131 (-0.389, 0.652)	0.6103	0.058 (-0.662, 0.777)	0.8712
Animal	115.9 ± 2.8	115.9 ± 2.8	121.4 ± 2.1	0.844 (0.284, 1.405)	0.0044	0.726 (0.071, 1.382)	0.0310
Dairy	114.8 ± 2.2	115.7 ± 2.4	120.8 ± 2.4	0.399 (-0.341, 1.140)	0.2800	-0.138 (-0.973, 0.698)	0.7391
Plant	119.9 ± 2.2	116.8 ± 2.1	113.5 ± 2.5	-0.506 (-0.953, -0.059)	0.0278	0.285 (-0.395, 0.966)	0.3989
<b>HDL cholesterol, mg/dL (n = 9478)</b>							
Total	51.2 ± 0.9	52.1 ± 0.7	54.7 ± 0.7	0.297 (0.105, 0.489)	0.0035	0.165 (-0.117, 0.447)	0.2425
Animal	52.7 ± 0.8	51.8 ± 0.8	53.5 ± 0.8	0.117 (-0.150, 0.384)	0.3779	0.009 (-0.263, 0.281)	0.9475
Dairy	52.0 ± 0.6	52.7 ± 0.8	52.1 ± 0.6	0.069 (-0.034, 0.172)	0.1834	0.076 (-0.080, 0.232)	0.3266
Plant	52.2 ± 0.7	52.1 ± 0.7	54.4 ± 0.7	0.210 (0.050, 0.370)	0.0117	0.234 (-0.013, 0.481)	0.0620
<b>Triglycerides, mg/dL (n = 4314)</b>							
Total	126.0 ± 4.3	130.2 ± 4.6	126.5 ± 6.5	0.177 (-1.563, 1.917)	0.8370	1.662 (-0.090, 3.415)	0.0623
Animal	129.4 ± 4.0	133.7 ± 5.7	133.4 ± 5.9	0.526 (-1.073, 2.124)	0.5075	1.386 (-0.236, 3.007)	0.0912
Dairy	134.4 ± 6.1	134.3 ± 5.7	132.8 ± 6.3	-0.748 (-2.254, 0.758)	0.3191	-1.211 (-2.911, 0.488)	0.1561
Plant	124.7 ± 4.3	129.6 ± 4.9	127.0 ± 5.1	0.446 (-1.040, 1.933)	0.5446	1.886 (-0.316, 4.087)	0.0906

<sup>1</sup>Values are least-squares means ± SEs. \*Significant regression coefficient.

<sup>2</sup>Data were analyzed with the use of ANOVA and adjusted for age, sex, BMI, ethnicity, physical activity, poverty-to-income ratio, and individual usual intake (g/kg) for each of the other 2 protein types (animal, dairy, and plant).

<sup>3</sup>Data were adjusted in addition for carbohydrate, total fat, saturated fat, and fiber intake.

<sup>4</sup>Significance was set at a Bonferroni-corrected *P* value of <0.0008 (0.05/60).

a by-product of amino acid oxidation and integral to the disposal of nitrogen waste. Furthermore, plant protein was associated with increased GFR and decreased BUN and creatinine in model 1, but

no longer related after additional adjustment for macronutrients. Again, this suggests that other nutrients in foods high in plant protein may account for the relation, not the protein, per se. A

**TABLE 4**Association of individual usual protein-type intake deciles with markers of kidney function in US adults: NHANES 2007–2010<sup>1</sup>

	Decile of individual usual protein intake, g/kg			Model 1 decile trend <sup>2</sup>		Model 2 decile trend <sup>3</sup>	
	1	5	10	$\beta$ (95% CI)	$P^4$	$\beta$ (95% CI)	$P^4$
Glomerular filtration rate, mL · min <sup>-1</sup> · 1.73 m <sup>-2</sup> (n = 9453)							
Total	92.5 ± 0.8	95.0 ± 0.7	94.7 ± 0.7	0.177 (0.005, 0.349)	0.0440	0.042 (-0.172, 0.256)	0.6908
Animal	95.2 ± 0.7	95.4 ± 0.7	93.9 ± 0.9	-0.138 (-0.334, 0.059)	0.1632	-0.125 (-0.333, 0.083)	0.2291
Dairy	94.4 ± 0.6	95.5 ± 0.7	95.1 ± 0.7	0.048 (-0.103, 0.198)	0.5217	0.028 (-0.112, 0.167)	0.6868
Plant	93.4 ± 0.8	94.4 ± 0.6	96.7 ± 0.6	0.284 (0.147, 0.420)*	0.0002	0.125 (-0.132, 0.383)	0.3289
Blood urea nitrogen, mg/dL (n = 9453)							
Total	12.2 ± 0.2	13.1 ± 0.2	14.8 ± 0.3	0.273 (0.222, 0.325)*	<0.0001	0.431 (0.364, 0.497)*	<0.0001
Animal	11.6 ± 0.2	12.7 ± 0.2	14.9 ± 0.3	0.306 (0.246, 0.365)*	<0.0001	0.313 (0.248, 0.379)*	<0.0001
Dairy	12.7 ± 0.2	12.8 ± 0.2	13.9 ± 0.2	0.142 (0.095, 0.189)*	<0.0001	0.195 (0.139, 0.251)*	<0.0001
Plant	13.9 ± 0.3	13.3 ± 0.2	12.8 ± 0.2	-0.103 (-0.140, -0.066)*	<0.0001	-0.065 (-0.146, 0.016)	0.1097
Creatinine, mg/dL (n = 9453)							
Total	0.94 ± 0.02	0.88 ± 0.01	0.87 ± 0.01	-0.006 (-0.008, -0.003)*	0.0002	-0.003 (-0.006, 0.000)	0.0389
Animal	0.89 ± 0.01	0.89 ± 0.01	0.88 ± 0.01	-0.001 (-0.004, 0.001)	0.3425	-0.001 (-0.004, 0.001)	0.3225
Dairy	0.89 ± 0.01	0.87 ± 0.01	0.88 ± 0.01	-0.001 (-0.003, 0.002)	0.5692	0.000 (-0.002, 0.002)	0.9971
Plant	0.92 ± 0.02	0.88 ± 0.01	0.85 ± 0.01	-0.006 (-0.008, -0.003)*	0.0001	-0.002 (-0.006, 0.002)	0.2586

<sup>1</sup>Values are least-squares means ± SEs. \*Significant regression coefficient.<sup>2</sup>Data were analyzed with the use of ANOVA and adjusted for age, sex, BMI, ethnicity, physical activity, poverty-to-income ratio, and individual usual intake (g/kg) for each of the other 2 protein types (animal, dairy, and plant).<sup>3</sup>Data were adjusted in addition for carbohydrate, total fat, saturated fat, and fiber intake.<sup>4</sup>Significance was set at a Bonferroni-corrected  $P$  value of <0.0008 (0.05/60).

recent publication that also used NHANES data showed that increasing quartiles of sodium were positively associated with GFR ( $P < 0.0001$ ) (39). Furthermore, a substudy of the OmniHeart Trial used a randomized, crossover, controlled-feeding design to investigate the effects of carbohydrate (15% protein and 27% fat), unsaturated fat (15% protein and 37% fat), and protein (25% protein and 27% fat) diets on kidney function (40). Similar to our findings, the protein diet, which was 48% plant-based, increased GFR and decreased creatinine compared with both the carbohydrate and unsaturated fat diets (40).

It is important to note that the GFR, BUN, and creatinine concentrations reported for each decile were within the normal range for healthy adults (normal ranges:  $\geq 90$  mL · min<sup>-1</sup> · 1.73 m<sup>-2</sup>; 7–20 mg/dL; and men: 0.7–1.3 and women: 0.6–1.1 mg/dL, respectively). A recent meta-analysis combined data from dietary intervention studies comparing higher-protein to normal- or low-protein diets in subjects with no history of CKD and found that GFR [mean difference: 7.18 mL · min<sup>-1</sup> · 1.73 m<sup>-2</sup> (4.45, 9.91 mL · min<sup>-1</sup> · 1.73 m<sup>-2</sup>),  $P < 0.001$ ] and urea [mean difference: 1.75 mmol/L (1.13, 2.37 mmol/L),  $P < 0.001$ ] were increased with higher-protein diets, demonstrating normal physiologic adaptations to increased protein intake in healthy adults (10). The argument that higher-protein diets cause a strain on the kidneys because of transient or sustained increases in GFR has never been translated to long-term disease burden in individuals with normal renal function (41). Thus, WHO and Institute of Medicine recommendations recognize higher-protein diets as safe in individuals without CKD (3, 42).

Limitations of the current study, as with any observational investigation, include an inability to infer causation. In addition, recent debate about the validity of self-reported dietary data

highlights the importance of acknowledging the inherent limitations, such as over- and underreporting (43). However, the biological endpoints measured in this study, including BUN, were greater with increasing protein intake, adding validity to the self-reported measures. Although our study was observational, it may provide the basis for controlled interventions to test the mechanisms by which dietary protein from different sources affects cardiometabolic and kidney health. The 2015 Scientific Report of the Dietary Guidelines Advisory Committee (44) makes recommendations based on food groups, not specific macronutrients, which is likely the best model for such future study designs that will guide public health recommendations.

In conclusion, we showed that animal and plant protein intake is inversely associated with WC, BMI, and body weight and that plant and dairy protein consumption is not associated with any biological marker of increased cardiometabolic disease risk. In healthy adults with no history of renal disease, GFR, BUN, and creatinine remain within normal physiologic ranges with increasing consumption of animal, dairy, and plant protein. These findings suggest that diets higher in plant and animal protein, independent of other dietary factors, are associated with cardiometabolic benefits, particularly improved central adiposity, but not impaired kidney function in US adults.

The author's responsibilities were as follows—SA and VLF: conducted the research; SMP: had primary responsibility for the final content; and all authors: designed the research, analyzed the data, wrote the manuscript, and read and approved the final manuscript. SA performs consulting and technical services for various food and beverage companies and related entities as President of NutriScience; VLF performs consulting and database analyses for various food and beverage companies and related entities as Senior Vice President of Nutrition Impact; CEB, HRL, and SMP did not report any conflicts of interest related to the study.

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