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Original Article

Fluid intake and all-cause mortality, cardiovascular mortality, and kidney function: a population-based longitudinal cohort study

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ABSTRACT

Background. Drinking eight glasses of fluid or water each day is widely believed to improve health, but evidence is sparse and conflicting. We aimed to investigate the association between fluid consumption and long-term mortality and kidney function.

Methods. We conducted a longitudinal analysis within a prospective, population-based cohort study of 3858 men and women aged 49 years or older residing in Australia. Daily fluid intake from food and beverages not including water was measured using a food frequency questionnaire. We did multivariable adjusted Cox proportional hazard models for all-cause and cardiovascular mortality and a boot-strapping procedure for estimated glomerular filtration rate (eGFR).

Results. Upper and lower quartiles of daily fluid intake corresponded to >3 L and <2 L, respectively. During a median follow-up of 13.1 years (total 43 093 years at risk), 1127 deaths (26.1 per 1000 years at risk) including 580 cardiovascular deaths (13.5 per 1000 years at risk) occurred. Daily fluid intake (per 250 mL increase) was not associated with all-cause [adjusted hazard ratio (HR) 0.99 (95% CI 0.98–1.01)] or cardiovascular mortality [HR 0.98 (95% CI 0.95–1.01)]. Overall, eGFR reduced by 2.2 mL/min per 1.73 m^2 (SD 10.9) in the 1207 (31%) participants who had repeat creatinine measurements and this was not associated with fluid intake [adjusted regression coefficient 0.06 mL/min/1.73 m^2 per 250 mL increase (95% CI −0.03 to 0.14)].

Conclusions. Fluid intake from food and beverages excluding water is not associated with improved kidney function or reduced mortality.

Keywords: chronic kidney disease, fluid intake, glomerular filtration rate, mortality

INTRODUCTION

The intake of at least eight glasses of water [1] or fluid [2] daily to improve health is a widely held belief that is reinforced by national health bodies. It is biologically plausible that increased water intake can prevent chronic kidney disease (CKD); fluid ingestion suppresses arginine vasopressin (AVP), a circulating hormone that increases renal plasma flow and glomerular hyperfiltration [3, 4]. AVP inhibition lowers blood pressure, proteinuria and glomerulosclerosis in experimental CKD [5] and water intake ameliorates experimental tubulointerstitial injury following kidney ablation [6] to prevent progressive CKD and mortality in rodents [7].

However, despite the broad promotion and adoption of encouraged fluid or water intake in the general population, clinical studies evaluating consumption and risks of cardiovascular-related death appear conflicting [8, 9], and data for kidney function are sparse. In the Adventist Health Study, higher water intake was associated with reduced fatal coronary heart disease [9], whereas in the Netherlands Cohort study, higher fluid or water consumption had no association with mortality from heart disease or stroke [8]. A small randomized trial of 'encouraged water intake' found no effects on kidney function or quality of life [10]. In a cross-sectional study among older Australians, we found those with a daily fluid intake from food and beverages (not including water) of ≥3.2 L or more had an adjusted risk of CKD [estimated glomerular filtration rate (eGFR) <55 mL/min/1.73 m^2] half that of participants ingesting ≤1.8 L. Recently, a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES) showed that a water intake <2 L/day had an imprecise and non-significant association with CKD compared with a higher water intake (>4.3 lL/day) [11]. While non-randomized and experimental data may suggest benefits for fluid consumption, this health strategy is not without potential harm, as drinking in excess of thirst may lead to hyponatremia [12].

We undertook a longitudinal analysis of the Blue Mountains Eye Study cohort to evaluate higher dietary fluid intake as a strategy to reduce mortality and preserve kidney function in the general population.

MATERIALS AND METHODS

Study population

We conducted an analysis within an existing population-based cohort study in men and women, aged 49 years or older, living within a geographically defined region near Sydney, Australia (the Blue Mountains Eye Study). Participants had been identified by a door-to-door census of all residents in two urban postcode areas in the Blue Mountain region [13], recruited from 1992 to 1994 ($N = 3654$) and from 1999 to 2000 ($N = 1174$). Ethical approvals for the study were obtained from the Western Sydney Area Health Service Human Ethics Committee, and written informed consent was obtained from all participants. The research was conducted according to the recommendations of the Declaration of Helsinki.

Assessment of exposure

Participants were sent a 145-item self-administered food frequency questionnaire (FFQ), which they returned at the time of the baseline visit. The FFQ was a semi-quantitative instrument modified from the Willett FFQ [14] for the Australian diet and vernacular and included portion sizes. We found that the modified FFQ provided valid estimates of nutrient intake compared with weighed food records during three 4-day assessments for a subset of the cohort [15]. Baseline exposure data included the estimated total fluid content of food and beverages (including tea, coffee, milk, juices, sweetened drinks and alcohol) but not water. Water intake was not available as an exposure of interest, as daily water intake was not investigated by the FFQ. We categorized intake into quartiles which corresponded to <2.0 L/day, 2.0–2.4 L/day, 2.5–3.0 L/day and >3.0 L/day. All FFQs with between 13 and 25 missing values were checked and corrected for any data errors. After data cleaning, if >12 questions (8% of the questionnaire) or an entire page (even if fewer than 12 blank questions) remained incomplete, then the participant was excluded ($N = 3$).

At baseline, all eligible individuals participated in a detailed medical examination and collection of sociodemographic information. For the cohort recruited from 1992 to 1994, the serum creatinine level was assessed using the modified kinetic Jaffe reaction (Abbott Laboratories, North Chicago, IL, USA). The assessment method for creatinine changed to Isotope Dilution Mass Spectrometry (IDMS) (Roche Products Ltd, NSW, Australia) for the cohort recruited in 2002 to 2004. As a result of the change in methods, we applied a correction to creatinine data obtained using the Jaffe assay as follows: creatinine (IDMS) = creatinine (Jaffe) × 1.086–26 μmol/L [16]. The coefficient of variation was <2.3% for both analyses.

Outcomes

To identify participants who died during follow-up, we cross-matched demographic information with Australian National Death Index (NDI) data using probabilistic record linkage [17, 18]. We interrogated the NDI for mortality events occurring before 31 December 2007. Cause of death was also provided by the NDI using the *International Classification of Diseases* (ICD) *9th and 10th Revision* cause of death codes. We defined cardiovascular death using ICD-9 (410.0–9, 411.0–8, 412, 414.0–9) and ICD-10 (I21.0–9, I22.0–9, I23.0–8, I24.0–9, I25.0–9) [17]. Australian NDI data have previously been reported to have high sensitivity and specificity for both mortality (93.7 and 100%) and cardiovascular mortality (92.5 and 89.6%) [18, 19]. We estimated the change in kidney function between baseline and end of follow-up using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [20] and conducted sensitivity analyses using the Modification of Diet in Renal Disease (MDRD) equation [21].

Statistical analysis

We calculated baseline characteristics as number (proportion), mean [standard deviation (SD)] or median (range) where appropriate. We used the Cochran Mantel-Haenszel method to test for trends in baseline characteristics across quartiles of increasing fluid intake. We estimated overall survival using the Kaplan–Meier method according to quartiles of baseline reported fluid intake, using <2 L/day as the reference category. Cumulative incidence rates for all-cause and cardiovascular mortality were also calculated per 250 mL increase in daily intake. We applied univariable and multivariable-adjusted Cox proportional hazard models to assess the relationship between all-cause and cardiovascular mortality and fluid consumption while controlling for age, sex, history of acute myocardial infarction, stroke, diabetes, or cancer, smoking, education, employment, blood pressure, eGFR, and serum HDL cholesterol, platelet count, white cell count, and fibrinogen. We calculated hazard ratios (HRs) and their 95% confidence intervals (CI) for the association between fluid intake (per 250 mL increase) and all-cause (and cardiovascular)

mortality. HRs were also calculated using unadjusted and adjusted multivariable models comparing drinking >2.0 L/day, in quartiles with those drinking <2.0 L/day. To assess the robustness of the analyses, we also adjusted for the effects of fluid intake relative to the body weight in all analyses by considering the fluid intake per unit of body weight at baseline as the exposure of interest.

We assessed the association between fluid intake and change in kidney function during follow-up using the boot-strapping procedure proposed by Heymans *et al.* [22]. Boot-strapping was used because it is a standard method of assigning measures of accuracy to the sample estimates when the underlying distribution for the test statistics is not known. Boot-strapping uses the available 'sample' as the surrogate of the population from which an approximate distribution of a test statistic can be made. First, we performed a sampling with replacement to generate 1000 bootstrap replicates. Second, for every bootstrap replicate, we then performed linear regression and identified the optimal set of predictor variables using the Bayesian information criterion (BIC) considering variables included in the models for mortality. Finally, we determined the percentage of bootstrap replicates in which a predictor variable was selected using BIC. The variables that were selected in at least 40% of the bootstrap replicates represented the most important predictors of change in kidney function. We used the open-source software R [R Foundation for Statistical Computing 2012, Vienna Austria (http://www.R-project.org/)] for analyses.

RESULTS

Characteristics of included participants and total fluid intake

A total of 4828 men and women were included in the survey. We could include 3858 (79.8%) participants from the overall population [1690 men, 2168 women; mean age 70.3 years (SD 9.9 years)] who provided useable data for fluid intake and baseline characteristics (Table 1). Average reported fluid consumption was 2.48 L/day, while 274 (7.1%) reported consumption <1.5 L/day. Higher intake at baseline was associated with younger age, being male, higher educational attainment, shared living, employment, better kidney function, higher haemoglobin, and higher intake of other nutrients and energy consumption.

Incidence rate of all-cause and cardiovascular mortality

The median length of follow-up was 13.1 (95% CI 11.1–13.9) years for a total of 43 093 years at risk. Of the total, 1127 cohort participants died (26.1/1000 years at risk) including 580 cardiovascular deaths (13.5/1000 years at risk). During follow-up, there were 301 deaths (143 cardiovascular deaths) for those who consumed <2 L, 318 deaths (171 cardiovascular deaths) for those who consumed 2.0–2.4 L, 289 deaths (154 cardiovascular deaths) for those who consumed 2.5–3.0 L and 219 deaths (112 cardiovascular deaths) for those who consumed >3.0 L.

We analysed risks of death considering daily fluid intake from food and beverages as a continuous variable (per 250 mL increase). We observed a significant association between lower intake and all-cause mortality in unadjusted analyses (HR: 0.97, 95% CI 0.95–0.99) but not cardiovascular mortality (HR, 0.98, 95% CI 0.95–1.01). When we categorized intake into quartiles of intake across the study population, the unadjusted HRs for all-cause mortality for each quartile of increasing fluid intake were: 0.89 (95% CI 0.76–1.05), 0.97 (95% CI 0.83–1.14) and 0.79 (95% CI 0.67–0.94) for fluid intake of 2.0–2.4 L/day, 2.5–3.0 L/day and >3.0 L/day compared with <2.0 L/day, respectively. The corresponding unadjusted HRs for cardiovascular mortality for each quartile of increasing fluid intake were 1.01 (95% CI 0.81–1.26), 1.08 (95% CI 0.86–1.36) and 0.85 (95% CI 0.66–1.09) for intake of 2.0–2.4 L/day, 2.5–3.0 L/day and >3.0 L/day compared with <2.0 L/day, respectively.

When we controlled analyses for clinical and demographic variables, the association between daily fluid intake and all-cause mortality was no longer significant [adjusted HR 0.99 (95% CI 0.98–1.01)] per 250 mL increase. The adjusted HR for cardiovascular mortality was 0.98 (95% CI 0.95–1.01) per 250 mL increase. When considered as quartiles of fluid intake, when compared with the lowest intake, the adjusted risk for death from any cause did not differ significantly for each quartile of increasing intake (Table 2 and Figure 1). The adjusted HRs for death were 0.96 (95% CI 0.74–1.23), 1.21 (95% CI 0.93–1.57) and 0.91 (95% CI 0.68–1.21) for intake of 2.0–2.4 L/day, 2.5–3.0 L/day and >3.0 L/day when compared with <2.0 L/day, respectively. Nor was there any association between cardiovascular mortality and intake across quartiles of increasing consumption (Table 2 and Figure 2).

Change in kidney function

Of the 3654 participants included in the first cross-sectional survey, 1479 (41%) had repeated measures of serum creatinine at the 10-year follow-up examination. We excluded a further 271 participants from the analyses because of missing values of fluid consumption and other variables of interest, leaving a total of 1207 (31% of 3858 overall) for the final analyses (Supplementary Table S1). The mean length of follow-up for kidney function was 10.8 (95% CI 10.5–11.4) years. The mean reduction in eGFR (at 10 years compared with baseline) was 2.2 (SD 10.9) mL/min/1.73 m^2.

Our bootstrap procedure identified six variables as important predictors of reduction in eGFR over time—age, systolic blood pressure, diastolic blood pressure and fibrinogen, diabetes and angina (Table 3). There was no statistically significant association between 'daily fluid intake' and change in eGFR. Next, we considered a linear model that explicitly included 'daily fluid intake' as a predictor variable in addition to the six predictor variables [23]. We observed that the 95% CI for 'daily fluid intake' included 0, which once again implied that the association between 'daily fluid intake' and change in eGFR was not statistically significant [adjusted regression coefficient, 0.06 mL/min/1.73 m^2 per 250 mL increase (95% CI −0.03 to 0.14)].

Sensitivity analyses

Adjustment for total fluid consumption with body weight showed no impact on the overall association between

Table 1. Baseline characteristics of participants (n = 3858)

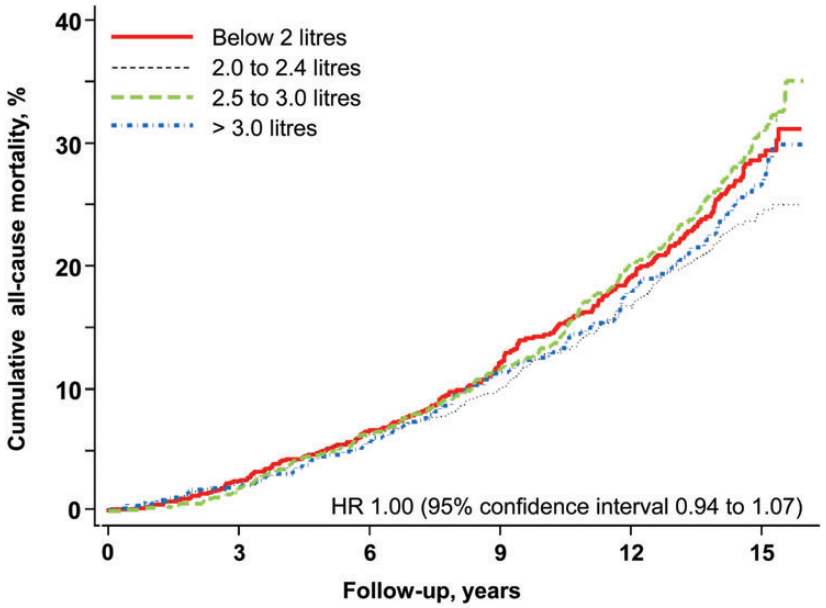
Characteristics	All participants N = 3858	Daily fluid intake				P-value[a]
		Quartile 1 (<2 L per day) N = 973	Quartile 2 (2–2.4 L per day) N = 1129	Quartile 3 (2.5–2.9 L per day) N = 914	Quartile 4 (≥3.0 L per day) N = 842	
Demographics						
Age, mean (SD), years	70.3 (9.9)	70.3 (9.9)	70.9 (9.9)	65.2 (9.5)	63.9 (8.8)	<0.001
Male, No. (%)	1690 (43.9)	385 (39.6)	470 (41.6)	395 (43.2)	440 (52.3)	<0.001
White race, No. (%)	3746 (97.2)	936 (96.2)	1097 (97.2)	897 (981)	816 (96.9)	0.5
Employed, No. (%)	1029 (26.7)	245 (25.2)	271 (24.0)	245 (26.8)	268 (31.8)	0.005
Ever smoked, No. (%)	1989 (51.6)	476 (49.0)	562 (49.8))	467 (51.1)	484 (57.5)	<0.001
eGFR (SD), mL/min per 1.73 m^2	66.9 (17.6)	66.2 (17.8)	65.9 (17.9)	66.3 (16.9)	69.7 (17.3)	<0.001
Prevalent disease, No. (%)						
Diabetes	214 (5.6)	59 (6.1)	52 (4.6)	51 (5.6)	52 (6.2)	0.2
Hypertension	1505 (39.0)	399 (41.0)	445 (39.4)	362 (39.6)	299 (35.5)	0.2
Angina	386 (10.0)	98 (10.1)	119 (10.5)	89 (9.7)	80 (9.5)	0.6
Myocardial infarction	288 (7.5)	77 (7.9)	84 (7.4)	61 (6.7)	66 (7.8)	0.3
Stroke	158 (4.1)	48 (4.9)	49 (4.4)	31 (3.4)	30 (3.6)	0.2
Cancer	751 (19.5)	186 (19.1)	209 (18.5)	194 (21.2)	162 (19.2)	0.5
Body mass index, mean (SD), kg/m^2	26.7 (4.7)	26.6 (4.8)	26.7 (4.9)	26.6 (4.6)	26.8 (4.2)	0.8
Body surface area (m^2)	1.8 (0.2)	1.8 (0.2)	1.8 (0.2)	1.7 (0.2)	1.8 (0.2)	0.1
Systolic blood pressure, mean (SD), mmHg	145.4 (38.8)	145.4 (35.4)	145.8 (41.4)	145.8 (21.3)	144.3 (36.2)	0.8
Diastolic blood pressure, mean (SD), mmHg	84.7 (31.3)	84.7 (31.1)	85.3 (40.0)	83.9 (10.5)	84.8 (33.2)	0.8
Serum cholesterol, mean (SD) (mg/dL)	5.9 (1.1)	5.9 (1.1)	5.9 (1.1)	5.9 (1.2)	5.9 (1.1)	0.6
HDL cholesterol, mean (SD), (mg/dL)	1.4 (0.4)	1.4 (0.4)	1.5 (0.4)	1.4 (0.4)	1.4 (0.4)	0.4
Serum triglycerides, mean (SD) (mg/dL)	1.7 (1.1)	1.7 (1.1)	1.7 (1.1)	1.7 (1.0)	1.8 (1.2)	0.3
Platelet count, mean (SD), ($\times 10^9$/L)	262.3 (63.9)	264.8 (67.1)	263.3 (64.9)	261.2 (62.5)	258.1 (60.0)	0.1
Haemoglobin, mean (SD), g/L	128.5 (12.6)	148.3 (13.2)	148.1 (12.5)	148.1 (12.4)	149.7 (12.2)	0.02
White cell count, mean (SD) ($\times 10^9$/L), g/L	6.5 (1.8)	6.5 (1.7)	6.5 (1.9)	6.4 (1.7)	6.4 (1.7)	0.4
Fibrinogen, mean (SD), g/L	4.0 (1.1)	4.0 (1.1)	4.0 (1.1)	40. (1.1)	3.9 (1.0)	0.2
Nutrition status						
Calcium intake, mean (SD), g	0.9 (0.4)	0.6 (0.3)	0.8 (0.3)	1.0 (0.3)	1.2 (0.5)	<0.001
Sodium intake, mean (SD), g	2.1 (0.8)	1.6 (0.6)	2.0 (0.6)	2.2 (0.7)	2.6 (0.8)	<0.001
Phosphate intake, mean (SD), g	1.5 (0.5)	1.1 (0.4)	1.4 (0.4)	1.7 (0.4)	2.0 (0.5)	<0.001
Potassium intake, mean (SD), g	3.8 (1.2)	2.7 (0.8)	3.5 (0.7)	4.1 (0.9)	5.0 (1.2)	<0.001
Sugar intake (per 100 g)	1.2 (0.5)	0.9 (0.4)	1.2 (0.4)	1.4 (0.5)	1.6 (0.6)	<0.001
Fibre intake (per 100 g)	0.3 (0.2)	0.2 (0.1)	0.3 (0.1)	0.3 (0.1)	0.4 (0.1)	<0.001
Protein intake (per 100 g)	0.9 (0.3)	0.7 (0.2)	0.8 (0.2)	1.0 (0.2)	1.1 (0.3)	<0.001
Fat intake (per 100 g)	0.8 (0.3)	0.6 (0.2)	0.7 (0.2)	0.8 (0.3)	0.9 (0.3)	<0.001
Carbohydrate intake (per 100 g)	2.4 (0.8)	1.8 (0.6)	2.2 (0.6)	2.5 (0.7)	3.0 (0.8)	<0.001
Energy intake, mean (SD), per 1000 kJ	8.5 (2.6)	6.6 (1.9)	8.0 (1.9)	9.2 (2.1)	10.8 (2.5)	<0.001
Fluid intake per body weight (mL/kg)	36.7 (11.8)	24.1 (6.6)	33.1 (6.8)	38.5 (7.8)	47.7 (10.7)	<0.001

[a]For trend across quartiles.

Table 2. Risk factors for mortality (n = 3858)

Variable adjusted for all others	All-cause mortality		Cardiovascular mortality	
	Adjusted HR	95% CI	Adjusted HR	95% CI
Demographics				
Age	1.02	1.01–1.03	1.05	1.04–1.06
Male	2.10	1.81–2.50	1.80	1.47–2.20
History of smoking	0.96	0.86–1.06	1.03	0.91–1.16
Higher tertiary qualification	1.16	1.01–1.33	1.20	0.97–1.41
Being employed	0.65	0.54–0.77	2.39	1.69–3.38
History of any cancer[a]	1.76	1.53–2.03	0.90	0.71–1.14
History of acute myocardial infarction	1.56	1.26–1.89	1.95	1.53–2.49
History of diabetes	1.30	1.03–1.64	0.86	0.60–1.22
History of stroke	1.49	1.17–1.90	1.68	1.22–2.30
Body mass index (kg/m^2)	0.98	0.96–0.99	0.98	0.96–1.00
Systolic blood pressure (per 10 mmHg increase)	1.11	1.07–1.15	1.10	1.05–1.16
Diastolic blood pressure (per 10 mmHg increase)	0.86	0.79–0.73	0.87	0.78–0.97
Laboratory measurements				
eGFR (per 10 mL/min per 1.73 m^2 decrease)	1.30	1.22–1.39	1.16	1.07–1.26
HDL cholesterol (mg/dL)	1.35	1.14–1.59	1.16	0.90–1.48
White cell count (×10^9), g/L	1.09	1.05–1.12	1.09	1.04–1.14
Platelet count (×10^9), g/L	0.79	0.70–0.89	0.72	0.61–0.85
Fibrinogen, g/L	1.19	1.12–1.26	1.12	1.07–1.26
Total daily fluid intake, L				
<2.0 (reference category)	1.00	Reference	1.00	Reference
2.0–2.4	0.96	0.74–1.23	0.97	0.77–1.24
2.5–2.9	1.21	0.93–1.57	1.15	0.90–1.48
≥ 3.0	0.91	0.68–1.21	0.91	0.70–1.19

[a]Excluding non-melanocytic skin cancers.

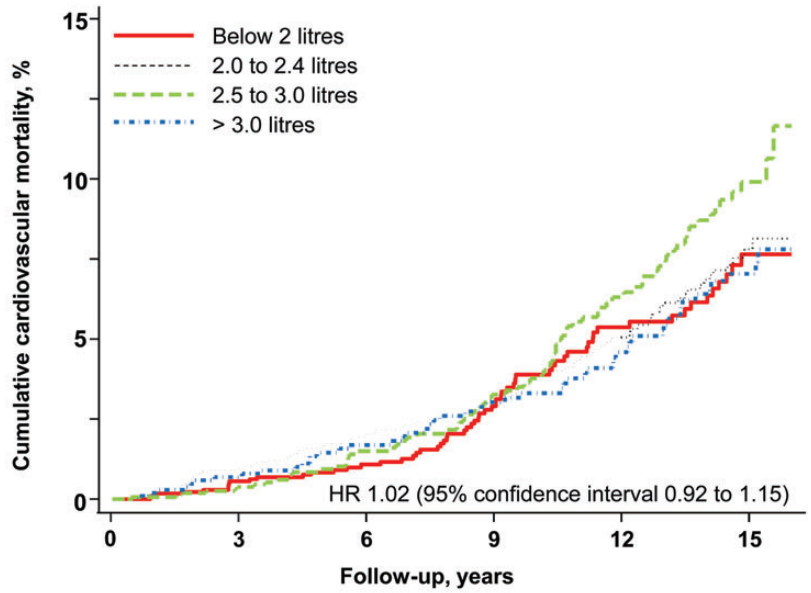


Number at risk

Less than 2.0 litres	578	549	507	463	416	210
2.0 to 2.4 litres	665	635	587	550	497	232
2.5 to 3.0 litres	584	563	517	477	425	211
>3.0 litres	520	504	475	440	402	206

FIGURE 1: All-cause mortality, stratified by self-reported daily fluid consumption (n = 3858).

cardiovascular and all-cause mortality in the adjusted model. The fully adjusted HRs of cardiovascular and all-cause mortality after taking into consideration of the total body weight were 1.02 (95% CI 0.98–1.05) and 1.01 (95% CI 0.98–1.05) for every millilitre per kilogram increase in total fluid intake, respectively. We also analysed mortality risk comparing very low fluid intake (<1.5 L) with 1.5 L or more and found no association with all-cause [adjusted HR 1.11 (95% CI 0.93–1.35)] or cardiovascular



Number at risk						
Less than 2.0 litres	578	549	507	463	416	210
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2.5 to 3.0 litres	584	563	517	477	425	211
>3.0 litres	520	504	475	440	402	206

FIGURE 2: Cardiovascular mortality, stratified by self-reported daily fluid consumption ($n = 3858$).

Table 3. Risk factors for change in kidney function ($n = 1207$)

Variable	Adjusted regression coefficient [change in eGFR (mL/min per 1.73 m^2) per 250 mL/day increase in fluid consumption]	P-value
Intercept	9.23	0.1
Age	−0.10	0.1
Systolic blood pressure	−0.086	0.004
Diastolic blood pressure	0.09	0.1
Fibrinogen	−0.63	0.06
History of angina	−3.62	0.02
Diabetes mellitus	−6.91	0.003
Fluid intake	0.06	0.6

mortality [adjusted HR 0.99 (95% CI 0.79–1.25)]. Using the MDRD equation to estimate GFR did not materially alter the association we observed between daily fluid intake and change in kidney function during follow-up.

DISCUSSION

In this analysis of a prospective, population-based cohort study of older adults, a higher daily fluid intake from food and beverages excluding water is not associated with a reduction in long-term all-cause or cardiovascular mortality or kidney function. Specifically, consuming over 3 L/day (roughly 12.5 glasses) does not alter risk of dying compared with an intake <2 L/day (~8 glasses) over ~13 years. We also found no evidence for increased mortality with very low fluid consumption (<6 glasses/day). In addition, increased fluid consumption (per 250 mL increase) is not associated with better kidney function over 10 years. Overall, these data do not support the hypothesis that fluid consumption above eight glasses per day lowers fatal events or protects against CKD.

There are widely and strongly held beliefs that people should consume eight or more glasses of water [1] or fluid [2] each day, even though supporting data are weak or conflicting [8, 9, 11, 24–26]. A cross-sectional study suggested a link between serum osmolality and prevalent coronary artery disease, leading to a hypothesis that dehydration might play a pathogenic role in atherosclerosis [27]. A randomized trial evaluated the clinical effects of water intake, although not on cardiovascular or mortality outcomes [10]. Advice to increase daily water intake by 1.5 L compared with placebo syrup in 141 healthy older men resulted in no difference in blood pressure, kidney function or quality of life between groups after 6 months, without episodes of hyponatremia [10]. The actual difference in water intake achieved between groups was small (~350 mL). To date, however, no randomized trial of water or fluid consumption on mortality or long-term kidney function has been reported.

Two previous longitudinal cohort studies evaluated the links between water or fluid consumption and cardiovascular mortality with conflicting results. In 20 297 white individuals living in Seventh-day Adventist households in California and without existing cardiovascular disease or diabetes, drinking five or more glasses of water/day compared with two or fewer was associated with reduced cardiovascular mortality over 6 years by one-half in men and one-third in women, whereas fluids other than water were associated with increased fatal coronary heart disease in men [9]. In the Netherlands Cohort Study of 3970 individuals aged between 55 and 69 years, no

association between total fluid intake (at least 1.5 L/day) and death due to ischaemic heart disease or stroke was observed during a decade of follow-up [8]. There was no association between water intake and cardiovascular mortality, although fresh water consumption was generally very low. The reasons for the differing conclusions in each of these studies and the current analysis are unclear but may relate to the volumes of fluid ingested, the potentially differing effects of water compared with fluid other than water on clinical outcomes, the analytical models used or baseline risks of cardiovascular disease.

The relationship between fluid or water intake and kidney function in existing data is similarly sparse and at high risk of bias. In a cross-sectional analysis, we recently found an inverse dose-dependent association between fluid intake from food and beverages except water and the prevalence of CKD (higher fluid intake was linked to a lower risk of kidney disease) [28]. In contrast, in a cross-sectional analysis of the general US population from the NHANES, higher water intake (greater than the 80th percentile of 4.3 L/day) was associated with an imprecise and non-significant adjusted risk of CKD compared with the lowest water intake (<2.0 L/day). Additionally, in the MDRD study (baseline GFR, 25–55 mL/min per 1.73 m^2), higher urine volumes were associated with more rapid progression of pre-existing moderately severe CKD although whether larger urine volumes were a cause or consequence of CKD remains speculative [29]. Longer term fluid restriction potentially stimulates the release of AVP (or antidiuretic hormone), which in turn may both increase glomerular filtration [30] (leading possibly to chronic glomerular hyperfiltration [31]) and lower sodium excretion [32]. Both may lead to chronic kidney damage [33] or hypertension [34], in part via volume expansion, although these clinical sequelae of vasopressin action remain hypothetical. Even in individuals with polycystic kidney disease, balancing the relative benefits of drinking water (reducing AVP release, which has a potentially pathogenic role in kidney cyst formation [35]) against the potential harms of increasing urine flow (potentially associated with more rapid progression of CKD [29]) remains problematic.

Our study has a number of important strengths. The cohort was community-based and included all residents of a particular geographic area and had a high participation rate, thus minimizing the potential for selection bias. The findings should therefore be generally applicable to older community-dwelling adults of European descent. We recorded over 1000 deaths and 500 cardiovascular deaths during follow-up of over 13 years, providing sufficient power to adjust for potential confounding variables in our analyses, although residual confounding from measured and unmeasured variables is likely. We minimized loss to follow-up (attrition-bias) for mortality to ensure all relevant outcome events were captured using a comprehensive national database for deaths.

Our study does have some important potential limitations. We estimated total fluid consumption excluding water intake, as the FFQ we used did not include a specific question about water consumption. Accordingly, any potential differences in associations between water intake, as opposed to the intake of beverages other than water, with mortality and kidney function which have been observed in previous studies could not be discerned. Furthermore, we did not have data for fluid intake during follow-up. It is possible that there was loss of separation between groups for fluid intake over time which may have underestimated a link between fluid intake and clinical outcomes. As such, an intervention trial—if feasible—would be needed to establish a causal relationship between intake and kidney disease progression and mortality. Our population was predominantly white; clinically relevant racial differences exist in water and sodium handling that might modulate the effects of fluid intake [36] and limit the applicability of our findings to non-Caucasian populations. Our study only assessed fluid intake in older adults. We did not record fluid intake in younger adults or know whether the fluid consumption recorded by the participants accurately reflected fluid intake through the earlier years of their adult lives or was stable during follow-up. Lower fluid consumption at a younger age may have influenced long-term neurohormonal activation, such as increased AVP release or elevated activity of the renin-angiotensin-aldosterone axis, which in turn may adversely influence cardiovascular risk and kidney function, but which could not be explored. We used a novel and robust model for assessing kidney function across the study period; however, substantial loss to follow-up occurred for measurements of kidney function, and an additional study with prospective evaluation of kidney function is now required. A change in the laboratory technique for creatinine for each contributing cohort may have confounded our analysis.

This study does not support the recommendation that people should consume at least eight glasses of fluid each day. More and better evidence is needed before encouraged fluid or water intake is known to be both beneficial and safe. Until then, we suggest specific fluid intake targets are not appropriate in general health advisory statements. Similarly, specific water intake advisories are not warranted based on the lack of currently available evidence. Given the limitations of our study and the importance of new strategies to improve health in the general population, additional prospective studies of fluid intake including those of encouraged water consumption on key health outcomes including CKD and mortality are needed. However, given that non-randomized studies will be limited by confounding, these data suggest a clustered randomized trial of encouraged water intake versus no intervention is needed to answer questions about the role of recommended minimum fluid targets on improving population health. Trials could also be undertaken in high risk populations such as those with urinary tract infections or renal calculi to evaluate kidney outcomes. One possibility would be to conduct small scale clinical trials to contribute to a prospective meta-analysis.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

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CONFLICT OF INTEREST STATEMENT

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