Diets higher in animal and plant protein are associated with lower adiposity and do not impair kidney function in US adults[1,2]

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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., non-dairy 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; ≥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 ± SE total protein intake was 82.3 ± 0.8 g/d (animal: 37.4 ± 0.5 g/d; plant: 24.7 ± 0.3 g/d; and dairy: 13.4 ± 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 ± 0.2 to 14.9 ± 0.3 mg/dL] and dairy [0.195 (0.139, 0.251), $P <$ 0.0001; decile 1–10: 12.7 ± 0.2 to 13.9 ± 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* 2016;104:743–9.

INTRODUCTION

Americans generally consume protein at amounts higher than the Recommended Dietary Allowance (RDA[6]; 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 ∼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 non-dialyzed 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

(RR: 0.68; 95% CI: 0.55, 0.84) compared with higher protein intake (≥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 ≥19 y) who completed a 24-h dietary recall, excluding pregnant or lactating women, individuals with a BMI (in kg/m^2) ≤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 ± 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 α of $P < 0.0008$ [$P < 0.05$ divided by 60 (4 protein source groups and 15 sets of variables analyzed)].

RESULTS

Protein intake

Mean ± SE total protein intake was 82.3 ± 0.8 g/d, of which 37.4 ± 0.5 g/d (range: 2.9 ± 0.1 to 98.0 ± 1.7 g/d) was animal protein, 13.4 ± 0.3 g/d (range: 0.03 ± 0.003 to 41.7 ± 0.9 g/d) was dairy protein, and 24.7 ± 0.3 g/d (range: 7.6 ± 0.2 to 52.1 ± 0.6 g/d) was plant protein. Approximately 6.8 ± 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**).
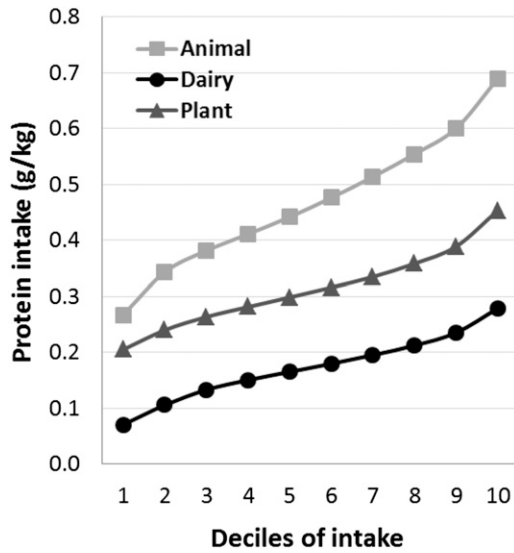
FIGURE 1 Deciles of total and source-specific (nondairy animal, dairy, and plant) protein intake in adults aged ≥19 y: NHANES 2007–2010 ($n = 11,111$)

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[1]

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

[1]Values are means ± 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[1]

	Decile of individual usual protein intake, g/kg			Model 1 decile trend[2]		Model 2 decile trend[3]	
	1	5	10	β (95% CI)	P[4]	β (95% CI)	P[4]
Body weight, kg (n = 9966)							
Total	97.3 ± 1.1	82.3 ± 0.7	67.6 ± 0.7	−2.896 (−3.107, −2.684)*	<0.0001	−1.516 (−1.750, −1.283)*	<0.0001
Animal	84.3 ± 0.8	82.3 ± 0.9	76.7 ± 0.8	−0.707 (−0.908, −0.505)*	<0.0001	−0.629 (−0.837, −0.422)*	<0.0001
Dairy	81.9 ± 0.9	84.0 ± 0.9	77.7 ± 0.6	−0.578 (−0.749, −0.407)*	<0.0001	−0.284 (−0.482, −0.087)	0.0062
Plant	94.9 ± 1.3	84.0 ± 1.0	71.0 ± 0.4	−2.431 (−2.694, −2.167)*	<0.0001	−1.018 (−1.378, −0.659)*	<0.0001
BMI, kg/m² (n = 9966)							
Total	33.9 ± 0.4	28.8 ± 0.3	24.2 ± 0.2	−0.956 (−1.018, −0.894)*	<0.0001	−0.497 (−0.577, −0.417)*	<0.0001
Animal	29.5 ± 0.3	28.9 ± 0.3	27.2 ± 0.3	−0.231 (−0.296, −0.167)*	<0.0001	−0.199 (−0.265, −0.134)*	<0.0001
Dairy	28.6 ± 0.3	29.2 ± 0.3	27.3 ± 0.2	−0.210 (−0.269, −0.152)*	<0.0001	−0.113 (−0.185, −0.042)	0.0030
Plant	32.9 ± 0.4	29.2 ± 0.3	25.3 ± 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 ± 0.9	98.7 ± 0.5	86.3 ± 0.6	−2.251 (−2.405, −2.096)*	<0.0001	−1.193 (−1.357, −1.029)*	<0.0001
Animal	99.5 ± 0.5	98.7 ± 0.7	93.7 ± 0.6	−0.541 (−0.668, −0.414)*	<0.0001	−0.505 (−0.641, −0.370)*	<0.0001
Dairy	97.9 ± 0.7	99.3 ± 0.7	94.8 ± 0.5	−0.434 (−0.576, −0.291)*	<0.0001	−0.235 (−0.397, −0.073)	0.0059
Plant	107.5 ± 1.1	99.4 ± 0.7	88.9 ± 0.4	−1.929 (−2.141, −1.718)*	<0.0001	−0.826 (−1.114, −0.538)*	<0.0001

[1]Values are least-squares means ± SEs. *Significant regression coefficient.

[2]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).

[3]Data were adjusted in addition for carbohydrate, total fat, saturated fat, and fiber intake.

[4]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% ± 1.7% compared with highest quintile: 22.8% ± 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 ∼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[1]

	Decile of individual usual protein intake, g/kg			Model 1 decile trend[2]		Model 2 decile trend[3]	
	1	5	10	β (95% CI)	P[4]	β (95% CI)	P[4]
Diastolic blood pressure, mm Hg (n = 9633)							
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
Systolic blood pressure, mm Hg (n = 9672)							
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
Glucose, mg/dL (n = 4345)							
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
Glycated hemoglobin, % (n = 9532)							
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
Insulin, μU/mL (n = 4286)							
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
HOMA-IR (n = 4286)							
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
LDL cholesterol, mg/dL (n = 4235)							
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
HDL cholesterol, mg/dL (n = 9478)							
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
Triglycerides, mg/dL (n = 4314)							
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

[1]Values are least-squares means ± SEs. *Significant regression coefficient.

[2]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).

[3]Data were adjusted in addition for carbohydrate, total fat, saturated fat, and fiber intake.

[4]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[1]

	Decile of individual usual protein intake, g/kg			Model 1 decile trend[2]		Model 2 decile trend[3]	
	1	5	10	β (95% CI)	P[4]	β (95% CI)	P[4]
Glomerular filtration rate, mL · min^{-1} · 1.73 m^{-2} (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

[1]Values are least-squares means ± SEs. *Significant regression coefficient.

[2]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).

[3]Data were adjusted in addition for carbohydrate, total fat, saturated fat, and fiber intake.

[4]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: ≥90 mL · min^{-1} · 1.73 m^{-2}; 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^{-1} · 1.73 m^{-2} (4.45, 9.91 mL · min^{-1} · 1.73 m^{-2}), 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.

REFERENCES

1. Fulgoni VL. Current protein intake in America: analysis of the National Health and Nutrition Examination Survey, 2003–2004. Am J Clin Nutr 2008;87:1554S–7S.
2. Pasiakos SM, Lieberman HR, Fulgoni VL 3rd. Higher-protein diets are associated with higher HDL cholesterol and lower BMI and waist circumference in US adults. J Nutr 2015;145:605–14.
3. Institute of Medicine. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients). Washington (DC): The National Academies Press; 2005.
4. Pasiakos SM, Agarwal S, Lieberman HR, Fulgoni VL. Sources and amounts of animal, dairy, and plant protein intake of US adults in 2007-2010. Nutrients 2015;7:7058–69.
5. Mirmiran P, Hajifaraji M, Bahadoran Z, Sarvghadi F, Azizi F. Dietary protein intake is associated with favorable cardiometabolic risk factors in adults: Tehran Lipid and Glucose Study. Nutr Res 2012;32:169–76.
6. Marckmann P, Osther P, Pedersen AN, Jespersen B. High-protein diets and renal health. J Ren Nutr 2015;25:1–5.
7. Cuenca-Sánchez M, Navas-Carrillo D, Orenes-Pinero E. Controversies surrounding high-protein diet intake: satiating effect and kidney and bone health. Adv Nutr 2015;6:260–6.
8. Clinical practice guidelines for nutrition in chronic renal failure. K/DOQI, National Kidney Foundation. Am J Kidney Dis 2000;35(6 Suppl 2):S1.
9. Fouque D, Laville M. Low protein diets for chronic kidney disease in non diabetic adults. Cochrane Database Syst Rev 2009;(3):CD001892.
10. Schwingshackl L, Hoffmann G. Comparison of high vs. normal/low protein diets on renal function in subjects without chronic kidney disease: a systematic review and meta-analysis. PLoS One 2014;9:e97656.
11. Center for Disease Control and Prevention & National Center for Health Statistics. National Health and Nutrition Examination Survey data. Hyattsville (MD): US Department of Health and Human Services, CDC; 2013.
12. USDA Agricultural Research Service. Food and nutrient database for dietary studies release 1-5.0 [Internet]. [cited 2014 Jan 22]. Available from: http://www.ars.usda.gov/Services/docs.htm?docid=18354.
13. USDA Agricultural Research Service. USDA national nutrient database for standard reference release 16-24 [Internet]. [cited 2014 Jan 10]. Available from: http://www.ars.usda.gov/main/site_main.htm?modecode=80-40-05-25.
14. USDA Agricultural Research Service. What we eat in America, food categories [Internet]. [cited 2014 Jan 5]. Available from: http://www.ars.usda.gov/Services/docs.htm?docid=23429.
15. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.
16. National Health and Nutrition Examination Survey—examination files. Atlanta (GA): CDC National Health Center for Health Statistics; 2010.
17. National Health and Nutrition Examination Survey—laboratory files. Atlanta (GA): CDC National Health Center for Health Statistics; 2010.
18. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412–9.
19. Johnson CL, Paulose-Ram R, Ogden CL, Carroll MD, Kruszon-Moran D, Dohrmann SM, Curtin LR. National Health and Nutrition Examination Survey: analytic guidelines, 1999–2010. Vital Health Stat 2 2013; (161):1–24.
20. Tooze JA, Kipnis V, Buckman DW, Carroll RJ, Freedman LS, Guenther PM, Krebs-Smith SM, Subar AF, Dodd KW. A mixed-effects model approach for estimating the distribution of usual intake of nutrients: the NCI method. Stat Med 2010;29:2857–68.
21. Feinman RDRD. Thermodynamics and metabolic advantage of weight loss diets. Metab Syndr Relat Disord 2003;1:209–19.
22. Fine EJ, Feinman RD. Thermodynamics of weight loss diets. Nutr Metab (Lond) 2004;1:15.
23. Abete I, Romaguera D, Vieira AR, Lopez de Munain A, Norat T. Association between total, processed, red and white meat consumption and all-cause, CVD and IHD mortality: a meta-analysis of cohort studies. Br J Nutr 2014;112:762–75.
24. Larsson SC, Orsini N. Red meat and processed meat consumption and all-cause mortality: a meta-analysis. Am J Epidemiol 2014;179:282–9.
25. Chen GC, Lv DB, Pang Z, Liu QF. Red and processed meat consumption and risk of stroke: a meta-analysis of prospective cohort studies. Eur J Clin Nutr 2013;67:91–5.
26. Wang X, Lin X, Ouyang YY, Liu J, Zhao G, Pan A, Hu FB. Red and processed meat consumption and mortality: dose-response meta-analysis of prospective cohort studies. Public Health Nutr 2016;19:893–905.
27. Kaluza J, Wolk A, Larsson SC. Red meat consumption and risk of stroke: a meta-analysis of prospective studies. Stroke 2012;43:2556–60.
28. Micha R, Michas G, Mozaffarian D. Unprocessed red and processed meats and risk of coronary artery disease and type 2 diabetes—an updated review of the evidence. Curr Atheroscler Rep 2012;14:515–24.
29. Pan A, Sun Q, Bernstein AM, Schulze MB, Manson JE, Stampfer MJ, Willett WC, Hu FB. Red meat consumption and mortality: results from 2 prospective cohort studies. Arch Intern Med 2012;172:555–63.
30. Pan A, Sun Q, Bernstein AM, Manson JE, Willett WC, Hu FB. Changes in red meat consumption and subsequent risk of type 2 diabetes mellitus: three cohorts of us men and women. JAMA Intern Med 2013;173:1328–35.
31. Pan A, Sun Q, Bernstein AM, Schulze MB, Manson JE, Willett WC, Hu FB. Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. Am J Clin Nutr 2011;94:1088–96.
32. Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. Meat intake and mortality: a prospective study of over half a million people. Arch Intern Med 2009;169:562–71.
33. Rohrmann S, Overvad K, Bueno-de-Mesquita H, Jakobsen M, Egeberg R, Tjonneland A, Nailler L, Boutron-Ruault M-C, Clavel-Chapelon F, Krogh V, et al. Meat consumption and mortality—results from the European Prospective Investigation into Cancer and Nutrition. BMC Med 2013;11:63.
34. Zheng J, Huang T, Yu Y, Hu X, Yang B, Li D. Fish consumption and CHD mortality: an updated meta-analysis of seventeen cohort studies. Public Health Nutr 2012;15:725–37.
35. Larsson SC, Orsini N. Fish consumption and the risk of stroke: a dose-response meta-analysis. Stroke 2011;42:3621–3.
36. Haring B, Gronroos N, Nettleton JA, von Ballmoos MCW, Selvin E, Alonso A. Dietary protein intake and coronary heart disease in a large community based cohort: results from the Atherosclerosis Risk in Communities (ARIC) study. PLoS One 2014;9:e109552.
37. Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Speizer FE, Hennekens CH, Willett WC. Dietary protein and risk of ischemic heart disease in women. Am J Clin Nutr 1999;70:221–7.
38. Bernstein AM, Sun Q, Hu FB, Stampfer MJ, Manson JE, Willett WC. Major dietary protein sources and risk of coronary heart disease in women. Circulation 2010;122:876–83.
39. Sharma S, McFann K, Chonchol M, de Boer IH, Kendrick J. Association between dietary sodium and potassium intake with chronic kidney disease in US adults: a cross-sectional study. Am J Nephrol 2013;37:526–33.
40. Juraschek SP, Appel LJ, Anderson CA, Miller ER 3rd. Effect of a high-protein diet on kidney function in healthy adults: results from the OmniHeart trial. Am J Kidney Dis 2013;61:547–54.
41. Martin WF, Armstrong LE, Rodriguez NR. Dietary protein intake and renal function. Nutr Metab (Lond) 2005;2:25.
42. Joint WHO/FAO/UNU Expert Consultation. Protein and amino acid requirements in human nutrition. World Health Organ Tech Rep Ser 2007;(935):1–265 (back cover.).
43. Subar AF, Freedman LS, Tooze JA, Kirkpatrick SI, Boushey C, Neuhouser ML, Thompson FE, Potischman N, Guenther PM, Tarasuk V, et al. Addressing current criticism regarding the value of self-report dietary data. J Nutr 2015;145:2639–45.
44. USDA & DHHS. Scientific Report of the Dietary Guidelines Advisory Committee. 2015 [cited 2015 Dec 10]. Available at: http://health.gov/dietaryguidelines/2015-scientific-report/.