Total volume and composition of fluid intake and mortality in older women: a cohort study

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ABSTRACT

Objectives: The health benefits of “drinking at least 8 glasses of water a day” in healthy individuals are largely unproven. We aimed to examine the relationship between total fluid intake and the sources of fluid composition, risk of rapid renal decline, cardiovascular disease (CVD) mortality and all-cause mortality in elderly women.

Design, setting and participants: We conducted a longitudinal analysis of a population-based cohort study of 1055 women aged ≥70 years residing in Australia.

Main outcome measures: The associations between total daily fluid intake (defined as total volume of beverage excluding alcohol and milk) and the types of fluid (water, black tea, coffee, milk and other fluids) measured as cups per day and rapid renal decline, CVD and all-cause mortality were assessed using adjusted logistic and Cox regression analyses.

Results: Over a follow-up period of 10 years, 70 (6.6%) experienced rapid renal decline and 362 (34.4%) died, of which 142 (13.5%) deaths were attributed to CVD. The median (IQR) intake of total fluid was 10.4 (8.5–12.5) cups per day, with water (median IQR) 4 (2–6) cups per day and black tea (median IQR 3 (1–4) cups per day) being the most frequent type of fluid consumed. Every cup per day higher intake of black tea was associated with adjusted HRs of 0.90 (95% CI 0.81 to 0.99) and 0.92 (95% CI 0.86 to 0.98) for CVD mortality and all-cause mortality, respectively. There were no associations between black tea intake and rapid renal decline, or between the quantity or type of other fluids, including water intake, and any clinical outcomes.

Conclusions: Habitual higher intake of black tea may potentially improve long-term health outcomes, independent of treating traditional CVD risk factors, but validation of our study findings is essential.

INTRODUCTION

It is a widely held belief that adequate water intake improves health outcomes, including reducing the risk of chronic kidney disease (CKD) and cardiovascular disease (CVD). The notion that high water intake could potentially prevent the development of CKD, in part, be attributed to the inhibition of arginine vasopressin (AVP), a hormone known to be associated with glomerular hyperfiltration and injury. In addition to the effects on the glomerulus, high water intake had been shown to ameliorate tubulointerstitial injury in animal models, possibly via inhibition of the profibrotic cytokine, tumour necrosis factor-β. The association between water or total fluid intake and the risk of CVD is less clear; however, it is well established that CVD risk is highly associated with increasing severity of CKD. The potential beneficial effects of water and other fluid ingestion may, in part, be attributed to its effect on preventing pre-renal states, thus preservation of kidney function. Nevertheless, the exact association between fluid intake and CKD is often difficult to discern as dietary modifications, including fluid restriction, could potentially follow a diagnosis of CKD rather than precede it and therefore evaluating CVD mortality and all-cause mortality may be more appropriate clinical outcomes.

Epidemiological studies of fluid intake have reported conflicting findings. The Adventist Health population cohort study,
comprising 20,000 participants of both genders, suggested that a higher intake of water (but excluding other types of fluid) may be protective with a 40% reduction in CVD mortality among those drinking over five or more glasses of water per day compared with two or fewer glasses per day. On the contrary, the Netherlands cohort study of over 120,000 participants aged 55–69 years of both genders did not find any association between higher amounts of fluid consumption and CVD or stroke mortality.8–10 With the ongoing uncertainty of the beneficial health effects of water and other fluid consumption, plus the known differential effect of gender on CVD mortality, it is therefore crucial to examine the effects of the quantity of daily total fluid consumption and the types of fluid consumption on long-term health outcomes in gender-specific populations.

We hypothesise that a higher intake of fluid consumption, particularly water intake, is associated with improved health outcomes in elderly women. The aims of this analysis are twofold. First, to determine whether a higher total daily fluid consumption is associated with a slower renal function decline and reduction in 10-year risk of CVD mortality and all-cause mortality; and second, to evaluate the relative kidney-related CVD mortality and all-cause mortality benefits of the different types of fluid compositions, including water and other beverages.

METHODS
Study population
One thousand five hundred women aged over 70 years, with a majority from higher socioeconomic groups, were recruited in 1998 in Perth, Western Australia to a 5-year prospective randomised controlled trial of oral calcium supplements (1.2 g of elemental calcium daily or matching placebo from 1998 to 2003) to prevent osteoporotic fractures. The details of the recruitment into this Calcium Intake Fracture Outcome Study (CAIFOS; Australian Clinical Trials Registry Registration Number: ACTRN012607000055404) have been previously published.11 At the completion of CAIFOS, participants were followed in an observational study for a further 10 years (2003–2013). Our study data and analyses are derived from these two associated studies. The Human Research Ethics Committee of the Western Australian Department of Health (DOHWA HREC) approved the data linkage study (approval number #2009/24) between CAIFOS and the follow-up observational study.

Baseline data
Details of baseline data collection have been previously published.11 In brief, baseline medical history (including diabetes, hypertension, smoking history) and medications were obtained from all participants, the latter verified with participants’ general practitioners where required. Body mass index (BMI) measurements were obtained at baseline and at 5 years postrandomisation (1998 and 2003). At baseline, an average of three blood pressure readings were measured and recorded after the participants had been rested and seated for 5 min. Socioeconomic status (SES) was assessed using relative social advantage related to residential postcodes according to the Australian Bureau of Statistics method.12 This variable was divided into six categories: one being the most disadvantaged and six being the least disadvantaged.

Fluid assessment
A validated beverage intake questionnaire developed by the Cancer Council Victoria (Melbourne, Australia),13 which quantified habitual beverage consumption during the 12 months prior to study enrolment, was completed by each participant in 2003. Total fluid consumption, comprising water, black tea, coffee and other beverages (eg, chocolate beverages, herbal tea, juices and sugar beverages), excluding alcoholic beverages (including beer, wine and spirits), was calculated. The exposure study variable is cups (1 cup=250 mL) of total and types of fluids (specifically water, black tea, coffee, milk and other fluids) per day.

Biochemistry
Fasting blood samples were collected in 1998, 2003 and 2008 with sera stored in a -70°C freezer until analysis. Creatinine measurements were performed using stored sera with measurements of creatinine in 2003 and 2008 samples being available for 689 women (45.9%). Serum creatinine was analysed using an isotope dilution mass spectrometry traceable Jaffe kinetic assay for creatinine on a Hitachi 917 analyser (Roche Diagnostics GmbH, Mannheim, Germany). Estimated glomerular filtration rate (eGFR) was derived using the creatinine-based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.14

Assessment of clinical outcomes
Participants’ general practitioners verified their medical histories and medications where possible, and were coded using the International Classification of Primary Care—Plus (ICPC-Plus) method.15 Prevalent CVD was determined from hospital discharge data between 1980 and 1998 and were defined using diagnosis codes from the International Classification of Diseases, Injuries and Causes of Death Clinical Modification (ICD-9-CM, 390-459).16 Prevalent renal disease was collected between 1980 and 1998 using ICD-9-CM 17. These codes included glomerular diseases (ICD-9-CM codes 580–583); renal tubulointerstitial diseases (ICD-9-CM codes 593.3–593.5, 593.7); renal failure (ICD-9-CM codes 584–586) and hypertensive renal disease (ICD-9-CM code 403). The search for renal disease hospitalisations included any diagnosis code.

The primary outcomes of the study were CVD mortality and all-cause mortality retrieved from the Western
Australian Data Linkage System (WADLS) for each of the study participants from 2003 to 2013. CVD mortality was defined using primary death codes from ICD—the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM), 100-199.17 Text fields from the death certificate were used to ascertain the cause(s) of deaths where coded death data were not yet available from the WADLS.

Statistical analysis
Baseline characteristics were expressed as mean and SD or median and IQR for continuous variables or as number and proportion for categorical variables. Correlation between total fluid intake and alcohol (gram/day (g/d)) was examined using Spearman’s coefficient. Associations between fluid consumption and change in eGFR (absolute change in eGFR between 2003 and 2008) and risk of rapid renal decline (defined as reduction in eGFR of ≥3 mL/min/1.73 m² annually between 2003 and 2008) were assessed using unadjusted and adjusted linear and logistic regression analyses, respectively. Restricted cubic splines were modelled to determine the linearity of the association between cups of fluid consumption per day and mortality. Associations between the total and types of fluids, CVD mortality and all-cause mortality were examined using the Cox proportional hazard regression models. The Cox models included covariates recorded at baseline in 1998 (ie, smoking history, SES, diabetes status, hypertension, systolic blood pressure, prevalent CVD, medications and treatment code (calcium supplementation vs no calcium supplementation)) and those recorded in 2003 (ie, fluid status, age, BMI and eGFR). Selection of covariates for inclusion in the multivariable-adjusted models were undertaken in two analytical approaches: (1) covariates with p<0.10 in the univariate models were selected (for each outcome including change in eGFR, rapid renal decline, CVD mortality and all-cause mortality), and (2) the β coefficient of each of the independent covariate and its association with each outcome in the univariate analyses was evaluated. If the coefficient of the independent covariate in the regression analyses changed by more than 10%, it was considered to be a confounder, and thus included in the final multivariable model. The covariates that were included in the multivariable models were selected from both analytical approaches. Fluid status and treatment code were included in all multivariable models irrespective of their associations in the univariate models. p Values of <0.05 in two-tailed testing were considered statistically significant. The proportional hazard assumptions of all Cox models were checked graphically by plotting the Schoenfield residuals, but there was no evidence of departures from proportional hazards for total and types of fluid intake. The data were analysed using SPSS (V.15; SPSS, Chicago, Illinois, USA) and STATA (V.11 StataCorp LP, College Station, Texas, USA).

RESULTS
Baseline characteristics
The baseline characteristics of the 1055 participants are shown in table 1. The mean age and burden of comorbidities of the 445 participants who were excluded (died between 1998 and 2003 or had missing data) were similar to the included cohort (data not shown). Over a follow-up time of 10 years between 2003 and 2013, 70 (6.6%) experienced rapid renal decline, and 362 (34.4%) died with 142 (13.5%) deaths attributed to CVD (table 2). The annual CVD mortality rate in our study cohort was 1346 deaths per 100 000 participants, as compared with an annual CVD mortality rate of 979 deaths per 100 000 population for women aged 75–84 years reported to the Australian Institute of Health and Welfare (AIHW; http://www.aihw.gov.au/cardiovascular-disease/deaths/#dt).

Table 1 Baseline characteristics of participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cohort (n=1055)</th>
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<tbody>
<tr>
<td><strong>Patient characteristics</strong></td>
<td></td>
</tr>
<tr>
<td>Age (years in 2003, mean±SD)</td>
<td>80.0±2.6</td>
</tr>
<tr>
<td>Body mass index at entry (kg/m², mean±SD)</td>
<td>27.2±4.5</td>
</tr>
<tr>
<td>Body mass index at 60 m (kg/m², mean±SD)</td>
<td>27.2±4.7</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg, mean±SD)</td>
<td>137.8±18.1</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg, mean±SD)</td>
<td>73.1±10.9</td>
</tr>
<tr>
<td>Previous and current smokers (n, %)</td>
<td>375 (36.5)</td>
</tr>
<tr>
<td>Diabetes (n, %)</td>
<td>53 (5.0)</td>
</tr>
<tr>
<td>Prevalent acute/chronic kidney disease (n, %)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Prevalent cardiovascular disease (n, %)</td>
<td>227 (21.5)</td>
</tr>
<tr>
<td>Socioeconomic status (n, %)*</td>
<td></td>
</tr>
<tr>
<td>Top 10% most highly disadvantaged</td>
<td>42 (4.0)</td>
</tr>
<tr>
<td>Highly disadvantaged</td>
<td>126 (11.9)</td>
</tr>
<tr>
<td>High–medium disadvantaged</td>
<td>172 (16.3)</td>
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<tr>
<td>Medium–low disadvantaged</td>
<td>162 (15.4)</td>
</tr>
<tr>
<td>Low disadvantaged</td>
<td>213 (20.2)</td>
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<tr>
<td>Top 10% least disadvantaged</td>
<td>333 (31.6)</td>
</tr>
<tr>
<td><strong>Medication use (n, %)</strong></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>194 (18.4)</td>
</tr>
<tr>
<td>Statin</td>
<td>198 (18.8)</td>
</tr>
<tr>
<td>Treatment with calcium supplements (n, %)</td>
<td>536 (50.8)</td>
</tr>
<tr>
<td>Total and type of fluid composition in cups/day (median, IQR)</td>
<td></td>
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<tr>
<td>Total fluid</td>
<td>10.4 (8.5–12.5)</td>
</tr>
<tr>
<td>Water</td>
<td>4 (2–6)</td>
</tr>
<tr>
<td>Black tea</td>
<td>3 (1–4)</td>
</tr>
<tr>
<td>Coffee</td>
<td>1 (0–2)</td>
</tr>
<tr>
<td>Milk</td>
<td>1.5 (0.8–1.5)</td>
</tr>
<tr>
<td>Other fluids</td>
<td>0.4 (0–1)</td>
</tr>
</tbody>
</table>

Data expressed as number (percentage), mean±SD or as median (IQR).
*Missing socioeconomic status (n=7).
The median (IQR) intake of total fluid was 10.4 (8.5–12.5) cups per day, with water (median (IQR) 4 (2–6) cups per day) and black tea (median (IQR) 3 (1–4) cups per day) being the most frequent types of fluid consumed. Almost 22% of participants had prevalent CVD but no participants had prevalent CKD. Almost 70% of participants were from low-medium or low disadvantaged groups. There was no significant correlation between total fluid intake and alcohol intake (Spearman’s correlation −0.024, p=0.45).

Assessment of the relationship between total and types of fluid intake and outcomes
The restricted cubic spline curves demonstrated that the relationship between total fluid intake and both CVD mortality and all-cause mortality was predominantly linear. Similarly, the relationships between water, black tea, coffee and other fluid intake and CVD mortality and all-cause mortality were also linear (see online supplementary figures S1 and S2).

Association between total fluid intake, 10-year CVD mortality and all-cause mortality
There was no significant association between total fluid intake and CVD or all-cause mortality in the unadjusted and adjusted models. The unadjusted HRs for every cup per day higher intake of total fluid for CVD mortality and all-cause mortality were 0.96 (95% CI 0.91 to 1.01) and 1.01 (95% CI 0.96 to 1.05), respectively, whereas the adjusted HRs were 1.02 (95% CI 0.95 to 1.10) and 0.99 (95% CI 0.95 to 1.04), respectively. For every cup per day higher intake of black tea, the unadjusted HRs of CVD mortality and all-cause mortality were 0.89 (95% CI 0.82 to 0.98) and 0.91 (95% CI 0.86 to 0.96), respectively. The adjusted HRs for every cup per day higher intake of black tea for CVD mortality and all-cause mortality were 0.90 (95% CI 0.81 to 0.99) and 0.92 (95% CI 0.86 to 0.98), respectively (figure 2). There were no associations between coffee, milk and other fluid types (excluding water, black tea and coffee) intake and CVD mortality and all-cause mortality in the unadjusted and adjusted models.

Association between total type of fluid intake and renal function decline
There was no association between total fluid intake and odds of rapid renal decline, with unadjusted and adjusted ORs of 1.02 (95% CI 0.95 to 1.10) and 1.04 (95% CI 0.96 to 1.12), respectively, for every cup per day higher intake of total fluid. There was no association between fluid type and rapid renal decline. The adjusted OR for every cup per day higher intake of water and black tea were 1.04 (95% CI 0.94 to 1.16) and 1.03 (95% CI 0.90 to 1.18), respectively, adjusted for age, BMI, hypertension and diabetes. Only diabetes was associated with rapid renal decline with an adjusted OR of 3.38 (95% CI 1.47 to 7.75).

There was no association between total fluid intake and change in eGFR. For every cup per day higher intake of total fluid, there was a −0.12 mL/min/1.73 m² (95% CI −0.38 to 0.13) and −0.18 mL/min/1.73 m² (95% CI −0.42 to 0.07) reduction in 5-year eGFR, respectively, in the unadjusted and adjusted models. There was no association between fluid types and eGFR filtration rate.
change in eGFR. Only the presence of diabetes was associated with a decline in eGFR over 5 years of \(-6.28 \text{ mL/min/1.73 m}^2\) (95% CI \(-10.38\) to \(-2.19\)).

**DISCUSSION**

The long-standing advice that drinking adequate amounts of fluid to avoid dehydration may lead to an improvement in health outcomes is currently not supported by consistent evidence. In this analysis of a prospective contemporary population-based cohort of older women over the age of 75 years, we have found no association between total fluid intake and 10-year hazards of CVD mortality and all-cause mortality. However, higher consumption of black tea was associated with a significant reduction in CVD mortality and all-cause mortality, independent of traditional CVD risk factors.

Similar to our study, another Australian prospective, population-based cohort study of 3858 men and women aged over 48 years found no association between total fluid intake (from food and beverages excluding water) and all-cause and CVD mortality.\(^8\) Similar findings (water and other fluids excluding food were evaluated) were corroborated in another large population-based cohort of 120,852 men and women aged between 55 and 69 years recruited in the Netherlands.\(^9\) In contrast, an inverse association between pure water intake (excluding water from food) and risk of fatal coronary artery disease (CAD) was shown in a large cohort of 20,297 men and women aged at least 38 years without prevalent vascular disease or diabetes in the USA. Compared with individuals who consumed two or less glasses of water per day, those who consumed five or more glasses of water per day had experienced over 30% reduction in the risk of fatal CAD.\(^10\) The beneficial effects of higher fluid intake in reducing the rates of vascular events including recurrent stroke, myocardial infarction or all-cause mortality were further shown in a small prospective study of 465 patients with stroke.\(^11\) Our study could not find an association between total fluid intake and CVD mortality and all-cause mortality, even though we established a best-fit linear relationship between the continuous exposure factor, total fluid intake and outcomes. The challenges in comparing and interpreting the results from these epidemiological studies include the vastly different populations with varying characteristics, different eras, variations in the definition of fluid consumption and dissimilar follow-up periods. The basis of the suggestion that fluid intake is associated with beneficial health outcomes has been extrapolated from studies involving surrogate markers of health outcomes and as such the evidence supporting this assertion is weak. For example, mechanistic theories suggest that adequate fluid intake to avoid dehydration can lead to suppression of AVP and avoidance of adverse physiological processes such as elevated plasma viscosity and fibrinogen (putative surrogate markers of CVD),\(^12\)\(^13\) which potentially may improve renal blood flow and perfusion resulting in improved kidney function and health outcomes.\(^3\) To shed light on the inconsistent negative association between quantity of total fluid consumption and important health outcomes, the next logical step is to evaluate the association between composition of beverage consumption and health outcomes.

In our study, we have shown an independent inverse association between consumption of black tea and CVD mortality and all-cause mortality. Higher intake of black tea was associated with a reduction in the relative hazards of CVD mortality and all-cause mortality. Nevertheless, our findings are in contrast to those of other epidemiological studies where no consistent patterns between types of beverages and clinical outcomes could be found. In the US study, a higher intake of fluid other than water (not examined by specific fluid types) was associated with an increased risk of fatal CAD in women but not in men, whereas the Netherlands study suggests that the inverse relationship between tea intake and CVD mortality was only apparent in men. A gender differential in the risk of CVD mortality and stroke mortality has been shown and although epidemiological studies have suggested that traditional vascular risk factors remain important in predicting mortality in men and women, it does raise the question of whether differences in lifestyle, dietary or behavioural factors may contribute to the gender disparity in CVD mortality.\(^21\)

While the health benefits of black tea have been attributed to the antioxidant and anti-inflammatory properties of flavonoids (a major composition in tea—100–300 mg per serving of tea),\(^22\)\(^23\) there may be other beneficial components in black tea that remain unexplored. In a survey of US adults, women were more

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**Figure 2** Forest plots showing the association between types of fluid consumption (every one cup higher intake per day), including water, black tea, coffee, milk and other fluids and risk of CVD and all-cause mortality, adjusted for age, blood pressure, prevalent CVD, diabetes and eGFR. CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate.
likely to consume a greater amount of flavonoids in their diet compared with men and the greatest source of intake of flavonoids was from tea.25 Of note, the flavonoid content in non-herbal tea depends on the strength, type of tea (particularly black tea) and the process of oxidisation. Furthermore, there are other food and beverage sources of flavonoids such as chocolate, nuts and red wine that may have modified the association between black tea and outcomes. The finding of a significant inverse association between tea consumption and CVD and all-cause mortality in women with CKD is intriguing but requires validation in other cohorts.

Finally, we have previously shown that increased consumption of proanthocyanidins, a class of flavonoids, was associated with improved kidney function and reduced risk of kidney disease-related clinical events but did not address the association of renal function decline.26 In this study, there was no association between total fluid, water or black tea consumption and eGFR decline or risk of rapid renal decline, findings that have been contradicted in other large cohort studies. A cross-sectional analysis of 3427 adults with a mean age of 46 years from the National Health and Nutrition Examination Survey (NHANES) showed that CKD, defined as eGFR between 30 and 60 mL/min/1.73 m², was associated with a lower intake of plain water of <2 L/day with adjusted OR of 2.36 (95% CI 1.10 to 5.06), compared with those with a higher water intake of >4.3 L/day.27 A similar protective effect between high fluid intake and development of CKD has also been shown in a cohort of older men and women with mean ages of 65 years.28 However, these studies defined CKD using a single time-point eGFR in the absence of other markers of CKD such as albuminuria. This association needs to be examined in other population cohorts using other markers of CKD and change in eGFR before this assertion can be substantiated.

Our study has several strengths and limitations. The prospective nature and completeness of the data set suggest that selection and ascertainment biases between the exposure factor and outcomes are minimised. The analytical data on fluid intake were calculated before examination of the relation to clinical outcome data and were subjected to meticulous covariate analysis in an attempt to identify important collinearity that may have accounted for the observed associations. Identification of causality is limited by the potential for recall bias, the complexity of estimating total fluid intake and the variability of the composition of the various beverages. Our analysis only focused on baseline fluid consumption but not change in fluid consumption over time, which may have modified our result findings. In addition, fluid derived from dietary consumption, which is likely to account for a small percentage of overall daily fluid intake, amount/intensity of exercise and energy expenditure were not included in this study because of the uncertainty over the accuracy of this information but could have modified the association between fluid intake and outcomes. In addition, we had excluded alcohol in the estimation of total fluid intake because epidemiological studies have shown an independent association between alcohol intake and health outcomes (including CVD mortality).29 However, despite these limitations, the association between volume of black tea consumption and mortality remains significant even after adjustment for other factors. Future studies will determine the generalisability of our results to a wider population, including men and younger individuals.

**CONCLUSION**

We found no association between the amount or type of daily fluid intake and renal function decline. However, an inverse linear relationship between the daily amount of black tea ingested and long-term hazards of CVD mortality and all-cause mortality was found in a cohort of elderly women. External validation of our findings in men and women of varying ages is required to establish the true clinical significance of black tea intake.

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**Contributors** All authors participated in the design of the work, interpretation of the data (WHL, GW and JRL participated in the conception and analysis), drafting of the work, given final approval and are accountable for all aspects of the work. The lead author (WHL) affirms that the manuscript is an honest, accurate and transparent account of the study being reported; and that any discrepancies from the study as planned have been explained.

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