

# Dietary Patterns and Clinical Outcomes in Chronic Kidney Disease: The CKD.QLD Nutrition Study

Shu Ning Wai, MNutrDiet,\* Jaimon T. Kelly, MNutrDiet,\* David W. Johnson, PhD,†‡ and Katrina L. Campbell, PhD\*‡§

**Objective:** Emerging evidence suggests that dietary patterns are associated with survival in people with chronic kidney disease (CKD). This study evaluated the relationship between dietary habits and renal-related clinical outcomes in an established CKD cohort.

**Design:** Prospective cohort study.

**Setting:** Three outpatient nephrology clinics in Queensland, Australia.

**Subjects:** A total of 145 adult patients with Stage 3 or 4 CKD (estimated glomerular filtration rate 15-59 mL/minute/1.73 m<sup>2</sup>).

**Intervention:** Dietary intake was measured using 24-hour recall and the HeartWise Dietary Habits Questionnaire (DHQ), which evaluates 10 components of dietary patterns in relation to cooking habits and intake of food groups.

**Main Outcome Measure:** The primary outcome was a composite end point of all-cause mortality, commencement of dialysis, and doubling of serum creatinine. Secondary outcome was all-cause mortality alone. Multivariate cox regression analyses calculated hazard ratios (HRs) for associations between DHQ domains and occurrence of composite outcome and adjusted for confounders, including comorbidities and renal function.

**Results:** Over a median follow-up of 36 months, 32% (n = 47) reached the composite end point, of which 21% died (n = 30). Increasing DHQ score was associated with a lower risk of the composite end point with increasing intake of fruits and vegetables (HR: 0.61; 95% CI, 0.39-0.94) and limiting alcohol consumption (HR, 0.79; 95% CI: 0.65-0.96). For the secondary outcome of all-cause mortality, there was a significant association with adequate intake of fruits and vegetables (HR: 0.35; 95% CI, 0.15-0.83).

**Conclusion:** Healthy dietary patterns consisting of adequate fruits and vegetables and limited alcohol consumption are associated with a delay in CKD progression and improved survival in patients with Stage 3 or 4 CKD.

© 2016 by the National Kidney Foundation, Inc. All rights reserved.

## Introduction

CHRONIC KIDNEY DISEASE (CKD) is a major public health issue,<sup>1</sup> with a worldwide prevalence of approximately 10%-15% in the adult population.<sup>2-5</sup> CKD is associated with poor quality of life, adverse clinical outcomes, and high health care costs.<sup>6,7</sup> There is

growing demand for effective and low-cost interventions to tackle this serious health burden.

Current evidence-based guidelines recommend dietary intervention targeting single nutrients, such as sodium, protein, potassium, and phosphorus, to manage CKD and associated cardiovascular risk factors.<sup>8-10</sup> However, single-nutrient interventions have been examined in CKD and demonstrated small, but largely inconclusive effects on CKD outcomes and cardiovascular risk.<sup>11-14</sup> As patients with earlier stages of CKD view dietary interventions as an essential approach to preventing disease progression,<sup>6</sup> research into the optimal dietary intervention that these populations should follow to protect residual kidney function and mitigate cardiovascular disease risk is needed.

Although dietary interventions are considered paramount in CKD management, there are limited and conflicting studies examining the association between dietary patterns and renal-related clinical outcomes in CKD populations.<sup>15-20</sup> Dietary patterns, such as plant-based diet and Mediterranean diet, have been associated with survival.<sup>15-17</sup> In contrast, other studies have shown no such associations.<sup>18-20</sup> An important caveat to each of these studies is they were based on subgroup analyses of subjects with renal impairment (typically estimated glomerular

\*Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Queensland, Australia.

†Department of Nephrology, Princess Alexandra Hospital, Brisbane, Queensland, Australia.

‡School of Medicine, University of Queensland, Brisbane, Queensland, Australia.

§Department of Nutrition and Dietetics, Princess Alexandra Hospital, Brisbane, Queensland, Australia.

Support: This research received funding support from University of Queensland CKD. QLD small grant to support the data collection.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Address correspondence to Dr. Katrina L. Campbell, PhD, Faculty of Health Sciences and Medicine, Bond University, 14 University Drive, Robina, Queensland 4226, Australia. E-mail: [kcampbel@bond.edu.au](mailto:kcampbel@bond.edu.au)

© 2016 by the National Kidney Foundation, Inc. All rights reserved.

1051-2276/\$36.00

<http://dx.doi.org/10.1053/j.jrn.2016.10.005>

filtration rate [eGFR] <60) from largely “healthy” cohort studies or randomized controlled trials in nonrenal populations.<sup>16–20</sup> Therefore, there is a need to establish the association between dietary patterns and outcome in a referred population seeking treatment for CKD.

Therefore, the aim of this prospective cohort study is to investigate the associations between dietary patterns and diet-related habits with the incidence of renal-related end points in patients with Stage 3 or 4 CKD.

## Methods

### Study Population

The study included adult patients, aged  $\geq 18$  years, with Stage 3 or 4 CKD (defined as an eGFR between 15 and 59 mL/minute/1.73 m<sup>2</sup>) referred to 1 of 3 nephrology outpatient units in Queensland, Australia, between January 1, 2011 and December 31, 2012. Any patients who were unable to provide informed consent or participate in accurately reporting dietary information because of cognitive or other impairments were excluded from the study. Ethics was approved by Metro South Health Service District Human Research Ethics Committee.

### Dietary Assessment

Information was collected by trained dietitians who obtained data during routine outpatient appointments, as per the Evidence-based Guidelines for Nutritional Management of CKD.<sup>21</sup> At baseline, dietitians recorded dietary data using the HeartWise Dietary Habits Questionnaire (DHQ) and multiple-pass 24-hour recall method,<sup>22,23</sup> which is a validated dietary assessment tool in the cardiac (non-CKD) rehabilitation population. The DHQ was chosen as it is validated to measure dietary fat, fiber, and sodium intake, which are proxy markers for CKD progression risk factors, and is also a tool that quickly assesses dietary habits and can identify priorities for individual dietary education. The DHQ captures responses of usual intake from a week to over the past month. Dietary patterns and habits were identified across 22 items covering 10 dietary categories, specifically intake of whole grains, fruits, and vegetables, omega-3 fatty acid intake, food preparation methods, food choices, take-away snacks, sources of dietary fat intake, fiber intake, sodium intake, and alcohol consumption. The score for each category ranges from 1 to 5 with a rating of 1 demonstrating poor habits and a rating of 5 healthy dietary habits.<sup>23</sup>

### Data Collection

Participant characteristics of age, gender, nationality, social history (living arrangements, cooking, shopping, and employment), comorbidities, and previous diet interventions were recorded at baseline. Comorbidities were defined according to the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) registry.<sup>24</sup> Although C-reactive protein was recorded along with the patient's full laboratory results, it was only available in 8%

of patients; hence, this was not reported or investigated as potential confounder.

### Clinical Outcome

Outcomes for participants were monitored for up to 4 years. The primary outcome was a composite outcome of renal endpoints: all-cause mortality, commencement of dialysis, and doubling of serum creatinine (from the baseline measure). The secondary outcome of interest was all-cause mortality, which was ascertained by linking cohort data to the Registrar General Death data. Commencement of dialysis was assessed via linkage with the ANZDATA. Serum creatinine level was obtained from the latest biochemistry laboratory results, through until November 30, 2014. Any patients who were lost to follow-up in the database were cross-referenced with the ANZDATA for outcome data.

### Statistical Analysis

Descriptive statistics were used to examine baseline characteristics. Cox regression analyses were used to examine associations between DHQ scores of each domain (categorical and total DHQ score) and occurrence of composite primary outcome (all-cause mortality, commencement of dialysis, or doubling of serum creatinine). The relationships were expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). In the categorical cox models, dietary domains were analyzed as those with a high DHQ score ( $\geq 3$ ), with the low DHQ score ( $< 3$ ) serving as the referent group. Based on previous studies in the area,<sup>17</sup> model 1 adjustments were made for age, gender, smoking status, and eGFR. In model 2, adjustments were made for model 1 plus malnutrition status (subjective global assessment), body mass index, diabetes, and number of comorbidities. Preliminary analyses were also done to decide if parameters were to be adjusted in each model. Proportional hazards assumptions were checked by Schoenfeld residuals. A 2-sided  $P < .05$  was considered statistically significant. All analyses were performed with SPSS Statistics (version 23; SPSS Inc., Chicago, IL).

## Results

### Participants Characteristics

Of 156 consecutive patients approached, 145 participants were consented and included in the analyses (93% consent rate). The percentage of patients who had Stage 3 CKD was 58%, and 41% had Stage 4 CKD. Mean age was  $71 \pm 12$  years, 59% were men, 54% had diabetes, mean eGFR was  $32 \pm 12$  mL/minute/1.73 m<sup>2</sup>, and mean systolic blood pressure was  $136 \pm 20$  mm Hg. Baseline characteristics by DHQ score are provided in Table 1. Those who had a high DHQ score had higher eGFR, were more likely to be on cholesterol lowering medications and less likely to smoke (Table 1). Figure 1 illustrates the flow of participants through the study.

**Table 1.** Baseline Characteristics Classified by Low and High DHQ Scores\*

Characteristic	Low DHQ Score (n = 52)	High DHQ Score (n = 86)	P Value
Age (y)	72 ± 12	73 ± 10	.24
Male gender (n, %)	30 (57.7)	53 (61.6)	.65
Social factors (n, %)			
Cooking (self)	26 (61.9)	39 (58.2)	.70
Shopping (self)	24 (63.2)	39 (56.5)	.50
Employed	9 (17.6)	11 (12.9)	.45
BMI (kg/m <sup>2</sup> )	29 ± 6	31 ± 7	.28
Current smoker (n, %)	7 (15.9)	4 (4.8)	.03
SGA score A (n, %)	46 (88.5)	75 (88.2)	.97
eGFR (ml/min/1.73 m <sup>2</sup> )	30 ± 14	35 ± 11	.02
No. of comorbidities ≥ 4 (n, %) <sup>†</sup>	19 (36.5)	37 (43)	.76
Diabetes (n, %)	22 (42.3)	52 (60.4)	.08
Hypertension (n, %)	37 (71.2)	66 (76.7)	.47
CVD (n, %)	15 (28.8)	24 (27.9)	.90
Systolic blood pressure (mm Hg)	135 ± 21	136 ± 19	.77
Energy intake (kcal/kg/d)	23 ± 27	22 ± 30	.28
Protein intake (g/kg/d)	1.1 ± 0.3	1.1 ± 0.4	.83
Statin use (n, %)	26 (50.0)	60 (69.8)	.02

BMI, body mass index; CVD, cardiovascular disease; DHQ, Heart-Wise Dietary Habits Questionnaire; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; SGA, subjective global assessment.

Values for categorical variables are given as number (percentage); values for continuous variable are given as mean ± standard deviation.

\*Low DHQ score (<3) and high DHQ score (≥3).

<sup>†</sup>Comorbidities include cardiovascular (myocardial infarction, use of warfarin, congestive heart failure, and hypertension), diabetes (DM 1, DM 2, diabetes nephropathy, and diabetes retinopathy), cancer (metastatic cancer, any tumor, leukemia, and lymphoma), other (mild liver disease, moderate/severe liver disease, peptic liver disease, peripheral vascular disease, depression, connective tissue disease, AIDS, hemiplegia, and skin ulcers/cellulitis).

## Dietary Patterns and Composite Primary Outcome

During a median follow-up of 36 months, 32% subjects (n = 47) reached the composite clinical end point, of which 21% died (n = 30), 8% (n = 12) commenced dialysis, and 3% (n = 5) experienced a doubling serum creatinine.

Based on both categorical (adequate intake cut-off of score ≥ 3) and continuous (increasing total DHQ score) predictors, the risk of the composite primary outcome was significantly lower in 8 of 10 domains of the DHQ with adequate and/or increasing intake of whole grains, fruits, and vegetables, fiber, healthier sources of dietary fat, limiting sodium intake, healthier food preparation methods, limiting take-away snacks, and limiting alcohol consumption (Table 2).

There were lower risks of reaching the composite clinical outcome with increasing DHQ scores across for whole grains, fruits, and vegetables, fiber, healthier food preparation

methods, limiting take-away snacks, and alcohol consumption (Table 2). The relationship however was only significant for adequate intake of fruits and vegetables (HR model 2, 0.38; 95% CI, 0.18–0.82) after adjustment for confounders.

For every 1-point increase in DHQ score, there was a significantly lower risk of composite clinical outcome with increasing intake of fruits and vegetables (HR model 2, 0.61; 95% CI, 0.39–0.94) and limiting alcohol consumption (HR model 2, 0.79; 95% CI, 0.65–0.96; Fig. 2). The association was no longer significant after adjustment for confounders for increasing intake of whole grains, increasing intake of fiber, healthier food preparation methods, and limitation of take-away snacks (Table 2).

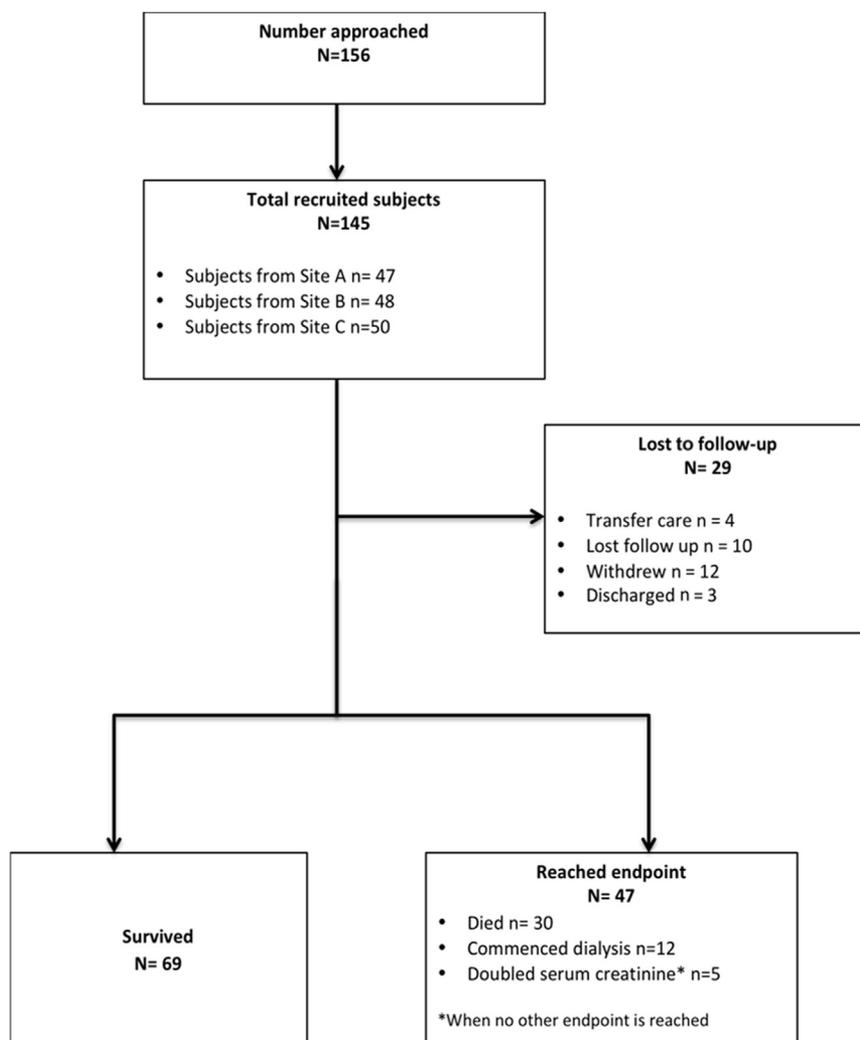
## Dietary Patterns and All-Cause Mortality

Over a median follow-up period of 32 months, 30 subjects died (21%). Survival rates were higher for those who had an adequate intake of fruits and vegetables (high DHQ (≥3), HR model 2, 0.35; 95% CI, 0.15–0.83; Fig. 3). The relationship with consumption of healthier sources of dietary fat, limiting sodium intake, and limiting alcohol consumption was no longer significant after adjusting for confounders (Table 2). Associations of each domain of the DHQ to commencing dialysis and doubling serum creatinine were also explored; however, there was no significant relationship (data not shown).

## Discussion

This study has shown that a dietary pattern with adequate intake of fruits and vegetables and limited alcohol consumption is associated with lower risk of a composite outcome of all-cause mortality, commencement of dialysis, or doubling of serum creatinine in Stages 3 and 4 CKD patients. Consuming an adequate amount of fruits and vegetables was also the only domain that demonstrated significance for all-cause mortality alone, with a diet higher in fruits and vegetables associated with a 65% reduced risk of all-cause mortality.

These results are in agreement with prior post-hoc analyses demonstrating an association between healthy dietary patterns and clinical outcomes including mortality in persons with and without established CKD.<sup>15–17,25</sup> The National Institutes of Health–American Association of Retired Person Diet and Health Study reported an association between healthy dietary patterns (according to diet quality index scores) and lowered risk of major renal composite outcome of death due to renal cause and initiation of dialysis.<sup>25</sup> The Uppsala Longitudinal Study of Adult Men similarly showed that greater adherence to the Mediterranean diet, a predominantly plant-based diet, was associated with higher survival rates in those with established CKD.<sup>16</sup> Another study showed CKD individuals from the Reasons for Geographic and Racial Differences in Stroke cohort,<sup>17</sup> who consumed a higher proportion of protein from plant-based



**Figure 1.** Flow diagram indicating pathways of outcomes of sample.

sources, characterized by high intake of fruits and vegetables, experienced a 23% reduced risk of death.<sup>17</sup> This type of dietary pattern was also shown to be associated with a 33% lower risk of mortality in a sub-population with established CKD from the Third National Health and Nutrition Examination Survey.<sup>15</sup>

One potential mechanism for this association may be the individual protective effect of fruits and vegetables on cardiovascular disease<sup>26</sup> and reduced risk of hypertension with limited alcohol consumption.<sup>27</sup> Other mechanisms explaining the positive effects of fruits and vegetables intake have been widely investigated in previous studies, including the ability to lower blood pressure,<sup>28-32</sup> control weight,<sup>32-35</sup> reduce the risk of diabetes,<sup>36</sup> and improve glycemic control.<sup>37</sup> One randomized controlled trial and 1 cross-sectional study have suggested higher intakes of fruits and vegetables may delay kidney function decline by reducing inflammation and improving acid-base balance.<sup>38,39</sup> Studies have also demonstrated that diets higher in fruits,

vegetables, whole grains, and low-fat dairy foods may be protective against eGFR decline and associated with lower urinary albumin-to-creatinine ratio and lower albumin excretion rate.<sup>38,39</sup> The antioxidant properties and fiber content of fruits and vegetables may have protective effects on inflammation markers, such as C-reactive protein and soluble intercellular adhesion molecule-1,<sup>40</sup> and explain the relationship with albuminuria and inflammation.<sup>41,42</sup> It was also suggested that the beneficial effect of proteins from plant-based foods was suggested to be favorable because of its effects on cholesterol metabolism,<sup>43</sup> decreased production of uremic toxins,<sup>44</sup> and its protective effect on albumin leakage over animal-based protein diets.<sup>38,45</sup>

In this study, no association was observed between the other DHQ domains (adequate intake of whole grains, fiber, healthier sources of dietary fat intake, omega-3 fatty acid, using ideal food preparation methods, better food choices, limiting take-away snacks, and limiting sodium intake) and primary and secondary outcomes. This may

**Table 2.** Association of Dietary Habits Questionnaire Domains With Composite Clinical Outcome and All-Cause Mortality in a Cohort of Chronic Kidney Disease Patients (n = 145)

Characteristic	Composite Clinical Outcome <sup>a</sup>		All-Cause Mortality	
	High DHQ Score ( $\geq 3$ ) (95% CI)	Every 1-Point Increase in DHQ Score (95% CI)	High DHQ Score ( $\geq 3$ ) (95% CI)	Every 1-Point Increase in DHQ Score (95% CI)
Increasing whole grains				
HR	0.49 (0.26-0.91)*	0.73 (0.55-0.97)*	0.64 (0.32-1.27)	0.86 (0.64-1.17)
HR model 1	0.74 (0.35-1.55)	0.86 (0.61-1.21)	0.60 (0.25-1.30)	0.85 (0.59-1.23)
HR model 2	0.77 (0.35-1.69)	0.83 (0.58-1.18)	0.58 (0.24-1.41)	0.87 (0.60-1.26)
Increasing fruits and vegetables				
HR	0.33 (0.17-0.63)*	0.54 (0.38-0.76)*	0.32 (0.16-0.68)*	0.67 (0.48-0.95)*
HR model 1	0.49 (0.24-1.03)	0.67 (0.44-1.01)*	0.43 (0.19-1.01)	0.80 (0.53-1.21)
HR model 2	0.38 (0.18-0.82)*	0.61 (0.39-0.94)*	0.35 (0.15-0.83)*	0.76 (0.49-1.18)
Healthier sources of dietary fat				
HR	0.53 (0.25-1.09)	0.73 (0.43-1.25)	0.41 (0.19-0.89)*	0.49 (0.28-0.89)*
HR model 1	0.66 (0.25-1.78)	1.00 (0.54-1.87)	1.23 (0.36-4.25)	0.81 (0.40-1.63)
HR model 2	0.46 (0.15-1.40)	0.84 (0.43-1.64)	1.07 (0.23-5.06)	0.74 (0.33-1.66)
Limiting sodium intake				
HR	0.68 (0.37-1.25)	0.82 (0.57-1.19)	0.49 (0.25-0.97)*	0.65 (0.44-0.95)*
HR model 1	0.87 (0.42-1.79)	0.99 (0.64-1.53)	0.76 (0.33-1.72)	0.90 (0.56-1.44)
HR model 2	0.80 (0.39-1.66)	0.85 (0.52-1.39)	0.74 (0.32-1.71)	0.58 (0.50-1.47)
Increasing fiber intake				
HR	0.55 (0.30-1.01)	0.60 (0.43-0.85)*	0.53 (0.27-1.06)	0.75 (0.53-1.07)
HR model 1	1.05 (0.52-2.11)	0.79 (0.51-1.21)	0.80 (0.35-1.79)	0.85 (0.55-1.31)
HR model 2	0.90 (0.43-1.88)	0.71 (0.45-1.12)	0.75 (0.31-1.85)	0.82 (0.52-1.29)
Omega-3 fatty acid intake				
HR	1.33 (0.71-2.49)	1.11 (0.83-1.47)	1.70 (0.87-3.34)	1.26 (0.93-1.72)
HR model 1	1.55 (0.77-3.09)	1.18 (0.85-1.64)	1.80 (0.84-3.86)	1.42 (0.99-2.01)
HR model 2	1.21 (0.57-2.56)	1.06 (0.74-1.52)	1.59 (0.70-3.58)	1.35 (0.92-1.97)
Food choice including quality of fat intake <sup>†</sup>				
HR	0.62 (0.32-1.20)	1.03 (0.76-1.39)	0.68 (0.33-1.41)	0.80 (0.59-1.09)
HR model 1	0.83 (0.40-1.73)	1.13 (0.81-1.57)	1.29 (0.55-2.99)	0.93 (0.65-1.33)
HR model 2	0.70 (0.32-1.53)	1.06 (0.74-1.51)	1.30 (0.52-3.27)	0.97 (0.66-1.42)
Healthier food preparation methods				
HR	0.63 (0.32-1.25)	0.72 (0.56-0.93)*	0.71 (0.33-1.52)	0.90 (0.69-1.18)
HR model 1	0.66 (0.26-1.16)	0.77 (0.55-1.05)	0.88 (0.32-2.42)	0.96 (0.67-1.37)
HR model 2	0.59 (0.22-1.54)	0.75 (0.54-1.04)	0.61 (0.22-1.71)	0.86 (0.61-1.22)
Limiting take-away snacks				
HR	0.44 (0.23-0.82)*	0.73 (0.56-0.95)*	0.60 (0.30-1.22)	0.89 (0.69-1.17)
HR model 1	0.67 (0.33-1.36)	0.86 (0.64-1.16)	0.87 (0.39-1.96)	1.02 (0.75-1.40)
HR model 2	0.60 (0.28-1.32)	0.78 (0.57-1.06)	1.07 (0.41-2.76)	0.95 (0.69-1.30)
Limiting alcohol consumption				
HR	0.33 (0.13-0.81)*	0.82 (0.72-0.95)*	0.38 (0.14-0.99)*	0.91 (0.78-1.07)
HR model 1	0.44 (0.14-1.33)	0.81 (0.69-0.96)*	0.66 (0.20-2.15)	0.99 (0.81-1.21)
HR model 2	1.67 (0.36-7.72)	0.79 (0.65-0.96)*	2.08 (0.25-17.56)	0.97 (0.78-1.23)

CI, confidence interval; DHQ, HeartWise Dietary Habits Questionnaire; HR, hazard ratio.

Model 1 is adjusted for age, gender, and eGFR. Model 2 is adjusted for variables in Model 1 and body mass index, malnutrition status (subjective global assessment), diabetes, and number of comorbidities. HR of high DHQ score is compared with low DHQ score; low DHQ score is used as the reference category.

<sup>a</sup>Refers to death, commencement of dialysis, or doubling of serum creatinine.

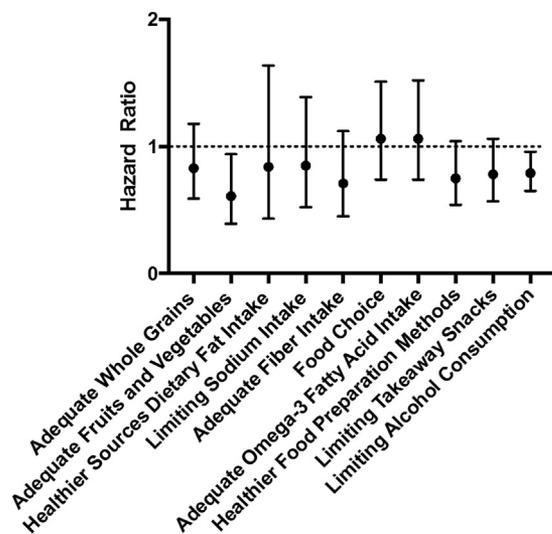
\*Result is significant as  $P$  value  $\leq .05$ .

<sup>†</sup>Food choice assesses the quality of fat intake in an individual's diet through frequency intake of low fat versus regular fat products intake of fish, processed meat, and type of spread consumed.

have been because of several reasons. First, given the relatively modest number of participants and events, there is a possibility that the analysis was underpowered to detect significant associations between the dietary domains and mortality. Second, the DHQ assessment was self-reported, which may have resulted in reporting errors because of reduced accuracy of dietary measurement, inability to

remember, underestimating or overestimating amount eaten and portion sizes, and social desirability bias.<sup>46</sup>

It is recognized that a diet with reduced sodium is a component of a dietary pattern that may lower the risk of cardiovascular events and all-cause mortality.<sup>11,47-50</sup> This relationship is suggested to be mediated by positive effects on blood pressure<sup>51</sup> and lipid profiles.<sup>50</sup> In contrast, this study



**Figure 2.** Risk of composite clinical end point with every 1-point increase in DHQ score stratified by dietary domains of the DHQ in a cohort of CKD patients ( $n = 145$ ). This figure represents adjusted model 2 that was adjusted for age, gender, eGFR, SGA, BMI, diabetes, and number of comorbidities. Error bars represent 95% confidence intervals. BMI, body mass index; CKD, chronic kidney disease; DHQ, Heart-Wise Dietary Habits Questionnaire; eGFR, estimated glomerular filtration rate; SGA, subjective global assessment.

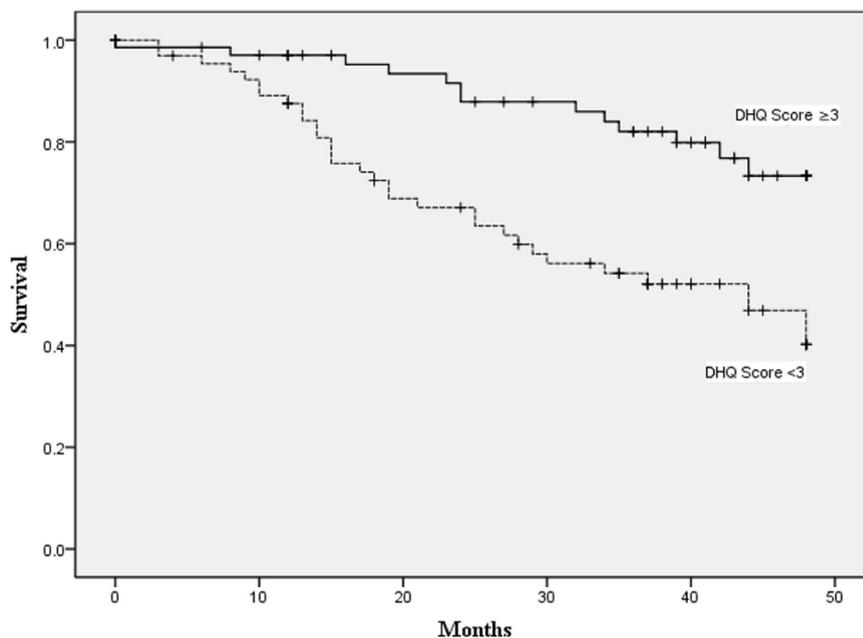
did not find an association between these dietary pattern components and adverse events. This may be because of the way sodium intake was captured on the DHQ. Intake of processed meats, pastries, and take-away style foods are not attributed to overall sodium intake in the DHQ scoring

domain, which some suggest is a substantial source of total sodium intake in the modern food supply.<sup>52</sup>

To the investigators' knowledge, this study is the first cohort study in an established CKD population to test the association of dietary patterns and clinical outcomes. A significant association was observed between consuming adequate fruits and vegetables and the composite outcome of mortality, doubling of serum creatinine and initiating dialysis, and all-cause mortality alone. A dietary pattern with adequate intake of whole grains was also associated with a reduction in the risk of composite outcome by 27%. This was in agreement with a recent systematic review that reported a 27% lower risk of death associated with healthy eating patterns characterized by higher intakes of fruits and vegetables, fish, legumes, cereals, and whole grains, and lower intakes of red meat, salt, and refined sugars.<sup>53</sup>

Despite these strengths, this study does have important limitations worth noting. First, the sample size was relatively small ( $n = 145$ ), and participants were only monitored for 48 months, such that the possibility of a type 2 statistical error cannot be excluded. Nonetheless, robust associations between important DHQ diet domains suggest that the study was adequately powered for the predictor of fruit and vegetable intake. Second, the DHQ consisted of 10 domains, which resulted in testing of multiple exposures, which may increase the risk of type 1 error. However, the findings were consistent with other prospective studies in this population.

In conclusion, the present study shows that consuming a dietary pattern characterized by adequate intake fruits and vegetables and limited alcohol consumption is associated



**Figure 3.** Kaplan–Meier survival curves stratified by low ( $<3$ ) and high ( $\geq 3$ ) DHQ scores of fruit and vegetable intake in a cohort of CKD patients ( $n = 145$ ). CKD, chronic kidney disease; DHQ, HeartWise Dietary Habits Questionnaire.

with a lower risk of the composite outcome of death, commencement of dialysis, or doubled serum creatinine levels. In current clinical practice, there can be a focus on restriction of fruits and vegetables because of concerns of higher dietary potassium and/or phosphate consumption with kidney dysfunction.<sup>54</sup> As single nutrient-focused diets are not typically reflective of a regular diet, our study reinforces the significance of an overall healthy diet, rather than confined focus on certain foods or single nutrients. The synergy between food and nutrients altogether may result in greater health benefits than each food component alone. This finding suggests a shift to focus on healthful dietary pattern with an intake of  $\geq 6$  pieces of fruits per week and  $\geq 3$  serves of vegetables per day is associated with a reduction in major renal outcomes in those with early or moderate stages of CKD. Intervention studies are needed to establish whether improving dietary patterns results can impact on major renal outcomes.

### Practical Application

This study adds to the growing momentum of evidence supporting the positive effects of plant-based dietary patterns and also encourages a shift in focus from single nutrient interventions to overall healthy diet interventions for CKD management. Dietary advice based on a whole food approach, encouraging increased fruit and vegetable intakes, could be an effective tool to reduce mortality in people with kidney disease.

### Acknowledgments

This study was supported by seed funding from the CKD.QLD Collaborative. The authors thank all of the dietitians involved in this study including April Campbell, Laura Cherry, Meri Manafi, Vicki Larkins, Eryn Murray, Chloe Jobber, Joanna Martin, and teams from Princess Alexandra Hospital, Gold Coast University Hospital, and Townsville Hospital involved in the data collection. The authors also thank Evelyne Rathbone from Bond University for data support and analysis. The authors are grateful to the participants in the study for their outstanding cooperation.

### References

- Bello AK, Nwankwo E, El Nahas AM. Prevention of chronic kidney disease: a global challenge. *Kidney Int.* 2005;68:S11-S17.
- Chadban SJ, Briganti EM, Kerr PG, et al. Prevalence of kidney damage in Australian adults: The AusDiab kidney study. *J Am Soc Nephrol.* 2003;14(Suppl 2):S131-S138.
- Chen J, Wildman RP, Gu D, et al. Prevalence of decreased kidney function in Chinese adults aged 35 to 74 years. *Kidney Int.* 2005;68:2837-2845.
- Singh NP, Ingle GK, Saini VK, et al. Prevalence of low glomerular filtration rate, proteinuria and associated risk factors in North India using Cockcroft-Gault and Modification of Diet in Renal Disease equation: an observational, cross-sectional study. *BMC Nephrol.* 2009;10:4.
- Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA.* 2007;298:2038-2047.
- Palmer SC, Hanson CS, Craig JC, et al. Dietary and fluid restrictions in CKD: a thematic synthesis of patient views from qualitative studies. *Am J kidney Dis.* 2015;65:559-573.
- Hemmelgarn BR, Manns BJ, Lloyd A, et al. Relation between kidney function, proteinuria, and adverse outcomes. *JAMA.* 2010;303:423-429.
- Ash S, Campbell K, MacLaughlin H, et al. Evidence based practice guidelines for the nutritional management of chronic kidney disease. *Nutr Diet.* 2006;63(Suppl 2):S33-S45.
- Kidney Disease Outcomes Quality Initiative. K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. *Am J kidney Dis.* 2004;43(5 Suppl 1):S1.
- Eknoyan G, Lameire N, Eckardt K, et al. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int.* 2013;3:5-14.
- McMahon EJ, Campbell KL, Bauer JD, Mudge DW. Altered dietary salt intake for people with chronic kidney disease. *Cochrane Database Syst Rev.* 2015;2:CD010070.
- 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;37:526-533.
- Robertson L, Waugh N, Robertson A. Protein restriction for diabetic renal disease. *Cochrane Database Syst Rev.* 2007;CD002181.
- Murtaugh MA, Filipowicz R, Baird BC, Wei G, Greene T, Beddhu S. Dietary phosphorus intake and mortality in moderate chronic kidney disease: NHANES III. *Nephrol Dial Transplant.* 2012;27:990-996.
- Chen X, Wei G, Jalili T, et al. The associations of plant protein intake with all-cause mortality in CKD. *Am J kidney Dis.* 2016;67:423-430.
- Huang X, Jimenez-Moleon JJ, Lindholm B, et al. Mediterranean diet, kidney function, and mortality in men with CKD. *Clin J Am Soc Nephrol.* 2013;8:1548-1555.
- Gutierrez OM, Muntner P, Rizk DV, et al. Dietary patterns and risk of death and progression to ESRD in individuals with CKD: a cohort study. *Am J Kidney Dis.* 2014;64:204-213.
- Ricardo AC, Anderson CA, Yang W, et al. Healthy lifestyle and risk of kidney disease progression, atherosclerotic events, and death in CKD: findings from the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J kidney Dis.* 2015;65:412-424.
- Ricardo AC, Madero M, Yang W, et al. Adherence to a healthy lifestyle and all-cause mortality in CKD. *Clin J Am Soc Nephrol.* 2013;8:602-609.
- Muntner P, Judd SE, Gao L, et al. Cardiovascular risk factors in CKD associate with both ESRD and mortality. *J Am Soc Nephrol.* 2013;24:1159-1165.
- Ash S, Campbell K, MacLaughlin H, et al. Evidence based practice guidelines for the nutritional management of chronic kidney disease. *Nutr Diet.* 2006;63(s2):S33-S45.
- Moshfegh AJ, Rhodes DG, Baer DJ, et al. The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *Am J Clin Nutr.* 2008;88:324-332.
- McKellar S, Horsley P, Chambers R, et al. Development of the diet habits questionnaire for use in cardiac rehabilitation. *Aust J Prim Health.* 2008;14:43-47.
- Australia and New Zealand Dialysis & Transplant Registry. *Definitions and Methodologies.* Available at: [http://www.anzdata.org.au/v1/definitions\\_methodologies.html](http://www.anzdata.org.au/v1/definitions_methodologies.html). Accessed June 1, 2016.
- Smyth A, Griffin M, Yusuf S, et al. Diet and major renal outcomes: a prospective cohort study. The NIH-AARP Diet and Health Study. *J Ren Nutr.* 2016;26:288-298.
- Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ.* 2014;349:g4490.
- Puddey IB, Rakic V, Dimmitt SB, Beilin LJ. Influence of pattern of drinking on cardiovascular disease and cardiovascular risk factors—a review. *Addiction.* 1999;94:649-663.
- Pienovi L, Lara M, Bustos P, Amigo H. [Fruit and vegetable intake, and blood pressure. A population research]. *Archivos Latinoam Nutr.* 2015;65:21-26.
- Aljuraiban GS, Griep LM, Chan Q, et al. Total, insoluble and soluble dietary fibre intake in relation to blood pressure: the INTERMAP Study. *Br J Nutr.* 2015;114:1480-1486.
- Radhika G, Sudha V, Mohan Sathya R, Ganesan A, Mohan V. Association of fruit and vegetable intake with cardiovascular risk factors in urban south Indians. *Br J Nutr.* 2008;99:398-405.

31. Erlund I, Koli R, Alfihan G, et al. Favorable effects of berry consumption on platelet function, blood pressure, and HDL cholesterol. *Am J Clin Nutr.* 2008;87:323-331.
32. Boeing H, Bechthold A, Bub A, et al. Critical review: vegetables and fruit in the prevention of chronic diseases. *Eur J Nutr.* 2012;51:637-663.
33. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. *Am J Clin Nutr.* 2003;78:920-927.
34. Mytton OT, Nnoaham K, Eyles H, Scarborough P, Ni Mhurchu C. Systematic review and meta-analysis of the effect of increased vegetable and fruit consumption on body weight and energy intake. *BMC Public Health.* 2014;14:886.
35. Alinia S, Hels O, Tetens I. The potential association between fruit intake and body weight—a review. *Obes Rev.* 2009;10:639-647.
36. Li M, Fan Y, Zhang X, Hou W, Tang Z. Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies. *BMJ Open.* 2014;4:e005497.
37. Du H, van der AD, Boshuizen HC, et al. Dietary fiber and subsequent changes in body weight and waist circumference in European men and women. *Am J Clin Nutr.* 2010;91:329-336.
38. Jacobs DR Jr, Gross MD, Steffen L, et al. The effects of dietary patterns on urinary albumin excretion: results of the Dietary Approaches to Stop Hypertension (DASH) Trial. *Am J kidney Dis.* 2009;53:638-646.
39. Nettleton JA, Steffen LM, Palmas W, Burke GL, Jacobs DR Jr. Associations between microalbuminuria and animal foods, plant foods, and dietary patterns in the Multiethnic Study of Atherosclerosis. *Am J Clin Nutr.* 2008;87:1825-1836.
40. Lin J, Fung TT, Hu FB, Curhan GC. Association of dietary patterns with albuminuria and kidney function decline in older white women: a subgroup analysis from the Nurses' Health Study. *Am J kidney Dis.* 2011;57:245-254.
41. Pedrinelli R, Dell'Omo G, Di Bello V, et al. Low-grade inflammation and microalbuminuria in hypertension. *Arterioscler Thromb Vasc Biol.* 2004;24:2414-2419.
42. Barzilay JI, Peterson D, Cushman M, et al. The relationship of cardiovascular risk factors to microalbuminuria in older adults with or without diabetes mellitus or hypertension: the cardiovascular health study. *Am J kidney Dis.* 2004;44:25-34.
43. Jenkins DJ, Kendall CW, Vidgen E, et al. High-protein diets in hyperlipidemia: effect of wheat gluten on serum lipids, uric acid, and renal function. *Am J Clin Nutr.* 2001;74:57-63.
44. Frassetto LA, Todd KM, Morris RC Jr, Sebastian A. Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. *Am J Clin Nutr.* 1998;68:576-583.
45. Teixeira SR, Tappenden KA, Carson L, et al. Isolated soy protein consumption reduces urinary albumin excretion and improves the serum lipid profile in men with type 2 diabetes mellitus and nephropathy. *J Nutr.* 2004;134:1874-1880.
46. Martin GS, Tapsell LC, Batterham MJ, Russell KG. Relative bias in diet history measurements: a quality control technique for dietary intervention trials. *Public Health Nutr.* 2002;5:537-545.
47. Huang T, Xu M, Lee A, Cho S, Qi L. Consumption of whole grains and cereal fiber and total and cause-specific mortality: prospective analysis of 367,442 individuals. *BMC Med.* 2015;13:59.
48. Kim Y, Je Y. Dietary fibre intake and mortality from cardiovascular disease and all cancers: A meta-analysis of prospective cohort studies. *Arch Cardiovasc Dis.* 2016;109:39-54.
49. Chiuve SE, McCullough ML, Sacks FM, Rimm EB. Healthy lifestyle factors in the primary prevention of coronary heart disease among men: benefits among users and nonusers of lipid-lowering and antihypertensive medications. *Circulation.* 2006;114:160-167.
50. Mekki K, Bouzidi-bekada N, Kaddous A, Bouchenak M. Mediterranean diet improves dyslipidemia and biomarkers in chronic renal failure patients. *Food Funct.* 2010;1:110-115.
51. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med.* 2001;344:3-10.
52. Gutierrez OM. Sodium- and phosphorus-based food additives: persistent but surmountable hurdles in the management of nutrition in chronic kidney disease. *Adv Chronic Kidney Dis.* 2013;20:150-156.
53. Kelly JT, Campbell KL, Wai SN, et al. Healthy eating patterns, mortality and end-stage kidney disease in CKD: A systematic review and meta-analysis. *Clin J Am Soc Nephrol* (in press). 2016;11.
54. Noori N, Kalantar-Zadeh K, Kovesdy CP, Bross R, Benner D, Kopple JD. Association of dietary phosphorus intake and phosphorus to protein ratio with mortality in hemodialysis patients. *Clin J Am Soc Nephrol.* 2010;5:683-692.