

1-1-2020

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[10.1007/s00394-019-02160-9](https://doi.org/10.1007/s00394-019-02160-9)

This is a post-peer-review, pre-copyedit version of an article published in the European Journal of Nutrition. The final authenticated version is available online at: <https://doi.org/10.1007/s00394-019-02160-9>

Bondonno, N. P., Blekkenhorst, L. C., Bird, A. L., Lewis, J. R., Hodgson, J. M., Shivappa, N., ... & Lim, W. H. (2020). Dietary inflammatory index and the aging kidney in older women: a 10-year prospective cohort study. *European Journal of Nutrition*, 59, 3201–3211.

This Journal Article is posted at Research Online.

<https://ro.ecu.edu.au/ecuworkspost2013/8351>

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Dietary inflammatory index and the ageing kidney in older women: a 10-year prospective cohort study

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Keywords: Dietary inflammatory index; chronic kidney disease; renal disease; renal decline; prospective cohort study.

Acknowledgments

The authors wish to thank the staff at the Data Linkage Branch, Hospital Morbidity Data Collection and Registry of Births, Deaths and Marriages for their work on providing data for this study.

The study was supported by Kidney Health Australia grant S07 10, Healthway Health Promotion Foundation of Western Australia, Sir Charles Gairdner Hospital Research Advisory Committee Grant and by project grants 254627, 303169 and 572604 from the National Health and Medical Research Council of Australia. The salary of JRL is supported by a National Health and Medical Research Council of Australia Career Development Fellowship (ID: 1107474). NPB is funded by a National Health and Medical Research Council Early Career Fellowship (Grant number APP1159914), Australia. The salary of JMH is supported by a National Health and Medical Research Council of Australia Senior Research Fellowship, Australia (Grant number APP1116937). WL is supported by the Raine/University of Western Australia clinical fellowship. NS and JRH were supported by the United States National Institute for Diabetes, Digestive and Kidney Diseases (grant no. R44DK103377). None of the funding agencies had any role in the conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

Abstract

Purpose: Chronic inflammation plays a role in the pathogenesis of age-related renal disease and the diet can moderate systemic inflammation. The primary objective of this study was to examine the associations between a dietary inflammatory index (DII®) score and renal function, the trajectory of renal function decline, and renal disease-related hospitalizations and/or mortality over 10 years.

Methods: The study was conducted in 1422 Western Australian women without prevalent chronic kidney disease and aged ≥ 70 years. Baseline dietary data, obtained from a validated food frequency questionnaire, were used to calculate a DII score for each individual.

Results: In this cohort the mean [range] DII score was 0.19 [-6.14 – 6.39]. A higher DII score was associated with poorer renal function and a greater renal function decline over 10 years; after multivariable adjustments a one-unit higher DII score was associated with a 0.55 mL/min/1.73m² lower eGFR at baseline ($p=0.01$), and a 0.06 mL/min/1.73m² greater annual decline in eGFR over 10 years ($p=0.05$). Restricted cubic splines provide evidence of a non-linear association between baseline DII score and risk of a renal disease-related event. Compared to participants in the lowest quintile, those in the highest quintile of DII score were at a higher risk of experiencing a renal disease-related event (adjusted HR: 2.06, 95% CI: 0.97, 4.37).

Conclusion: Recommending an increased consumption of foods with a higher anti-inflammatory potential could form part of a multifaceted approach to reduce the risk of renal disease through diet and lifestyle changes.

Introduction

Chronic kidney disease (CKD) has emerged as a major public health concern and significant driver of healthcare expenditures [1,2]. The incidence of CKD is steadily increasing, with a global prevalence of up to 13% [3].

Although a substantial proportion of older individuals in the general population have stage 2-3 CKD, individuals exhibiting a rapid decline in kidney function have the greatest risk of adverse health outcomes [4]. It has been suggested that chronic inflammation may play a critical role in the pathogenesis of age-related CKD and/or kidney function decline [1,5,6], suggesting that attenuation of an inflammatory response could potentially slow renal decline and/or reduce the risk of CKD-related adverse outcomes.

Over the last decade, the role that diet plays in the regulation of systemic inflammation has become increasingly apparent [7,8]. Epidemiological studies have shown that the intake of anti-inflammatory foods and nutrients, primarily fruit, vegetables, fibre, omega-3 polyunsaturated fatty acids and vitamins, are associated with lower serum levels of inflammatory biomarkers in persons at risk of developing CKD [9,6,10]. In contrast, pro-inflammatory diets typically high in refined grains, full fat dairy, red meat, total fat, and saturated fat are positively associated with higher levels of inflammatory biomarkers [11] and a higher incidence of CKD [12].

The literature-derived Dietary Inflammatory Index (DII®), based on 45 food parameters, is a suggested indicator of the inflammatory potential of whole dietary patterns[13]. Previous research has proposed independent associations between pro-inflammatory dietary patterns, indicated by high DII scores, and asthma[14], cardiovascular disease[15], diabetes[16] and several cancers[17-20]. There is evidence that pro-inflammatory diets are associated with systemic inflammation and reduced renal function[21]. However, associations between DII, temporal change in renal function and renal disease-related adverse health outcomes, a large and growing public health concern, remain unknown.

The aims of this study were to examine the associations between DII scores and renal function decline, and to estimate the risk of renal disease-related hospitalization and/or mortality in a cohort of elderly women in Australia. We hypothesized that, in a population of elderly women, a pro-inflammatory diet, characterized by a higher DII score, would be associated with poorer baseline renal function and a more rapid renal function decline as well as a higher risk of renal disease -related adverse health outcomes.

Methods

Study Population

Participants were originally recruited in 1998 for a 5-year double-blind, randomised, controlled trial of oral calcium supplements; the Calcium Intake Fracture Outcome Study (CAIFOS)[22]. Briefly, 1500 women aged 70 years and above were recruited from the Western Australian general population by mail using the Electoral Roll. All participants in the study were ambulatory and had an expected survival beyond 5 years. Participants received either 1.2 g of elemental calcium as calcium carbonate or a matching placebo daily. Following the completion of the study, participants were followed for a further ten years as part of the Perth Longitudinal Study of Aging in Women (PLSAW). Participants were similar to the age-matched general population in terms of disease burden and pharmaceutical consumption[22]. The current study reports on 1,422 of the total 1,500 participants included in the PLSAW. As shown in **Figure 1**, participants who did not complete a food frequency questionnaire (FFQ) at baseline and those with implausible energy intakes [$<2,092$ kJ/day (<500 kcal/day) and $>14,644$ kJ/day ($>3,500$ kcal/day)] were excluded from the analysis ($n=32$), which is consistent with other studies of this cohort[23,1]. Furthermore, all women with missing data ($n=21$) or a history of prevalent renal disease at baseline were excluded ($n=25$).

All participants provided written informed consent for the study and for the follow up of electronic health records. Ethics approval for the study was granted by The Human Ethics Committee of the University of Western Australia (approval number 05/06/004/H50) and the Human Research Ethics Committee of the Western Australian Department of Health (DOH HREC) approved the data linkage study (approval number #2009/24).

Dietary Assessment and Dietary Inflammatory Index Score

Diet was assessed at baseline (1998) using a semi-quantitative FFQ developed by the Cancer Council of Victoria[24]. This FFQ has been validated against two 7-day weighed food records and was found to have reasonable correlations for all nutrients, except retinol, due to the inclusion of liver in the weighed food records, but not the FFQ[25]. Nutrient and energy intakes were estimated based on usual portion size and the frequency of consumption[26]. The DII was intended for use in large epidemiological studies, with the intention of examining whether DII scores are associated with risk of chronic diseases. A description of the development of the DII is available elsewhere[13]. Briefly, the DII is based on 1,943 scientific articles published between 1950 and 2010 scoring 45 dietary components according to whether they increased (+1), decreased (-1) or had no

effect (0) on six inflammatory markers [interleukin (IL)-1 beta, IL-4, IL-6, IL-10, tumor necrosis factor-alpha, and C-reactive protein). Articles were weighted by study characteristics; using these weighted values, a specific inflammatory effect score was derived for each of the 45 food parameters. In the current study, the DII score was calculated using the corresponding 32 food parameters available from the FFQ used in this cohort. To calculate the DII score for each individual, the mean intake of each food parameter was standardized, converted to centered proportions and then multiplied by the respective food parameter specific inflammatory effect score. These parameter-specific DII scores were summed to create the overall DII score for each participant in the study[13]. The 32 food parameters included in the DII score are shown in **Supplemental Table 1**. Higher DII scores represent more pro-inflammatory dietary patterns, whereas lower DII scores represent more anti-inflammatory dietary patterns.

Exposure

DII was both considered as a continuous variable and was categorized into quintiles: Q1 (-6.14, -1.72); Q2 (-1.73, -0.38); Q3 (-0.39, 0.76); Q4 (0.77, 2.13); Q5 (2.14, 6.39).

Study outcomes

The primary outcomes in this study were the association between DII score and renal function at baseline, 10-year change in renal function, and renal disease-related hospitalizations and deaths (events) over the 10 years of follow-up.

Renal function (eGFR)

Fasting blood samples for creatinine and cystatin C were collected at baseline (1998), 5 years (2003), and 10 years (2008), as described elsewhere[27,4]. Estimated glomerular filtration rate (eGFR) at each of these time points was calculated from creatinine and cystatin C (CKD-EPI-creatinine and cystatin C) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[28]. The annual rate of change in eGFR over 10 years of follow-up was estimated by calculating the slope of the line between eGFR measurements at two or, when available, three time-points.

Biochemistry

Plasma total L-homocysteine (tHcy) was measured using a Fluorescence Polarization Immuno-assay as described previously [29]. High sensitivity C reactive protein (hs-CRP) was measured using a highly sensitive latex immunoassay with a measurement range of 0.02 to 48.00 mg/dL (CRP Vario, Sentinel Diagnostics, Abbott Diagnostics Europe, Milan, Italy).

10-year Renal Disease Hospitalisations and Mortality

Prevalent renal disease-related events were captured using a follow-up period of 18 years between 1980 and 1998 while incident events between 1998 and 2008 were retrieved from the Western Australian Data Linkage System (WADLS) using the diagnoses codes from the International Classification of Diseases, Injuries and Causes of Death Clinical Modification (ICD-9-CM)[30] and the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM)[31]. WADLS is a comprehensive, population-based linkage system connecting 40 years of data from over 30 health-related datasets for Western Australian residents using ICD codes[32]. A renal disease event was defined as first-time renal disease-related hospitalization or renal disease-related death. Codes used for identification of renal disease hospitalizations included ICD-9-CM codes 580–583, ICD-10-AM codes N00–08, ICD-9-CM codes 593.3–593.5, 593.7 and 590–591, ICD-10-AM codes N09–16, ICD-9-CM codes 584–586, ICD-10-AM codes N17–19, ICD-9-CM code 403, and ICD-10-AM codes I12 in either the participant’s primary discharge diagnosis or additional diagnoses fields. Renal disease-related death ICD codes included all available diagnostic information that comprised Parts 1 and 2 of the death certificate. All diagnosis text fields from the death certificate were used to ascertain the cause(s) of deaths where these data were not yet available from the WADLS.

Covariates

Baseline questionnaires were used to determine values for potential confounding variables including age, use of antihypertensive medication, use of statins, use of NSAIDs for musculoskeletal pain, and current/previous smoking. Smoking status was defined as non-smoker or ex-smoker/current smoker if a participant had ever consumed more than 1 cigarette per day for more than 3 months during their lifetime. Weight (kg) was measured using digital scales, height (m) was assessed using a stadiometer and body mass index (BMI) was calculated in kg/m². Physical activity was assessed by asking participants about their participation in regular physical activities undertaken in the three months prior to their baseline visit [33]. Activity levels (kJ/d) were calculated using a validated method, taking into consideration the type of activity, time engaged in the activity,

and body weight[34]. Total energy intakes were estimated from the FFQ. Prevalent cancer and atherosclerotic vascular disease (ASVD) at baseline was determined from primary discharge diagnoses from hospital records (1980–1998). ICD codes for prevalent cancer included (ICD-9-CM codes C00–C99). ICD codes for prevalent ASVD included: ischemic heart disease (ICD-9-CM codes 410–414); heart failure (ICD-9-CM code 428); cerebrovascular disease excluding hemorrhage (ICD-9-CM codes 433–438); and peripheral arterial disease (ICD-9-CM codes 440–444). Participants provided their previous medical history and current medications, with this information verified by their General Practitioner where possible. These data were coded using the International Classification of Primary Care – Plus (ICPC-Plus) method[35], allowing for aggregation of different terms for similar pathologic entities as defined by the ICD-10 coding system, and then used to determine the presence of diabetes at baseline.

Statistical Analysis

Analyses were undertaken using STATA/IC® 14.2 (StataCorp LLC), SAS® 9.4 (SAS Institute Inc) and R® statistics (R Core Team[36]). Statistical significance was set at $p \leq 0.05$ (two-tailed) for all tests. For all analyses, two models of adjustment were fit: 1) minimally-adjusted: age and energy intake; and 2) multivariable-adjusted: age, energy intake, treatment code (calcium or placebo), BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, and use of NSAIDs for joint pain. Generalized additive models were used to examine the association between DII and both baseline eGFR and the trajectory of eGFR change over the 10 years of follow-up. In the latter analysis, the time-points at which eGFR was measured was adjusted for. The associations of DII with biomarkers of inflammation, eGFR, and the trajectory of eGFR change were assessed by linear regression. Potential nonlinear relationships between DII and renal disease-related mortality and hospitalisation events were examined using restricted cubic splines, with hazard ratios (HRs) based on Cox proportional hazards models. HRs with 95% confidence intervals (CIs) were plotted for each unit of the exposure against the median DII score in quintile 1. Age- and multivariable-adjusted Cox proportional hazard ratios (HR) and 95% confidence intervals (CIs) for renal events were computed across quintiles of DII score, where the lowest (least inflammatory) quintile was the referent. Schoenfeld residuals were used to check the Cox proportional hazards assumptions, with no evidence of violation of this assumption. As the research question addressed in this paper was aetiological in nature, we did not apply a sub-distribution proportional hazards model to take into account competing risks[37]. Individuals who died or were lost to follow-up were censored. As a sensitivity analysis, all participants with a history of cancer at baseline were excluded and 1,336 were re-analysed. Statistical power was too limited to perform analysis for renal disease-

related hospitalisation and deaths separately (114 renal disease-related hospitalisations and 19 renal disease-related deaths).

Results

Baseline characteristics

In this population of 1,422 postmenopausal women, DII scores were normally distributed with a mean of 0.19 units and a SD of 2.14 units. The baseline characteristics of the study population, overall and stratified by DII score quintiles [Q1 (-6.14, -1.72); Q2 (-1.73, -0.38); Q3 (-0.39, 0.76); Q4 (0.77, 2.13); Q5 (2.14, 6.39)], are shown in **Table 1**. At baseline, subjects in the highest versus the lowest quintile of DII score had a lower energy intake, lower level of physical activity and lower eGFR. No other baseline characteristics appeared to differ across the DII quintiles. Baseline intakes of dietary components that were used to calculate the DII score, for the total cohort population and stratified by the occurrence of a renal disease-related event, are presented in **Supplemental Table 1**. Intakes of trans-fatty acids were higher in participants who suffered from a renal event ($p=0.01$). Intakes of the vitamins riboflavin, niacin, folate and vitamin E, the minerals iron, magnesium and zinc, and isoflavones (from sources other than tea) were lower in participants who had experienced a renal event ($p<0.05$ for all). Differences in baseline dietary intakes across DII quintiles are presented in **Supplemental Table 2**. After energy adjustment, with the exception of alcohol, retinol equivalents, and garlic, intakes of all other food parameters used to calculate the DII score were significantly different across DII quintiles ($p<0.05$). Aside from carbohydrates and iron, the intakes of food parameters that positively contribute to the DII score increased as DII quintiles increased while all food parameters that negatively contributed to the DII score decreased across DII quintiles.

Associations between DII and renal function estimates

Of 1,111 participants with eGFR measured at baseline, the mean \pm SD for eGFR was 65.9 ± 12.9 mL/min/1.73m². Evidence for a linear association between DII score and baseline eGFR can be seen in **Figure 2** ($p=0.01$). After multivariable adjustments a one-unit higher DII score was associated with a 0.55 mL/min/1.73m² lower eGFR at baseline ($p=0.01$; **Table 2**). Of the 1,342 participants still alive after 5 years of follow-up, eGFR was measured in 1,022; the mean \pm SD for eGFR was 61.33 ± 14.19 mL/min/1.73m². Of the 1,253 participants still alive after 10 years of follow-up, eGFR was measured in 738; the mean \pm SD for eGFR was 60.4 ± 15.8 mL/min/1.73m². The association between DII score and eGFR at both 5 and 10 years was linear

($p < 0.01$). After multivariable adjustments a one-unit higher DII score was associated with a 0.89 mL/min/1.73m² lower eGFR at 5 years ($p < 0.01$) and a 0.92 mL/min/1.73m² lower eGFR at 10 years ($p = 0.01$; **Table 2**). eGFR was calculated at two or more time points in 998 women, allowing for an estimation of renal function trajectory (annual rate of change in eGFR) in this subgroup. **Figure 3** provides weak evidence that there is a linear association between DII and renal function trajectory ($p = 0.08$). After multivariable adjustments a one-unit higher DII score was associated with a 0.06 mL/min/1.73m² greater annual decline in eGFR ($p = 0.05$; **Table 2**).

Associations between DII and biomarkers of inflammation

After multivariable adjustments, a one-unit higher DII score was associated with a 0.46 μ mol/L higher baseline plasma tHcy ($p < 0.001$; **Supplementary Table 3**). DII score was not significantly associated with baseline levels of hs-CRP ($p = 0.57$; **Supplementary Table 3**).

Associations with 10-year renal disease-related events

During 13,013 person-years of follow-up (median follow-up time = 10 years), 123 (8.6%) participants experienced a renal disease-related event (hospitalization or death). Restricted cubic splines provide evidence of a non-linear association between baseline DII score and risk of a renal disease-related event (p for non-linearity = 0.04; **Figure 4**). Compared to participants with a DII score of -2.6, those with a score > 4 had a significantly higher risk of experiencing a renal disease-related event (HR: 2.35, 95% CI: 1.16, 4.75). Minimal- and multivariable-adjusted associations between DII score and renal events are shown in **Table 3**. After multivariable adjustments, there was evidence that participants in the highest (most pro-inflammatory) quintile of DII score were at a higher risk of experiencing a renal disease-related event (HR: 2.06, 95% CI: 0.97, 4.37) compared to those in the lowest quintile.

Sensitivity analysis

Excluding participants with a history of cancer at baseline ($n = 86$) did not change the main findings of the study. After multivariable adjustments, a one-unit higher DII score was associated with a 0.57 mL/min/1.73m² (95% CI: 0.13, 1.01, $p = 0.01$) lower eGFR at baseline and a 0.06 mL/min/1.73m² (95% CI: 0.00, 0.12, $p = 0.05$) greater annual decline in eGFR. Furthermore, participants in the highest quintile of DII score had a two times higher

risk of experiencing a renal disease-related event (HR: 2.00, 95% CI: 0.973 4.28) compared to those in the lowest quintile.

Discussion

The relationships between the inflammatory potential of the diet, assessed using the DII, renal function and renal disease-related events were investigated in a cohort of 1,422 postmenopausal women. Evidence suggests that participants with a higher pro-inflammatory diet score had poorer renal function and a greater decline in renal function over 10 years of follow-up. Additionally, participants with high DII® score appeared to be at the highest risk of a renal disease-related event.

Diet is an important and potentially easily modifiable risk factor for chronic disease[38]. A Western-style diet, characterized by a high intake of added sugar, red meat, refined grains, and high-fat dairy products, contributes to systemic inflammation (with elevated inflammatory biomarkers)[11] and development of CKD[12]. Conversely, a Mediterranean-style diet, characterized by a high intake of fruits, vegetables and wholegrains with a low intake of red meats and saturated fat, attenuates systemic inflammation[39] and may be protective against the development of CKD[40]. Although the DII score is used to reflect the overall inflammatory potential of the participants' diets, the relationship between specific food components included in the calculation of the DII and renal disease events is more difficult to establish. However, women who experienced renal disease-related events had higher intakes of pro-inflammatory *trans*-fatty acids, a dietary component characteristic of a Western-style diet. Additionally, the intakes of anti-inflammatory dietary components including vitamins (riboflavin, niacin, folate and vitamin E), minerals (iron, magnesium and zinc), and isoflavones were lower in women who had experienced renal disease-related events.

Reduced kidney function has been shown to be an independent risk factor for cardiovascular disease and all-cause mortality in the general population, with the risk of end-stage kidney disease increasing exponentially with eGFR below 60 mL/min/1.73m²[4,41,42]. Although the association between CKD and mortality is well recognized, the extent of a direct causal pathway remains unclear, since considerable indirect effects exist via an excess of traditional CVD risk factors. Reduced kidney function is associated with significantly higher serum levels of inflammatory biomarkers [43,44]. In addition, the DII score is positively associated with circulating levels of the inflammatory biomarkers, CRP [45,46] and IL-6 [45,47,46,21], suggesting the likelihood of an inverse association between DII and kidney function. In the present study, participants with a higher DII score

had a lower eGFR at baseline, suggesting that a pro-inflammatory diet is associated with poorer kidney function. In line with our findings, recent cross-sectional studies have reported that a higher DII score was associated with worse kidney function, a higher prevalence of CKD [48], and, in participants with CKD, a higher risk of being in a later stage of CKD [49]. In a cross-sectional study of 1,942 elderly Swedish men and women, from two independent cohorts, researchers considered the association between an adapted DII (ADII) and kidney function[6]. The ADII differs from the DII used in this paper in that it is calculated by modifying an older version of the DII which uses fewer dietary parameters, is based on reviewing less articles (n=927) and is now obsolete for reasons described elsewhere [50]. Despite the methodologic deficiencies, the authors demonstrated that a 1 SD higher ADII score was associated with a 1.8% lower eGFR at baseline (β : -1.8%; 95% CI: -2.7%, -0.9%; $p < 0.001$). Mediation analyses revealed that 15% of the association could be explained by increased plasma levels of CRP. Whether dietary changes to incorporate more anti-inflammatory foods can improve renal function warrants further investigation.

Temporal change in eGFR may be a more accurate prediction of adverse long-term health outcomes in the general population compared to a single-time-point eGFR. In a study of 4,380 subjects with 7-year follow-up, individuals who had experienced a more rapid loss of kidney function, greater than 3 ml/min/1.73m², were at more than a 50% higher risk of death and developing CVD, independent of baseline eGFR and traditional CVD risk factors [51]. In a comparable population, consisting primarily of older white women, a Western-style dietary pattern correlated directly with a rapid decline of eGFR [52]. To our knowledge, no previous studies have examined the relationship between DII and renal function decline. Our results show that participants with the most pro-inflammatory diet had the lowest eGFR at each time-point and experienced the greatest decline in renal function over 10 years.

To date, no previous prospective cohort study has examined the relationship between DII and renal disease-related events. Our results suggest that the risk of a renal disease-related event is highest in participants with the most pro-inflammatory diet. However, our findings of a non-linear association suggest that only individuals with a highly pro-inflammatory diet are at a higher risk. If this proposed association is confirmed to be causal, individuals at the upper end of the DII score scale should be the primary target for dietary intervention, as they are likely to experience the most benefit. With projected expenditures of renal disease-related disease reaching 12 billion AUD by 2020 [2], such findings are of great clinical and economic significance.

There are a number of strengths of this study, including the use of a large prospective cohort of subjects with no loss to follow-up, combined with use of the literature-derived DII, validated against a variety of inflammatory markers [45,47,46,21], and the use of an eGFR equation based on creatinine and cystatin C which is a better measure of true GFR than eGFR equations using creatinine alone [53]. Renal disease-related events were ascertained through independently reported hospital records, removing the risk of recall bias. Furthermore, adjusting for a large number of potential confounding factors did not significantly alter the observed relationship between DII and eGFR. The strengths of this study must be balanced against the limitations; firstly this is an observational study and as such causality cannot be established. Secondly, the findings are in a cohort of women of European descent aged ≥ 70 years with adequate nutrition, therefore limiting the ability to generalize findings to males, other ethnic groups, younger individuals, and those with poor nutrition intakes. Participant DII scores could only be calculated from 32 of the original 45 dietary components that were available from the FFQ used in the PLSAW study. Participants only completed an FFQ at baseline meaning that changes in DII scores over time were not able to be assessed. Additionally, the modest number of event cases resulted in the inability to assess the risk of renal disease hospitalization and mortality separately.

Conclusion

In the present cohort of women ≥ 70 years of age, we have shown that a pro-inflammatory dietary pattern, reflected by a higher DII score, is associated with poorer renal function, a more rapid renal function decline over 10 years, and a higher risk of renal disease-related hospitalization and/or death. Further research is warranted to confirm the association between the inflammatory potential of the diet and kidney function as well as to verify these findings in other population groups.

300 **Conflict of interest**

301 The authors declare no conflict of interest.

302 **Disclosure**

303 Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company that has
304 licensed the right to his invention of the dietary inflammatory index (DII®) from the University of South
305 Carolina in order to develop computer and smart phone applications for patient counseling and dietary
306 intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI.

307 **Authorship**

308 W.H.L., J.R.L., D.A.K., and R.L.P. were responsible for the project conception; J.R.L., R.L.P. collected the
309 data; W.H.L., J.R.L., D.A.K., R.L.P., and J.M.H. developed the research plan; N.S. and J.R.H. contributed
310 expertise and algorithms to calculate the DII scores and consulted on DII-related analyses. N.P.B. analyzed the
311 data; N.P.B., L.C.B., and A.L.B. prepared the manuscript; all authors critically reviewed the manuscript.

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Table 1. Baseline characteristics of study population

	Total population n=1422	DII® quintiles					P value
		Q1 n=283	Q2 n=284	Q3 n=283	Q4 n=287	Q5 n=285	
DII, mean [range]	0.19 [-6.14, 6.39]	-2.83 [-6.14, -1.72]	-1.02 [-1.73, -0.38]	0.18 [-0.39, 0.76]	1.40 [0.77, 2.13]	3.18 [2.14, 6.39]	
<i>Demographics</i>							
Age (years)	75.2 ± 2.7	75.3 ± 2.7	75.0 ± 2.7	75.3 ± 2.7	75.2 ± 2.7	75.1 ± 2.8	0.69
Body mass index (kg/m ²)	27.2 ± 4.8	27.2 ± 4.8	27.0 ± 4.3	27.3 ± 4.6	27.5 ± 4.8	26.9 ± 5.1	0.77
Energy intake (MJ/d)	7.1 ± 2.1	9.2 ± 2.0	7.7 ± 1.7	7.0 ± 1.4	6.1 ± 1.4	5.4 ± 1.4	<0.001
Smoked ever, n (%)	530 (37.2)	107 (37.8)	103 (36.3)	96 (33.9)	106 (36.9)	118 (41.4)	0.53
Physical activity (kJ/day), median [IQR]	470 [114, 857]	554 [213, 901]	488 [219, 906]	469 [0, 800]	464 [100, 850]	354 [0, 795]	0.004
Alcohol intake (g/d), median [IQR]	0.8 [0.3, 9.8]	1.4 [0.1, 12.9]	2.0 [0.4, 9.9]	2.2 [0.3, 9.3]	1.9 [0.3, 9.8]	1.1 [0.2, 8.0]	0.34
Diabetes, n (%)	84 (5.9)	16 (5.7)	18 (6.3)	13 (4.6)	20 (7.0)	17 (6.0)	0.78
ASVD, n (%)	163 (11.4)	32 (11.3)	25 (8.8)	37 (13.1)	38 (13.2)	31 (10.9)	0.44
Cancer, n (%)	86 (6.0)	14 (4.9)	11 (3.9)	25 (8.8)	19 (6.6)	17 (6.0)	0.14
eGFR (mL/min per 1.73m ²)	65.9 ± 12.8	67.0 ± 12.1	67.5 ± 13.2	64.1 ± 12.9	65.8 ± 12.9	65.2 ± 12.9	0.03
<i>Medications, n (%)</i>							
Treatment (calcium)	744 (52.3)	157 (55.5)	154 (54.2)	152 (53.7)	140 (48.8)	141 (49.1)	0.54
Antihypertensive	612 (43.0)	126 (44.5)	141(49.6)	131 (46.3)	123 (42.9)	121 (49.5)	0.59
NSAIDs for joint pain	469 (33.0)	87 (30.7)	95 (33.5)	101 (35.7)	89 (31.0)	97 (34.0)	0.66
Statins	269 (18.9)	67 (23.7)	52 (18.3)	52 (18.4)	45 (15.7)	53 (18.6)	0.13

Data expressed as mean ± SD unless otherwise stated. P-values for comparisons between DII® score quintiles were derived by ANOVA, Kruskal-Wallis H test or x² test where appropriate. ASVD, atherosclerotic vascular disease; DII®, Dietary Inflammatory Index; eGFR, estimated Glomerular Filtration Rate.

Table 2. Association between DII score and eGFR at baseline (1998), 5 years (2003), and 10 years (2008) and annual rate of change in eGFR.

	N	Model 1		Model 2	
		β (95% CI)	p value	β (95% CI)	p value
eGFR at baseline	1,111	-0.49 (-0.94, -0.05)	0.03	-0.55 (-0.98, -1.22)	0.01
eGFR at 5 years	1,022	-0.82 (-1.34, -0.30)	<0.01	-0.89 (-1.38, -0.39)	<0.01
eGFR at 10 years	738	-0.80 (-1.51, -0.08)	0.03	-0.92 (-1.60, -0.24)	0.01
Annual change in eGFR*	998	-0.06 (-0.12, 0)	0.07	-0.06 (-0.12, 0)	0.05

Association between baseline dietary inflammatory index (DII®) score and estimated glomerular filtration rate (eGFR) at baseline, 5 years and 10 years of follow-up, and annual rate of change in eGFR. Estimates were obtained using linear regression analyses adjusted for age and energy (Model 1) and age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, and use of NSAIDs for joint pain (Model 2). *Adjusted for years in which eGFR was measured.

Table 3. Risk estimates of renal disease-related events during 10 years of follow-up

		N (events/total)	Model 1		Model 2	
			HR (95% CI)	p value	HR (95% CI)	p value
Baseline DII quintiles						
Q1 (<-1.72)	18/283	1.00 (Referent)		1.00 (Referent)		
Q2 (-1.73, -0.38)	23/284	1.35 (0.71, 2.56)	0.36	1.35 (0.70, 2.58)	0.37	
Q3 (-0.39, 0.76)	27/283	1.53 (0.80, 2.93)	0.20	1.51 (0.78, 2.93)	0.22	
Q4 (0.77, 2.13)	22/287	1.18 (0.57, 2.43)	0.65	1.12 (0.54, 2.33)	0.77	
Q5 (≥2.14)	33/285	1.96 (0.95, 4.05)	0.07	2.06 (0.97, 4.37)	0.06	

DII, Dietary inflammatory index.

Hazard ratios (HR) and 95% confidence intervals (CI) were obtained from Cox proportional hazards models adjusted for age and energy (Model 1) and age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, and use of NSAIDs for joint pain (Model 2).

Figure Legends:

Fig. 1 Consort flow diagram.; eGFR, estimated glomerular filtration rate; FFQ, food frequency questionnaire

Fig. 2 Graphic presentation of the multivariable adjusted effect of dietary inflammatory index (DII) on estimated glomerular filtration rate (eGFR) in 1,111 elderly Western Australian women at baseline (1998). The vertical axis is the difference in eGFR at each DII score relative to the eGFR for the mean DII score. The association was obtained from a generalized additive model adjusted for age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, and use of NSAIDs for joint pain.

Fig. 3 Graphic presentation of the multivariable adjusted effect of dietary inflammatory index (DII) on annual rate of change of estimated glomerular filtration rate (eGFR; $p=0.08$) in 998 elderly Western Australian women during 10 years of follow-up (1998 - 2008). The vertical axis is the difference in the annual rate of change of eGFR at each DII score relative to the annual rate of change of eGFR for the mean DII score. The association was obtained from a generalized additive model adjusted for age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, use of NSAIDs for joint pain, and time of eGFR measurements.

Fig. 4 Cubic spline curves describing the association between Dietary Inflammatory Index score and renal disease-related events (hospitalization or death); p for non-linearity = 0.04. Hazard ratios are based on Cox proportional hazards models adjusted for age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, use of NSAIDs for joint pain, and are comparing the specific Dietary Inflammatory Index score (horizontal axis) to the median score for participants in the quintile 1 (-2.6)

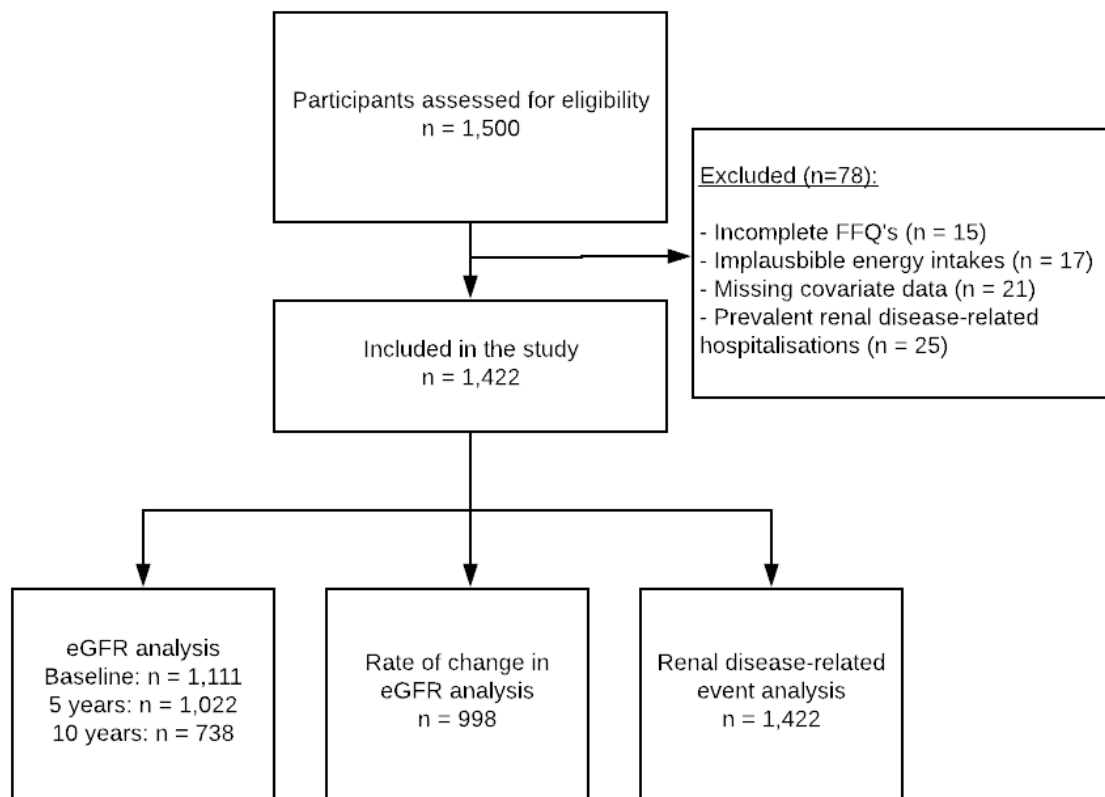


Figure 1. Consort flow diagram.; eGFR, estimated glomerular filtration rate; FFQ, food frequency questionnaire.

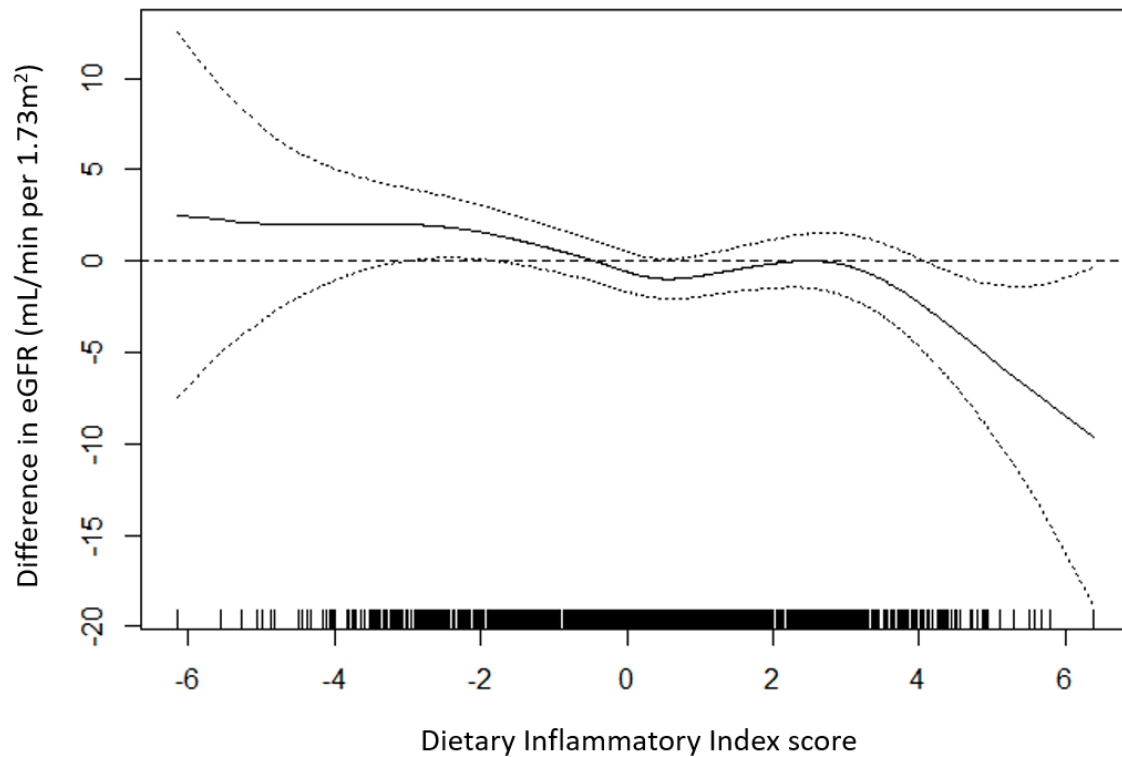


Figure 2. Graphic presentation of the multivariable adjusted effect of dietary inflammatory index (DII) on estimated glomerular filtration rate (eGFR) in 1,111 elderly Western Australian women at baseline (1998). The vertical axis is the difference in eGFR at each DII score relative to the eGFR for the mean DII score. The association was obtained from a generalized additive model adjusted for age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, and use of NSAIDs for joint pain.

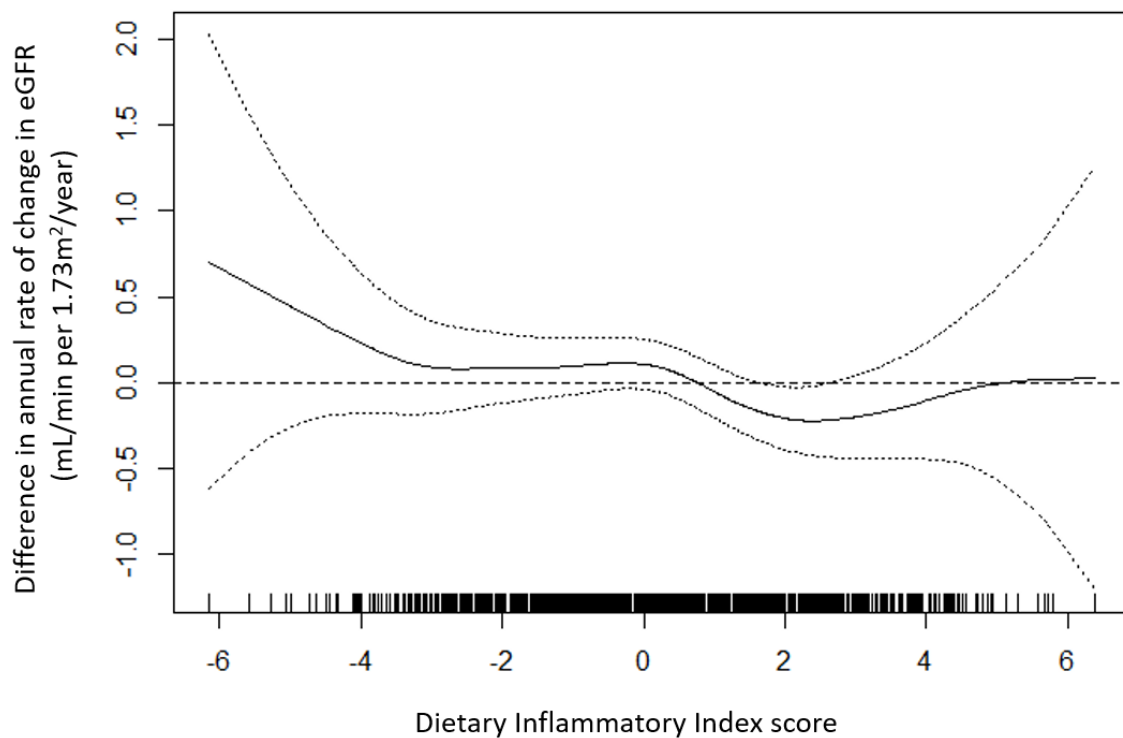


Figure 3. Graphic presentation of the multivariable adjusted effect of dietary inflammatory index (DII) on annual rate of change of estimated glomerular filtration rate (eGFR; $p=0.08$) in 998 elderly Western Australian women during 10 years of follow-up (1998 - 2008). The vertical axis is the difference in the annual rate of change of eGFR at each DII score relative to the annual rate of change of eGFR for the mean DII score. The association was obtained from a generalized additive model adjusted for age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, use of NSAIDs for joint pain, and time of eGFR measurements.

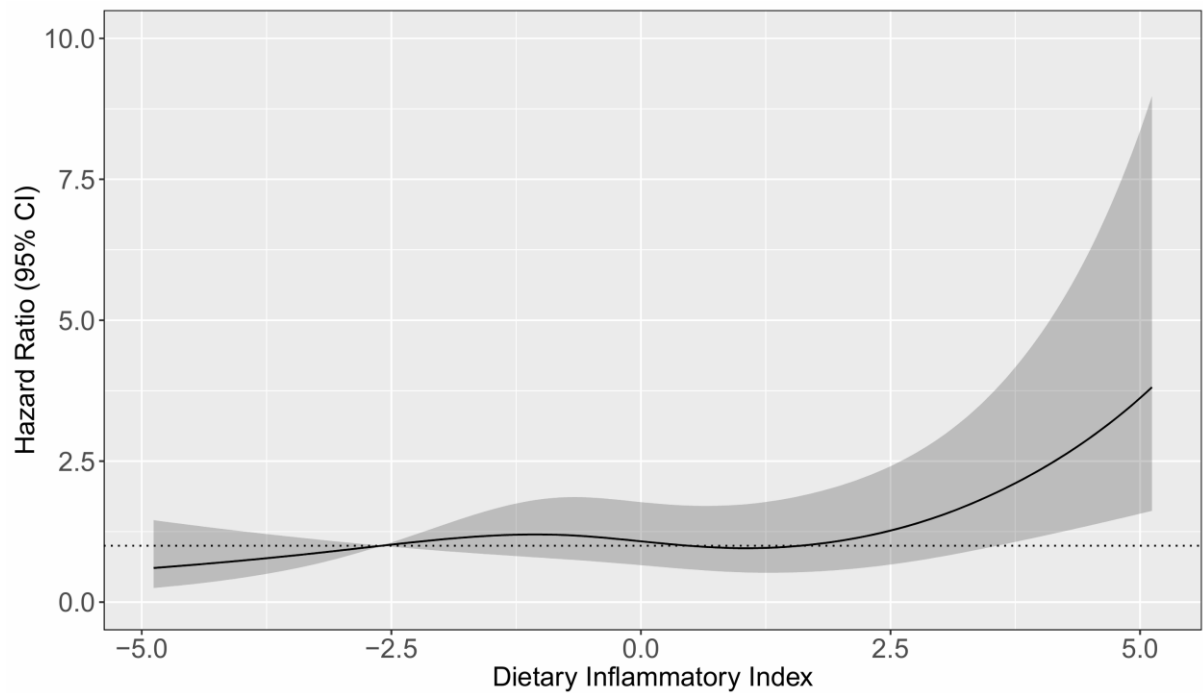


Figure 4. Cubic spline curves describing the association between Dietary Inflammatory Index score and renal disease-related events (hospitalization or death); p for non-linearity = 0.04. Hazard ratios are based on Cox proportional hazards models adjusted for age, energy intake, treatment code, BMI, smoking status, physical activity, alcohol intake, diabetes status, use of antihypertensive medication, prevalent ASVD, statin use, use of NSAIDs for joint pain, and are comparing the specific Dietary Inflammatory Index score (horizontal axis) to the median score for participants in the quintile 1 (-2.6).