

# Association between Water Intake, Chronic Kidney Disease, and Cardiovascular Disease: A Cross-Sectional Analysis of NHANES Data

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## Key Words

Chronic kidney disease · Glomerular filtration rate · Water intake · Fluid intake · Cardiovascular disease

## Abstract

**Background:** Evidence from animal and human studies suggests a protective effect of higher water intake on kidney function and cardiovascular disease (CVD). Here the associations between water intake, chronic kidney disease (CKD) and CVD were examined in the general population. **Methods:** We conducted a cross-sectional analysis of the 2005–2006 National Health and Nutrition Examination Survey. Non-pregnant adults with an estimated glomerular filtration rate (eGFR)  $\geq 30$  ml/min/1.73 m<sup>2</sup> who were not taking diuretics were included. Total water intake from foods and beverages was categorized as low ( $<2.0$  l/day), moderate (2.0–4.3 l/day) and high ( $>4.3$  l/day). We examined associations between low total water intake and CKD (eGFR 30–60 ml/min/1.73 m<sup>2</sup>) and self-reported CVD. **Results:** Of 3,427 adults (mean age 46 (range 20–84); mean eGFR 95 ml/min/1.73 m<sup>2</sup> (range 30–161)), 13% had CKD and 18% had CVD. CKD was higher among those with the lowest ( $<2.0$  l/day) vs. highest total water intake ( $>4.3$  l/day) (adjusted odds ratio (OR) 2.52; 95% confidence interval (CI) 0.91–6.96). When stratified by

intake of (1) plain water and (2) other beverages, CKD was associated with low intake of plain water: adjusted OR 2.36 (95% CI 1.10–5.06), but not other beverages: adjusted OR 0.87 (95% CI 0.30–2.50). There was no association between low water intake and CVD (adjusted OR 0.76; 95% CI 0.37–1.59). **Conclusions:** Our results provide additional evidence suggesting a potentially protective effect of higher total water intake, particularly plain water, on the kidney.

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## Introduction

Arginine vasopressin (AVP) is an antidiuretic hormone that regulates thirst and water conservation in mammals. While essential for water regulation, AVP has vasoconstrictive effects and there is evidence that increased plasma levels can have negative effects on renal hemodynamics, blood pressure, and ventricular function [1–7]. AVP infusion increases proteinuria, renal plasma flow, and hyperfiltration, while administration of AVP antagonists reduces proteinuria and lowers blood pressure [1, 3, 8–11]. Although AVP is difficult to measure reliably in humans, a new assay for copeptin — a surrogate marker of AVP — shows promise as both a diagnostic and research

tool. The BRAHMS copeptin assay (in combination with troponin T) may improve early diagnosis of myocardial infarction in the emergency room setting [6, 12–14]. Copeptin positively associates with microalbuminuria in the general population [5, 15], and higher levels predict faster renal decline in kidney transplant recipients [16].

Increased water intake suppresses plasma AVP [17, 18] and exerts other hemodynamic effects [19]. In animal models, increased water intake has been shown to reduce proteinuria and slow renal progression [18, 20]. In humans, several observational studies show that greater water intake may have a possible protective effect on renal and cardiovascular outcomes [21–26]. In a large Canadian cohort, lower urine volume at baseline predicted faster decline in estimated glomerular filtration rate (eGFR) over follow-up [22]. In the Adventist Health Study, cardiovascular mortality was inversely associated with water intake, although not with other fluids. Most recently, researchers identified chronic dehydration from heat stress as the most likely causal factor in a perplexing epidemic of chronic kidney disease (CKD) in Central America [24, 25]. To examine the cross-sectional associations between water intake, CKD and cardiovascular disease (CVD) in the general population, we analyzed data from the National Health and Nutrition Examination Survey (NHANES). We also examined whether the relationship with total water intake differed for low vs. high intake of plain water vs. beverages other than plain water.

## Methods

### Sample

NHANES is an ongoing survey conducted in the USA by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention. Data from the 2005–2006 cohort were analyzed in the present study. NHANES participants (non-institutionalized US residents) are selected using a stratified, multistage national probability sampling design. Ethics approval for NHANES was obtained from the NCHS Research Ethics Review Board. Data collection for NHANES was approved by the NCHS Research Ethics Review Board. Analysis of de-identified data from the survey is exempt from the federal regulations for the protection of human research participants. Additional information about the 2005–2006 NHANES survey and methodology is available at [www.cdc.gov/nchs/nhanes.htm](http://www.cdc.gov/nchs/nhanes.htm).

### Data Collection and Measures

Participants completed an in-person structured interview, a physical examination (including height, weight and blood pressure measurements), and a computer-assisted 24-hour dietary recall. The dietary recall is a 5-step interview that includes multiple passes through the previous 24 h using standardized questions to help respondents recall and describe foods and beverages consumed [27,

28]. Total water intake was estimated from all foods and beverages consumed within the previous 24 h. Water intake from beverages was grouped as follows: plain water (defined by the NCHS as tap water, water from a drinking fountain or water cooler, non-carbonated bottled water, and spring water); energy drinks, sugar- or artificially-sweetened drinks (carbonated or non-carbonated); alcoholic drinks; coffee or tea; fruit and vegetable juices, and milk, soy milk and other dairy drinks. In the absence of recommended daily intake values for fluid consumption based on physiological parameters and health outcomes, researchers often group respondents based on percentiles of total water intake [29–32]. As such, we defined *low water intake* as intake below the 20th percentile of total water intake ( $<2.0$  l/day), *moderate intake* as intake between the 20th and 80th percentile ( $2.0$ – $4.3$  l/day), and *high intake* as intake greater than the 80th percentile of total water intake ( $>4.3$  l/day). We applied the same algorithm to categorize total intake of (1) plain water and (2) beverages other than plain water. Kidney function was estimated from isotope dilution mass spectrometry (IDMS)-standardized serum creatinine values, and eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) [33]; CKD (stage III) was defined as eGFR between 30 and 59 ml/min/1.73 m<sup>2</sup> (those with eGFR  $<30$  were excluded) [34]. CVD was defined as a composite of a self-reported physician diagnosis of coronary heart disease, myocardial infarction, stroke, congestive heart failure, or angina pectoris. Hypertension was defined as average systolic/diastolic blood pressure  $\geq 140/90$  mm Hg or self-reported antihypertensive medication use. Diabetes was defined based on participant self-report of a physician diagnosis. Finally, participants were categorized as sedentary or active based on self-reported physical activity [35].

### Inclusion/Exclusion Criteria

We included all adults aged 20–84 years with 1 day of complete and reliable dietary intake data. We excluded participants who were pregnant or had kidney cancer since these conditions may affect eGFR assessment. We also excluded participants taking lithium or diuretics because these medications may affect thirst and diuretics are often used when patients with heart failure are told to restrict their fluid intake (due to edema). Finally, we excluded those who reported weak or failing kidneys or treatment with dialysis in the past year and those who had an eGFR  $<30$  ml/min/1.73 m<sup>2</sup> because some patients with advanced kidney disease may be told to restrict fluid consumption (due to edema).

### Statistical Analyses

All analyses were weighted using the NHANES dietary examination sample weights and adjusted for the complex sampling design using SAS Version 9.2 (SAS Institute, Inc., Cary, N.C., USA). Percentages are adjusted for survey sampling weights and are therefore discordant with percentages derived from raw frequencies; for this reason, weighted percentages with standard errors (SE) are presented, but raw frequencies are not [36]. Odds ratios (ORs) and 95% confidence intervals (CIs) for CKD and CVD were calculated using weighted logistic regression analysis; the reference group for all analyses was the high water intake group. All multivariable models included age (per year) and sex. In addition, the following variables were considered for inclusion: ethnicity, highest level of completed education, body mass index (BMI), smoking status, dietary sodium intake (mg/day), physical activity, hypertension, and diabetes. Models were reduced using backward elimination at  $\alpha = 0.20$  [37, 38], unless elimination changed the

**Table 1.** Sample characteristics, overall and stratified by daily total water intake<sup>a</sup>

	All (n = 3,427)	Total daily water intake <sup>b</sup>		
		low <2.0 l/day (n = 906)	moderate 2.0–4.3 l/day (n = 1,948)	high >4.3 l/day (n = 573)
Mean age, years	45.5 (0.6)	47.4 (1.6)	45.9 (0.5)	42.2 (1.0)
Age >65, %	12.6 (1.0)	21.8 (2.5)	12.1 (1.0)	4.9 (1.0)
Female, %	49.9 (0.7)	68.9 (1.8)	48.7 (1.3)	34.5 (2.3)
Ethnicity, %				
Mexican-American	8.2 (1.0)	13.2 (1.7)	7.5 (1.0)	5.7 (1.2)
Other Hispanic	2.8 (0.6)	3.7 (1.3)	2.8 (0.7)	1.7 (0.7)
Non-Hispanic White	73.4 (0.3)	56.5 (4.2)	76.0 (2.5)	82.8 (2.7)
Non-Hispanic Black	10.6 (1.9)	19.1 (3.1)	9.2 (1.7)	6.4 (1.5)
Other	5.0 (0.6)	7.5 (2.0)	4.6 (0.9)	3.5 (0.6)
Highest level of completed education, %				
Less than high school	16.0 (1.6)	25.9 (2.3)	13.8 (1.8)	12.9 (2.3)
High school	24.8 (1.1)	26.1 (2.5)	25.4 (1.6)	21.8 (2.1)
Some college or advanced degree	31.3 (1.2)	25.8 (2.3)	32.2 (1.2)	34.3 (2.2)
College diploma or university degree	27.9 (2.4)	22.2 (3.2)	28.7 (2.5)	31.1 (3.0)
Mean BMI	28.4 (0.3)	27.8 (0.4)	28.5 (0.4)	28.4 (0.4)
BMI categories, %				
Underweight (<18.5 kg/m <sup>2</sup> )	6.2 (0.6)	8.4 (0.9)	5.9 (0.8)	5.1 (1.0)
Normal (18.5–24.9 kg/m <sup>2</sup> )	28.9 (1.5)	30.5 (1.9)	28.3 (1.7)	29.1 (3.1)
Overweight (25.0–29.9 kg/m <sup>2</sup> )	32.7 (1.1)	33.0 (1.0)	32.3 (1.2)	33.9 (2.7)
Obese (>30.0 kg/m <sup>2</sup> )	32.2 (1.9)	28.2 (2.0)	33.6 (2.0)	31.9 (3.5)
Smoking status, %				
Never, <100 cigarettes ever	49.9 (0.90)	57.1 (3.0)	51.1 (1.4)	38.9 (2.4)
Former	23.5 (1.1)	20.9 (2.7)	24.4 (1.4)	23.5 (2.6)
Current	26.6 (0.9)	22.1 (3.0)	24.5 (1.6)	37.6 (2.9)
Mean eGFR, ml/min/1.73 m <sup>2</sup>	95 (1.0)	95 (2.1)	94 (0.9)	95 (0.9)
Mean dietary sodium intake, mg/day	3,594 (55)	2,595 (78)	3,560 (26)	4,697 (137)
Physical activity level: sedentary, %	79.0 (1.2)	76.3 (2.3)	49.6 (1.3)	49.9 (2.5)
Hypertension, %	27.5 (1.4)	31.4 (3.5)	26.5 (1.5)	26.4 (2.6)
Currently taking medication for hypertension <sup>c</sup> , %	80.6 (2.3)	83.5 (5.1)	80.1 (2.8)	77.9 (5.7)
Diabetes, %	7.9 (0.8)	10.7 (2.0)	7.01 (0.7)	7.5 (1.4)

<sup>a</sup> Weighted means or proportions (SE) were generated using sample weights provided by the National Center for Health Statistics. <sup>b</sup> Total water intake was estimated from all foods and beverages consumed during the 24 h preceding the interview. <sup>c</sup> Only asked of respondents who reported having hypertension.

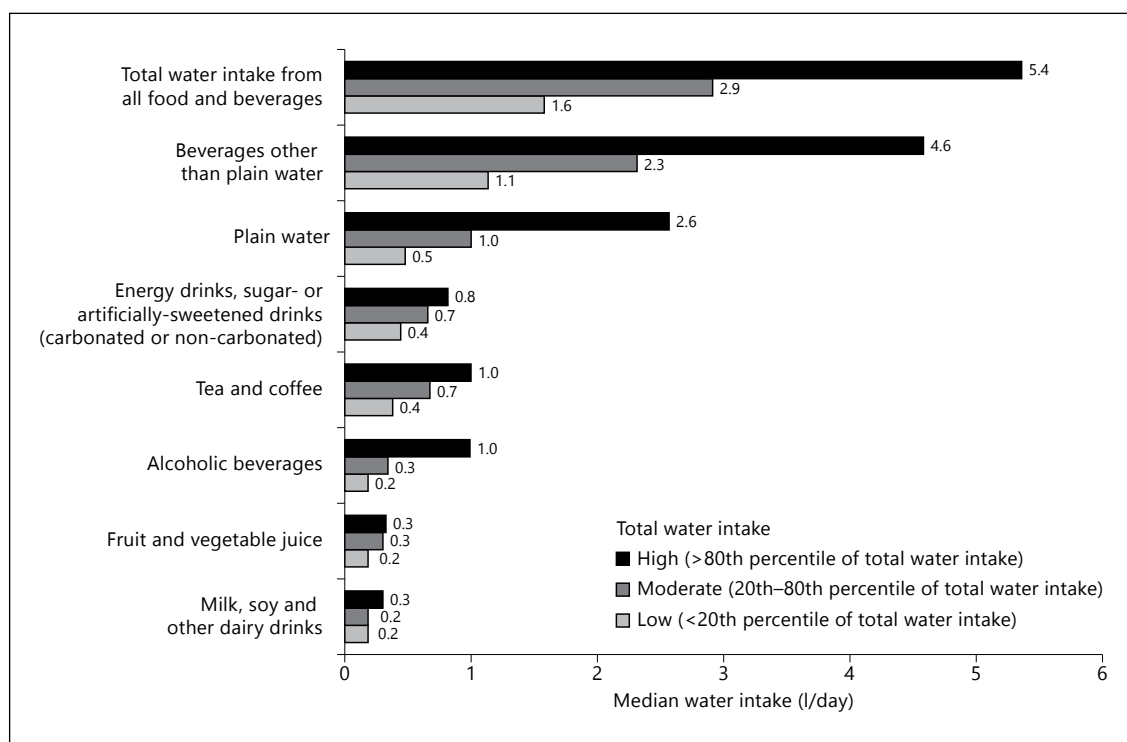
exposure outcome association by more than 10% [38, 39]. Separate analyses were run for low vs. high intake of (1) plain water and (2) beverages other than plain water. As recommended, we report 95% CIs, which incorporate the weighted variance estimates (rather than p values) to describe the precision of the estimates [40, 41].

## Results

The 2005–2006 NHANES cycle included 4,400 respondents aged 20–84 years who completed the dietary interview and physical examination. After exclusions for pregnancy (n = 316), kidney cancer, weak or failing kid-

neys, dialysis, or eGFR <30 ml/min/1.73 m<sup>2</sup> (n = 334), and lithium or diuretic medication use (n = 323), the final analytic sample included 3,427 participants. Sample characteristics, overall, and stratified by increasing water intake, are shown in table 1. Respondents were 50% female with a mean age of 46 (range 20–84) years; 13% were >65. Mean eGFR was 95 (range 30–161) ml/min/1.73 m<sup>2</sup>, and 13% had stage III CKD (eGFR 30–60 ml/min/1.73 m<sup>2</sup>).

Median daily water intake from all food and beverages was 2.9 liters, with 20% of total water coming from food. Median total water intake among those with low, moderate, and high intake was 1.6, 2.9, and 5.4 l/day, respec-



**Fig. 1.** Median daily water intake in liters (NHANES 2005–2006; n = 3,427).

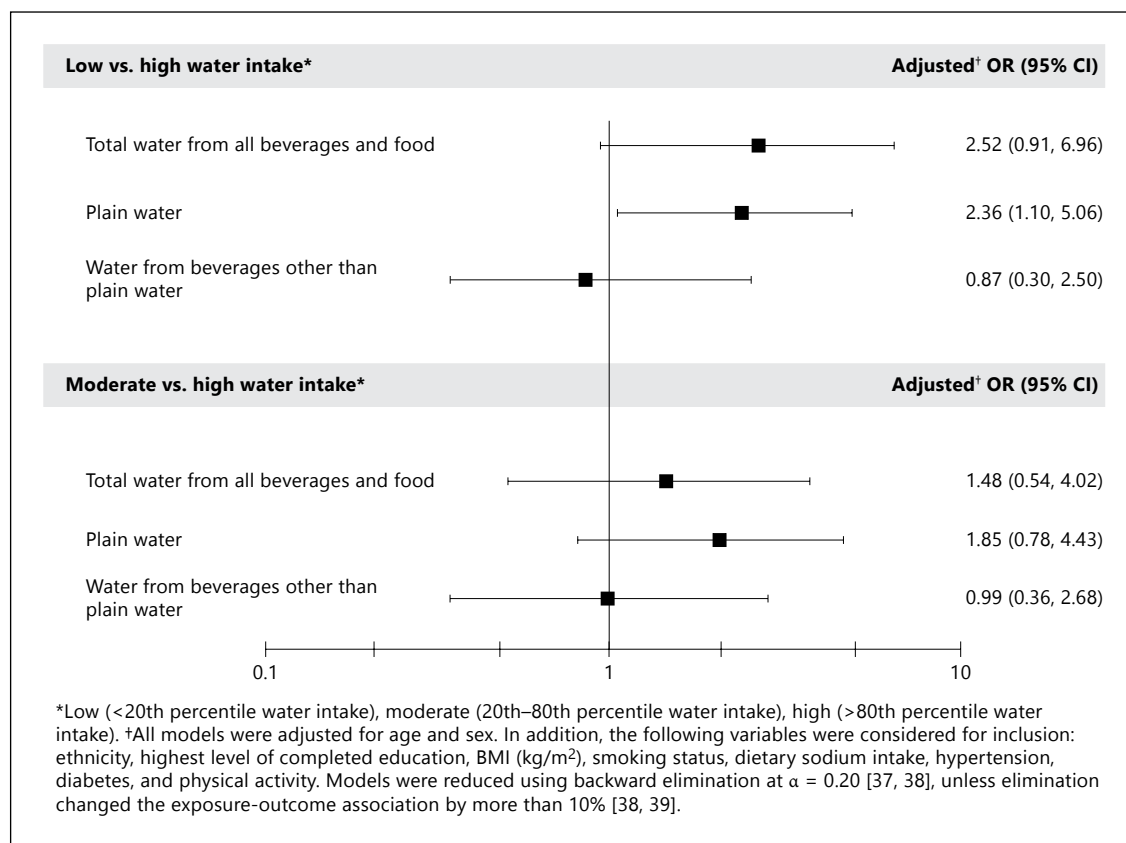
tively (fig. 1). Plain water was the most common beverage consumed (median intake 1.0 l/day) followed by energy drinks and sugar- or artificially-sweetened drinks (carbonated or non-carbonated): 0.7 l/day; tea and coffee: 0.7 l/day; alcoholic beverages: 0.4 l/day; fruit and vegetable juice: 0.3 l/day, and milk, soy and/or other dairy drinks: 0.2 l/day. Median daily intake for each beverage category among those with low, moderate and high total water intake is shown in figure 1.

Compared with those who had high water intake, those with low water intake were older (mean age 42 vs. 47), more likely to be female (35 vs. 69%), less likely to be non-Hispanic White (83 vs. 57%), less likely to have completed any education beyond high school (65 vs. 48%), less likely to be obese (32 vs. 28%), less likely to be current smokers (38 vs. 22%), more likely to be sedentary (50 vs. 76%), and to have hypertension (26 vs. 31%) or diabetes (8 vs. 11%) (table 1). Mean sodium intake was considerably higher in those with high vs. low water intake (4,697 vs. 2,595 mg/day).

The association between total water intake and reduced kidney function is shown in table 2. The prevalence of stage III CKD was highest among those with the lowest water intake (8.4%) and this decreased with increasing

water intake: 3.7 and 1.3% among those with moderate and high water intake, respectively. After adjusting for age, sex, ethnicity, BMI, smoking status, sodium intake, hypertension, and diabetes, the adjusted OR for CKD among those with low vs. high water intake was 2.52 (95% CI 0.91–6.96). As shown in figure 2, the association between water intake and CKD was qualitatively different for (1) plain water and (2) other beverages: the adjusted OR for CKD in those with low vs. high intake of plain water was 2.36 (95% CI 1.10–5.06). When beverages other than plain water were considered, the adjusted OR for low vs. high intake was 0.87 (95% CI 0.30–2.50).

CVD was reported by 18%. The association between water intake and CVD is shown in table 3. Compared with participants who had the highest water intake, those with lowest intake were more likely to report a history of coronary heart disease (1.7 vs. 3.3%), myocardial infarction (1.4 vs. 3.1%), stroke (1.8 vs. 2.6%), congestive heart failure (0.9 vs. 1.1%), and angina pectoris (1.3 vs. 1.6%). However, CVD was not associated with low water intake in multivariable analyses (adjusted OR 0.76; 95% CI 0.37–1.59). Results were similar when total water intake was restricted to plain water and to beverages other than plain water.



**Fig. 2.** Adjusted ORs and 95% CIs for CKD.

**Table 2.** Association between total water intake (from foods and beverages) and CKD

Total water intake	eGFR categories, ml/min/1.73 m <sup>2</sup> (prevalence, weighted percent)			Association with CKD <sup>a</sup> OR (95% CI)	
	30–60	60–90	>90	age and sex-adjusted	fully adjusted <sup>b</sup>
Low (<2.0 l/day)	8.4	32.5	59.1	2.15 (0.86–5.37)	2.52 (0.91–6.96)
Moderate (2.0–4.3 l/day)	3.7	34.6	61.7	1.42 (0.54–3.70)	1.48 (0.54–4.02)
High (>4.3 l/day)	1.3	32.3	66.3	reference	reference

<sup>a</sup> eGFR 30–60 ml/min/1.73 m<sup>2</sup>. <sup>b</sup> Adjusted for age (years), sex, ethnicity, BMI, dietary sodium intake (mg/day), smoking, hypertension, and diabetes.

## Discussion

In this cross-sectional analysis of a representative sample of the US population, the prevalence of stage III CKD was highest among those with the lowest water intake. Interestingly, the association between daily water

intake and CKD was only significant for low vs. high intake of plain water: OR 2.36 (95% CI 1.10–5.06), but not for low intake of beverages other than plain water: OR 0.87 (95% CI 0.30–2.50). No association was evident between low water intake and CVD: OR 0.76 (95% CI 0.37–1.59).

**Table 3.** Association between total water intake (from foods and beverages) and CVD

Total water intake	CVD (prevalence, weighted percent)						Association with CVD OR (95% CI)	
	coronary heart disease	heart attack	stroke	congestive heart failure	angina pectoris	composite of all CVD <sup>a</sup>	age- and sex-adjusted	fully adjusted <sup>b</sup>
Low (<2.0 l/day)	3.28	3.08	2.62	1.05	1.63	7.3	0.82 (0.43–1.55)	0.76 (0.37–1.59)
Moderate (2.0–4.3 l/day)	2.24	2.54	1.38	1.40	1.79	6.0	0.87 (0.43–1.77)	0.91 (0.44–1.89)
High (>4.3 l/day)	1.66	1.44	1.81	0.94	1.32	4.6	reference	reference

<sup>a</sup> Composite of coronary heart disease, myocardial infarction, stroke, congestive heart failure, and angina pectoris. <sup>b</sup> Adjusted for age (years), sex, ethnicity, BMI, physical activity, smoking, hypertension, and diabetes.

Although the relationship between hydration and health is controversial, with many unfounded claims in the popular media [42–44], our results are consistent with recent literature showing a specific beneficial effect of hydration on the kidney [18, 20, 22–25, 45–47]. In particular, our results [22] complement a longitudinal analysis of a Canadian cohort in which lower urine volume predicted faster renal decline over follow-up. Clark et al. [22] measured 24-hour urine volume in over 2,000 adults who were free of CKD at baseline. Kidney function was measured annually for 6 years. For each increasing category of baseline urine volume (<1, 1–1.9, 2–2.9, and ≥3 l/day), the percent annual eGFR decline was progressively slower (1.3, 1.0, 0.8, and 0.5%, respectively;  $p = 0.02$ ) — and those with the largest urine volumes were least likely to demonstrate rapid renal decline over follow-up. While Clark et al. did not collect data on the amount or type of fluid consumed, Strippoli et al. [23] conducted a cross-sectional analysis of an older Australian cohort (average age 66 years) and showed an inverse association between self-reported fluid intake and kidney function; however, they did not have data on plain water consumption and did not stratify by type beverage consumed. Participants with the highest quintile of fluid intake (>3.2 l/day) were significantly less likely to have CKD (eGFR <60 ml/min/1.73 m<sup>2</sup>) (OR 0.5; 95% CI 0.32–0.77). In contrast to these studies, in an observational study of patients with CKD, those with higher urine volumes had significantly faster renal decline [48]. This association may be partly explained by greater diuretic use among those with higher urine volumes. Also, because the kidneys concentrate urine less well as function declines, in patients with CKD, high urine volume could be the result, not the cause, of faster decline.

In addition to regulating fluid balance, the kidneys filter waste from the blood and may function more efficiently in

the presence of an abundant fluid supply [49, 50]. Higher water intake increases the clearance of sodium, urea and osmoles [51–53], and increased water intake is the most effective therapeutic measure to prevent kidney stones (and stones are also associated with loss of kidney function) [54–57]. Under conditions of low hydration, the kidneys produce more concentrated urine and there is some evidence that higher urine concentration may contribute to glomerular hyperfiltration and the development of albuminuria [8, 15, 46, 58, 59]. Exposure to chronic plasma volume depletion may make the kidneys more susceptible to subclinical injury, and accumulated damage from repeated insults may hasten the development of CKD [24]. This mechanism, exacerbated by heat stress, is believed to explain a recent epidemic of CKD among young male agricultural workers in Central America [24, 25].

Despite the robust relationships between vasopressin, copeptin, and cardiovascular outcomes, the relationship between water intake and CVD is less clear. Water drinking may elicit a pressor response mediated through sympathetic nervous system activation [19]. There is some evidence that dehydration might contribute to increased blood viscosity [60, 61], a known risk factor for ischemic heart disease and stroke [62, 63]. However, several interventions have failed to reduce blood viscosity with greater fluid intake [60, 61, 64, 65] — possibly because a benefit of greater water intake may not be realized in patients who are adequately hydrated, as appeared to be the case in one trial, where the baseline urine volume of patients was ~1.6 l/day [65]. Few studies have evaluated the direct effect of water intake on cardiovascular outcomes, and these have produced equivocal results. In the Adventist Health Study, fatal coronary heart disease was significantly lower among participants who drank ≥5 cups of water daily compared with <2 cups [21], however no associa-



tion was seen for high intakes of beverages other than water. In a Dutch cohort, neither total fluid intake nor plain water intake predicted fatal ischemic heart disease or stroke over 10 years of follow-up [66], however another prospective study found a significantly reduced risk of stroke recurrence among patients whose total self-reported water intake was  $>2$  l/day compared with  $\leq 2$  l/day [26].

In the present study and others, the association between water intake and renal and vascular outcomes appears to be modified by source of water, where a beneficial effect is seen with greater intake of plain water, but not other beverages [21, 67–69]. On the one hand, greater intake of plain water may be a marker for a healthier lifestyle. In a detailed dietary analysis of NHANES data by Kant et al. [28], plain water intake was positively correlated with education and fiber intake, and inversely correlated with age and sugar intake. The direction of these relationships reversed when other fluids were considered, and a positive correlation was seen between smoking and intake of other fluids. Despite this potential for confounding, a positive, causal effect of increased water consumption on kidney function is supported by several highly controlled studies of 5/6 nephrectomized rats, which show a consistent benefit of high water intake on preserving kidney function [18, 20, 45–47]. Even if increased hydration does in truth protect the kidney, any beneficial effect may be offset if total fluid consumption comes largely from sugar-sweetened beverages (usually sweetened with high-fructose corn syrup), which has been associated with the metabolic syndrome — and there is some evidence that fructose itself can cause kidney damage, perhaps by raising levels of uric acid [67, 70–72]. This is supported by data from large observational studies that link high intake of sugar-sweetened beverages ( $\geq 2$  cups/day) to albuminuria (OR 1.4; 95% CI 1.1–1.7), CKD (OR 2.3; 95% CI 1.4–3.7), and coronary heart disease (relative risk 1.4; 95% CI 1.1–1.69) [67–69].

Because this study was a cross-sectional analysis of observational data, conclusions about causality are not possible. Also, a 24-hour dietary recall may not accurately capture average long-term diet. Nonetheless, the 5-step multiple-pass dietary survey used in NHANES has been extensively studied and validated and is the most accurate method of dietary assessment for large population-based studies [27, 73, 74]. Moreover, our results are consistent with a diverse body of literature showing a beneficial effect of higher water intake on kidney function. We analyzed over 3,000 free-living adults in a nationally representative population in the USA. To minimize the potential for reverse causality, we also excluded those with advanced kidney disease ( $\text{eGFR} < 30$  ml/min/1.73 m<sup>2</sup>) and

those taking diuretics. Whereas CKD was defined using an objective measure of kidney function, CVD was defined based on self-reported physician diagnosis. Even though the sensitivity and specificity of self-reported cardiovascular outcomes are reasonably good, ranging from 66 to 90% [75–77] and from 98 to 99% [75, 77], respectively, outcome misclassification is likely, and this could have attenuated the association with this outcome. Although our results support a beneficial effect of higher water intake on kidney function, aggressive fluid loading should be avoided because of the attendant risk for hyponatremia [78, 79].

## Conclusion

Our analysis of a representative sample of the US population adds to a diverse body of literature showing a protective effect of higher water intake (particularly plain water) on the kidney. While our primary analysis considered total water intake from all foods and beverages combined, sensitivity analyses showed that CKD was inversely related to higher intake of plain water, but not other beverages, which is supported by other studies [21, 67–69]. Taken together, these findings are provocative, however evidence from a large, well-designed randomized controlled trial is needed to determine if higher water intake can truly protect the kidney and slow renal decline.

## Disclosure Statement

The present results have not been published previously in whole or part. Dr. W. Clark has received consulting fees or honorarium and support to travel to meetings from Danone Research.

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