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REVIEW

Dietary fiber effects in chronic kidney disease: a systematic review and meta-analysis of controlled feeding trials

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BACKGROUND/OBJECTIVES: Chronic kidney disease (CKD) is a major health concern associated with increased risk of cardiovascular disease, morbidity and mortality. Current CKD practice guidelines overlook dietary fiber, which is chronically low in the renal diet. However, increasing dietary fiber has been proposed to ameliorate the progress of CKD. We therefore conducted a systematic review and meta-analysis on the effect of dietary fiber intake on serum urea and creatinine as classical markers of renal health in individuals with CKD.

SUBJECTS/METHODS: We searched MEDLINE, EMBASE, CINHAL and the Cochrane Library for relevant clinical trials with a follow-up $\geqslant 7$ days. Data were pooled by the generic inverse variance method using random-effects models and expressed as mean difference (MD) with 95% confidence intervals (95% CIs). Heterogeneity was assessed by the Cochran Q statistic and quantified by I^2.

RESULTS: A total of 14 trials involving 143 participants met the eligibility criteria. Dietary fiber supplementation significantly reduced serum urea and creatinine levels in the primary pooled analyses (MD, − 1.76 mmol/l (95% CI, − 3.00, − 0.51), $P < 0.01$ and MD, − 22.83 mmol/l (95% CI, − 42.63, − 3.02), $P = 0.02$, respectively) with significant evidence of interstudy heterogeneity only in the analysis of serum urea.

CONCLUSIONS: This is the first study to summarize the potential beneficial effects of dietary fiber in the CKD population demonstrating a reduction in serum urea and creatinine, as well as highlighting the lack of clinical trials on harder end points. Larger, longer, higher-quality clinical trials measuring a greater variety of uremic toxins in CKD are required (NCT01844882).

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INTRODUCTION

Despite the accumulating evidence on the beneficial effects of dietary fiber in ameliorating uremic environments, guidelines make little or no reference to dietary fiber intake for chronic kidney disease (CKD).[1–6] In fact, the renal diet has chronically been deficient in dietary fiber due to concerns over increased potassium and phosphorus intake. As a result, the benefits of fiber including adequate laxation are often overlooked in those with CKD. Stephen and Cummings[7] in the early 1980s were among the first to show that dietary fiber consumption increased fecal bacterial mass and nitrogen excretion. Their findings for dietary fiber intake have since been validated by others and support the notion of a lower uremic toxin production by bacterial degradation of dietary and secretory proteins of the gastrointestinal tract,[8–11] as well as improved cardiovascular disease (CVD) risk factor profile and oxidative stress status.[12] A recent cohort study[13] concluded that participants with the highest dietary cereal fiber intake, compared with those with the lowest, had a 50% reduced risk for incidence of moderate CKD. Furthermore, in the recent Prevención con Dieta Mediterránea study, a significant association was found between greater fiber intake and reduced risk of CKD.[14] Unfortunately, according to NHANES III data, the average dietary fiber intake in the CKD population is about 15.4 g/day, which is much lower than the recommended 25–30 g/day intake for the general population.[15] Considering the potential benefits of dietary fiber and the very low average intake of this nutrient in the CKD population, we have conducted a systematic review and meta-analysis of controlled feeding trials to assess the effect of dietary fiber on serum urea and creatinine as clinical markers of uremia in individuals with CKD.

SUBJECTS AND METHODS

We conducted a systematic review and meta-analysis following the Cochrane Handbook for Systematic Reviews of Interventions[16] and have reported our findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17,18] The protocol is registered at Clinicaltrials.gov (NCT01844882).

Study selection

We searched MEDLINE, EMBASE, CINAHL and the Cochrane Library through 1 September 2014 using the search terms '(dietary fiber OR fiber$ OR fibre$ OR polysaccharides OR psyllium$ OR metamucil OR polymers OR carbohydrate$ OR dietary carbohydrate OR fermentable OR fructans OR Asteraceae OR fructooligosaccharide$ OR oligofructose$ OR chicory root$ OR jerusalem artichoke$ OR inulin OR Benefiber OR Unifiber OR lactulose) AND

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(chronic kidney disease OR CKD OR chronic renal failure OR CRF OR renal insufficiency OR hemodialysis OR haemodialysis OR dialysis)' (Table 1). There was no restriction placed on language and the search was supplemented with manual searches of the reference lists of all selected articles and review articles. We included controlled feeding trials investigating the effect of dietary fiber compared with non-fiber supplemented diets or low-fiber diets on serum urea and creatinine, as well as serum phosphorus, in patients with CKD or on hemodialysis (HD). Trials where protein content varied between treatments were not included in order to isolate the effects of fiber. Trials were excluded if they were <7 days of follow-up (fiber diet duration) or did not provide data on either of the end points of interest.

Data extraction

Each report was independently reviewed and had relevant data extracted by two independent reviewers (LC and AM). Each reviewer also assessed study quality using the Heyland Methodological Quality Score. Non–English language articles were translated. Extracted data included information on study setting, design, randomization, blinding, sample size and participant characteristics; fiber type, dose and comparator; follow-up; macronutrient profile of the background diet; and funding. Disagreements were reconciled by consensus.

Mean and s.d. data on serum urea and creatinine for end of treatment were extracted as the *a priori* end points, as well as phosphorus *post hoc*. All trials reported end of treatment values. Missing s.d. values were calculated from available statistics using standard formulae.[16] Missing s.d. values were imputed using the pooled s.d. of other trials which report s.d.[19] Correlation coefficients for individual trials were derived according to a standard formula.[16,20] In studies where correlation coefficients could not be derived from available data, a pooled correlation coefficient was applied. This pooled correlation coefficient was derived from a meta-analysis of the transformed *Z*-scores ± s.e. of available correlation coefficients. Selected authors were contacted to request additional information.

Statistical analyses

Data were analyzed using Review Manager (RevMan) version 5.2 (Copenhagen, Denmark) for primary pooled analyses and STATA version 11 (StataCorp, College Station, TX, USA) for subgroup analyses. Data were pooled using the generic inverse variance method with random-effects models and data expressed as mean differences (MDs) with 95% confidence intervals (CIs). Inter-study heterogeneity was assessed by the Cochran *Q* statistic (χ^2), with the significance at $P < 0.10$ and quantified by the I^2 statistic, where a value of $\geqslant$50% indicates substantial heterogeneity.[16] Potential sources of methodological heterogeneity were investigated by sensitivity analyses in which each individual trial was removed systematically and the pooled effect estimates recalculated as well as by *a priori* subgroup analyses for randomization (yes or no), fiber type (fermentable and non-fermentable), dose ($\leqslant$25 g/day, >25 g/day), follow-up ($\leqslant$4 week, >4 week), participant type (HD or non-HD) and Heyland Methodological Quality Score (<8, $\geqslant 8$). Meta-regression analyses were used to test for subgroup

Table 1. PRISMA flow diagram: search strategy for studies assessing the effect of dietary fiber on serum urea and creatinine in CKD

Database	*Search period*	*Search terms*
MEDLINE	1948 to 1 September 2014	1. Dietary fiber OR fiber$ OR fibre$ OR polysaccharides OR psyllium$ OR metamucil OR polymers OR carbohydrate$ OR dietary carbohydrate OR fermentable OR fructans OR Asteraceae OR fructooligosaccharide$ OR oligofructose$ OR chicory root$ OR jerusalem artichoke$ OR inulin OR Benefiber OR Unifiber OR lactulose 2. Chronic kidney disease OR CKD OR chronic renal failure OR CRF OR renal insufficiency OR hemodialysis OR haemodialysis OR dialysis 3. 1 and 2 4. Limit 3 to animals 5. 3 not 4
EMBASE	1948 to 1 September 2014	1. Dietary fiber OR fiber$ OR fibre$ OR polysaccharides OR psyllium$ OR metamucil OR polymers OR carbohydrate$ OR dietary carbohydrate OR fermentable OR fructans OR Asteraceae OR fructooligosaccharide$ OR oligofructose$ OR chicory root$ OR jerusalem artichoke$ OR inulin OR Benefiber OR Unifiber OR lactulose 2. Chronic kidney disease OR CKD OR chronic renal failure OR CRF OR renal insufficiency OR hemodialysis OR haemodialysis OR dialysis 3. 1 and 2 4. Limit 3 to randomized controlled trials
CINAHL	To 1 September 2014	1. Dietary fiber OR fiber$ OR fibre$ OR polysaccharides OR psyllium$ OR metamucil OR polymers OR carbohydrate$ OR dietary carbohydrate OR fermentable OR fructans OR Asteraceae OR fructooligosaccharide$ OR oligofructose$ OR chicory root$ OR jerusalem artichoke$ OR inulin OR Benefiber OR Unifiber OR lactulose 2. Chronic kidney disease OR CKD OR chronic renal failure OR CRF OR renal insufficiency OR hemodialysis OR haemodialysis OR dialysis 3. 1 and 2 4. Limit 3 to animals 5. 3 not 4
The Cochrane Library	To 1 September 2014	1. Dietary fiber OR fiber$ OR fibre$ OR polysaccharides OR psyllium$ OR metamucil OR polymers OR carbohydrate$ OR dietary carbohydrate OR fermentable OR fructans OR Asteraceae OR fructooligosaccharide$ OR oligofructose$ OR chicory root$ OR jerusalem artichoke$ OR inulin OR Benefiber OR Unifiber OR lactulose 2. Chronic kidney disease OR CKD OR chronic renal failure OR CRF OR renal insufficiency OR hemodialysis OR haemodialysis OR dialysis 3. 1 and 2

Abbreviations: CKD, chronic kidney disease; CRF, chronic renal failure. *For all databases, the original search date was 30 January 2012; updated searches were performed on 31 May, 17 July, 11 September 2012, 7 January, 29 April, 18 September 2013 and 1 September 2014.

differences. Meta-regression analyses were also performed to assess the possibility of dose–response associations. Where linear relationships were not found, dose response was formally tested using meta-regression, successively adding up to 4th degree (quartic) functions of dose, to assess for improved model fit. Publication bias was investigated by visual inspection of funnel plots and formally tested using Begg[21] and Egger[22] tests.

RESULTS

Search results

The flow of the literature for identifying trials is depicted in Figure 1. Eligible reports (8051) were identified by the search, and review of the titles and abstracts identified 72 potentially relevant reports for full review of which 60 were excluded. A total of 12 reports[8,23–33] providing data for 14 trials met the eligibility criteria for analyses. Thirteen trials reported data for serum urea ($n = 123$), 12 trials reported data for serum creatinine ($n = 120$) and 7 trials reported data for serum phosphorus ($n = 66$).

Trial characteristics

Trial characteristics are detailed in Table 2. There were 14 trials involving 143 participants described as having CKD or chronic renal failure, 74 of whom were on any type of HD. Participants tended to be middle-aged men (median age, 51.9 years (range: 22–72 years)). Median baseline serum urea was ~25.0 mmol/l (range: 4.9–42.0mmol/l) overall with 25.0 mmol/l (range: 4.9–42.0 mmol/l) for those with CKD and 26.9 mmol/l (range: 21.1–32.0 mmol/l) for HD participants. Median baseline serum creatinine was ~495.7mmol/l (range: 291.7–3180.0 mmol/l) overall with 415.5 mmol/l (range: 291.7–3180.0 mmol/l) for those with CKD and 936.0 mmol/l (range: 777.9–1060.8 mmol/l) for HD participants. Median baseline serum phosphorus was ~1.71 mmol/l (range: 1.1–2.2 mmol/l) overall and 1.45 mmol/l

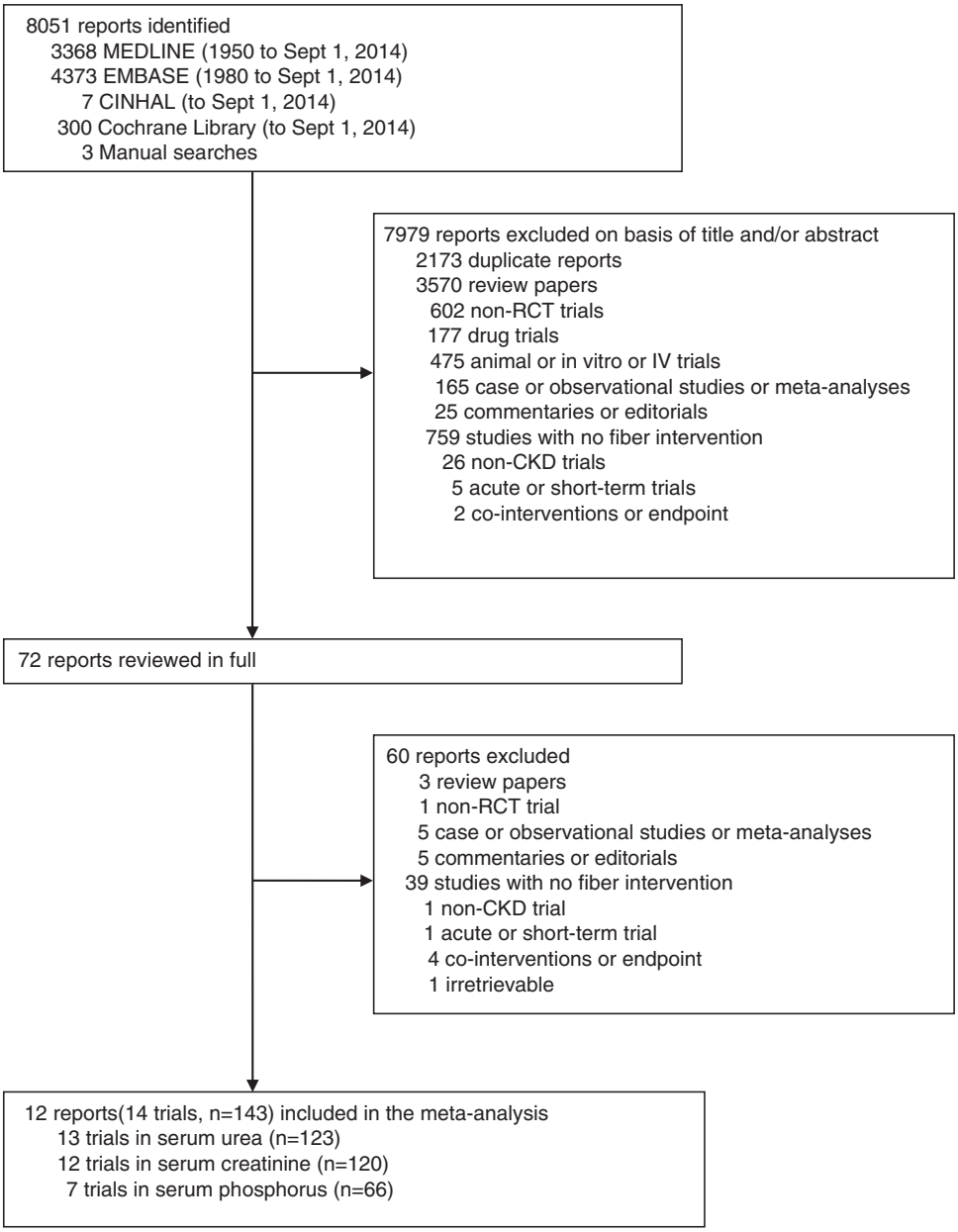

Figure 1. Flow of the literature.

Table 2. Characteristics of included trials investigating the effects of dietary fiber supplementation on the uremic solutes serum urea and creatinine in patients with chronic kidney disease

Study, year	*Participants*	*Mean age (s.d. or range), years*	*Setting*	*Feeding control*[a]	*Randomization*	*Fiber dose (s.d. or range) (g/day)*	*Fiber form*	*Follow-up (weeks)*	*MQS*[b]
Salmean *et al.*, 2013[23]	13 CKD (5M,8F)	67.0 ± 14.8	OP, USA	Met	N	26.4 ± 7.0	Pea hull fiber, corn fiber, inulin	6	4
Meijers *et al.*, 2010[8]	22 HD (15M,7F)	62.2 ± 12.8	OP, Belgium	Suppl	N	10.0–20.0	Oligofructose-enriched inulin	4	5
Younes *et al.*, 2006[24]	9 CRF (3M,6F)	67.7 ± 11.5	OP, France	Partial	Y	35.8 ± 4.6	Fermentable carbohydrates (bread+powder)	5	8
Rampton *et al.*, 1984 (T1)[25]	3 CRF (2M,1F)	18–62	OP, Great Britain	Suppl	N	30	Arabinogalactan	5	6
Rampton *et al.*, 1984 (T2)[25]	9 CRF (5M,4F)	22–64	OP, Great Britain	Suppl	N	7	Psyllium (isphagula husk)	8	6
Bliss *et al.*, 1996[26]	16 CRF (10M,6F)	20–72	OP, Great Britain	Suppl	Y	50	Gum arabic	4	4
Rivellese *et al.*, 1985[27]	5 CRF-DM (5M,0F)	46–68	IP, Italy	Met	Y	40	High-fiber foods versus low-fiber foods	1.4	7
Parillo *et al.*, 1988[28]	6 CRF-DM	48.5 ± 14.8	IP, Italy	Met	Y	43	High-fiber foods versus low-fiber foods	1.4	8
Burgess *et al.*, 1987[29]	9 HD	NR	OP, USA	Suppl	N	3.1	Wheat bran	4	6
Yatzidis *et al.*, 1980 (T1)[30]	3 CRF	22–45	IP, Greece	Suppl	N	50	Locust bean gum	[c]20	2
Yatzidis *et al.*, 1980 (T2)[30]	3 HD	22–45	IP, Greece	Suppl	N	25	Locust bean gum	[c]14	2
Miura *et al.*, 1989[31]	10 CRF	56	OP, Japan	Suppl	N	18	Lactulose	12	2
Miyazaki *et al.*, 1984[32]	15 CRF	48.4	IP, Japan	Met	N	18–36	Lactulose	2	5
Pender F, 1989[33]	20 HD (15M,5F)	54.4	OP, Scotland	Suppl	N	15	Wheat bran	4	2

Abbreviations: CKD, chronic kidney disease; CRF, chronic renal failure; DM, diabetes mellitus; F, female; HD, hemodialysis; IP, inpatient; M, male; Met, metabolic; MSQ, Methodological Quality Score; N, no; NR, not reported; OP, outpatient; suppl, supplemented; T1, trial 1; T2, trial 2; Y, yes. [a]Metabolic feeding control was the provision of all meals, snacks and study supplements (test fibers and foods) consumed during the study under controlled conditions. Supplemented feeding control was the provision of study supplements. [b]Trials with a score ⩾8 were considered to be of higher quality. [c]Denotes approximately.

(range: 1.1–2.2 mmol/l) for CKD and 2.0 mmol/l (range: 1.84–2.2 mmol/l) for HD participants.

The trials tended to be small (median number of participants, 9 (range: 3–22)) and to be conducted in European countries (6/14). Most trials were of short duration (median follow-up was 4.5 weeks (range: 1.4–20 weeks)). Four (29%) trials were randomized and all were crossover designs. All trials had a fiber supplemented/high-fiber diet group compared with a non-supplemented/low-fiber diet group. In the majority of studies (12 (86%) trials), fiber was supplemented as fermentable fiber (including gum arabic, psyllium and lactulose). Median fiber dose was 26.9 g/day (range: 3.1–50.0 g/day). The median protein intakes of the diets were ~57 g/day (range: 45–69 g/day). In all trials, intervention and control arms were matched for energy. The majority of trials (86%) were of low study quality as assessed by the Heyland Methodological Quality Score (<8). Blinding was reported in only two trials (14%), both of which were single-blinded. Funding was reported in only three trials (21%) and three trials (21%) reported having study products provided. Conflicts of interest were only reported in one trial (7%) within which no conflicts of interest were declared by the authors.

Pooled correlation coefficients were imputed and applied to five trials (38%) for serum urea, seven trials (58%) for serum creatinine and four trials (57%) for serum phosphorus.

The pooled effect of fiber on serum urea is shown in Figure 2. Fiber significantly reduced serum urea in the primary pooled analysis (MD, −1.76mmol/l (95% CI, −3.00, −0.51), $P=0.006$). There was significant evidence of interstudy heterogeneity. Sensitivity analyses in which each trial was systematically removed did not change the statistical significance of the interstudy heterogeneity or the urea lowering effects. The pooled effect of fiber on serum creatinine is shown in Figure 3. Similarly, dietary fiber supplementation significantly reduced serum creatinine in the overall analysis (MD, −22.83 (95% CI, −42.63, −3.02), $P=0.02$), however, without evidence of heterogeneity ($P=0.19$). *A priori* subgroup analyses did not reveal any significant effect modifications (Supplementary Figures 1 and 2). To assess the possibility of a dose–response association on serum urea, MD was plotted against mean dose, and no obvious linear or non-linear association between dose and MD was observed for urea (Supplementary Figure 3). Dose response was formally tested using meta-regression, successively adding up to 4th degree (quartic) functions of dose, and none of these improved model fit, confirming a lack of non-linear dose–response effects (Supplementary Table 1). However, there was a significant dose response observed for creatinine where increasing dose of fiber resulted in a greater reduction in serum creatinine (Supplementary Figure 4).

Overall, there was no significant pooled effect seen on serum phosphorus (Figure 4).

DISCUSSION

This study is the first to summarize in detail previously conducted controlled clinical trials on the effects of dietary fiber in CKD. This systematic review and meta-analysis of 14 controlled feeding trials in 143 participants with CKD demonstrated that dietary fiber can reduce serum concentrations of urea and creatinine with a dose-dependent response for serum creatinine.

By definition, dietary fibers are non-digestible carbohydrates and lignans that escape digestion and arrive intact in the large intestine. However, the physiological effects of various fibers depend in part on their physico-chemical properties that can result in non-fermentable or fermentable fibers. In the current meta-analyses of the effects on serum urea and creatinine, the majority of the trials (12 out of 13) used fermentable fiber types (psyllium, gum arabic, inulin and lactulose). Therefore, our *a priori* subgroup analyses were limited in their ability to detect a

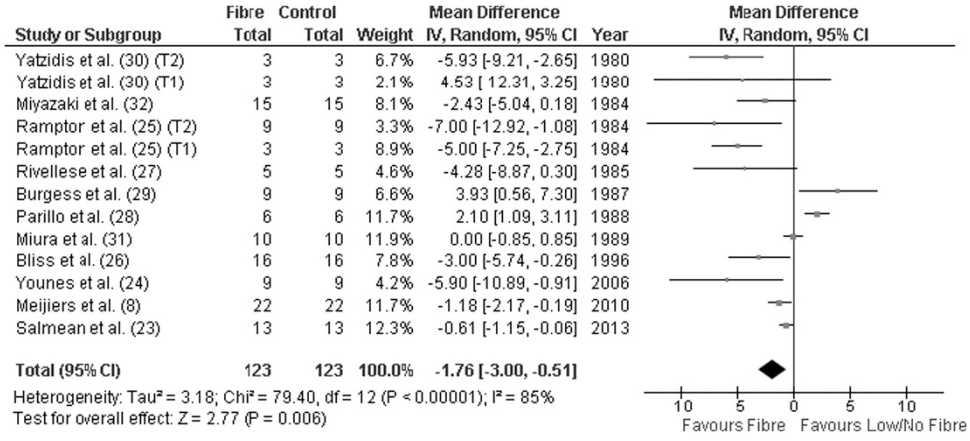

Figure 2. Forest plot for the effect of dietary fiber on serum urea concentration (mmol/l). Data are expressed as weighted mean differences (MDs) with 95% CI using generic inverse variance random-effects models. Pooled effect estimates are shown as diamonds. Inter-study heterogeneity was tested by Cochran's *Q* statistic (χ^2) at a significance level of $P < 0.10$ and quantified by I^2, where $I^2 \geqslant 50\%$ is considered to be evidence of substantial heterogeneity. Subgroup analysis for dose were assessed by χ^2at a significance level of $P < 0.05$. CI, confidence interval.

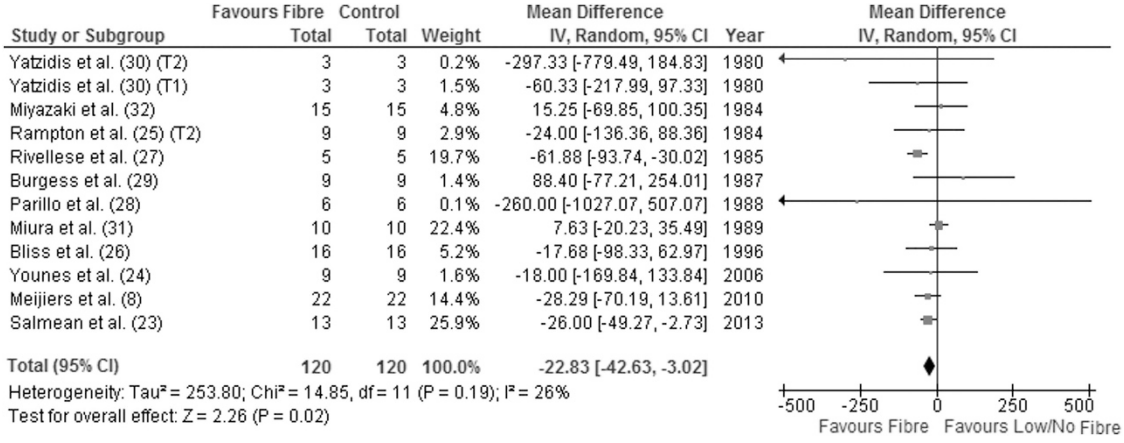

Figure 3. Forest plot for the effect of dietary fiber on creatinine concentration (mmol/l). Data are expressed as weighted mean differences (MDs) with 95% CI using generic inverse variance random-effects models. Pooled effect estimates are shown as diamonds. Inter-study heterogeneity was tested by Cochran's *Q* statistic (χ^2) at a significance level of $P < 0.10$ and quantified by I^2, where $I^2 \geqslant 50\%$ is considered to be evidence of substantial heterogeneity. Subgroup analysis for dose were assessed by χ^2 at a significance level of $P < 0.05$. CI, confidence interval.

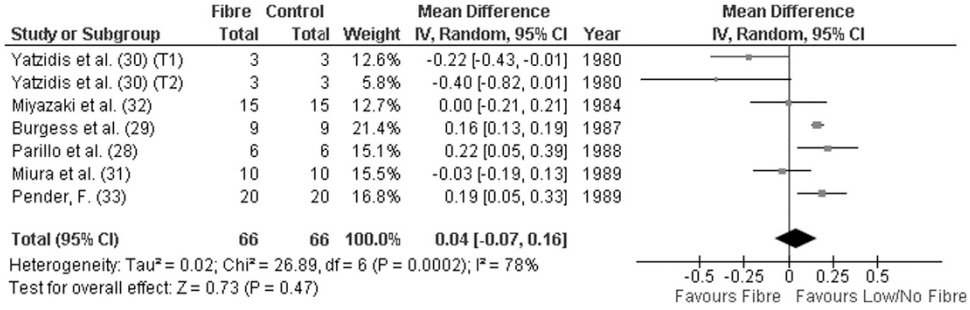

Figure 4. Forest plot for the effect of dietary fiber on phosphorus concentration (mmol/l). Data are expressed as weighted mean differences (MDs) with 95% CI using generic inverse variance random-effects models. Pooled effect estimates are shown as diamonds. Inter-study heterogeneity was tested by Cochran's *Q* statistic (χ^2) at a significance level of $P < 0.10$ and quantified by I^2, where $I^2 \geqslant 50\%$ is considered to be evidence of substantial heterogeneity. Subgroup analysis for dose were assessed by χ^2 at a significance level of $P < 0.05$. CI, confidence interval.

difference between fiber types as there was only one trial using non-fermentable fibers. Our subgroup analyses demonstrated that within those trials with fermentable fibers, the results were very similar to the overall analyses, thus the results of our primary analyses may be driven by fermentable fibers. Fermentable fibers are known to stimulate colonic bacterial growth, fecal mass and short-chain fatty acid production. These changes can, in CKD, influence the uremic environment.

Dietary fiber may reduce serum urea by altering the urea enterohepatic cycling, by causing the proliferation of

large-intestine microflora and the trapping of protein nitrogen in the microbial bodies, as well as in the elevation of ammonium (NH_4) in the feces due to the reduction in pH by short-chain fatty acids and the conversion of diffusible ammonia (NH_3) to the less-diffusible NH_4.[34] These processes result in increased nitrogen excretion via feces. Animal studies have demonstrated that active fermentation stimulates bacterial growth and leads to a considerable enlargement of the colonic contents and lead to cecal wall hypertrophy,[35–37] an effect that may be explained by an increase in short-chain fatty acids availability through carbohydrate (e.g. butyrate) fermentation.[38,39] Resistant starches (mainly undigestible carbohydrates) have shown to have the greatest trophic effects on colonic mucosa.[40–42] Although human data are lacking, it is possible that fermentable carbohydrates exert similar effects in humans.[43] This trophic effect in turn stimulates the exchanges of urea and ammonia nitrogen between blood and digestive lumen.[35,36,44,45] Urea has been demonstrated to be permeable through the colon.[46] Similarly, creatinine is transportable across the intestinal epithelium[47] and has been proposed to be metabolized by intestinal bacteria.[48,49] As creatinine is a metabolic byproduct of muscle metabolism and its plasma concentration is relatively constant due to low variability in muscle turnover, the reduction in serum creatinine observed may be due to increased creatinine degradation by bacterial creatinase throughout the bowel and thus potential loss to the creatinine pool.[49] Although the mechanism is unclear, creatinine is the most widely used indirect measure of the estimated glomerular filtration rate, which is the most commonly used marker of renal function clinically.

Of great importance is the fact that the majority of CKD patient deaths are due to CVD rather than progression to end-stage renal disease[50] and it has been well demonstrated that dietary fiber improves a variety of CVD risk factors. Intrinsically, dietary fiber has been demonstrated to dampen glycemic excursions, improve cholesterol and improve blood pressure,[51–53] which have been associated with improved renal function[54,55] as well as decreased CVD risk.[50,56–58] Extrinsically, dietary fiber consumed as either a supplement or through high-fiber foods, displaces other foods in the diet that may not be beneficial for renal function or increase the risk of CVD. For example, oats and barley may replace bread and rice, the former of which are rich in beta-glucan and have been demonstrated to lower cholesterol and blood pressure and elicit a lower glycemic response.[59,60] Finally, dietary fiber has been associated with reduced inflammation, which is elevated in CKD and CVD.[61] Krishnamurthy *et al.*,[15] using data from the National Health and Nutrition Examination Study III including just under 15 000 participants, concluded that a high total dietary fiber intake was associated with lower risk of inflammation and that these associations were stronger in those with kidney disease compared to those without. The study also found that a high total dietary fiber intake was inversely related to mortality in those with kidney disease. Therefore, there may be a potential for fiber to assist in reducing the burden of not only nitrogenous waste products that contribute to uremia, but also by reducing CVD risk factors such as inflammation, glycemic control, cholesterol and blood pressure.

From the present systematic review, all clinical trials of dietary fiber in CKD were retrieved and the discernible lack of trials assessing other uremic retention solutes was clearly evident. However, the limited studies that have been done suggest dietary fiber supplementation may also be beneficial. Protein-bound uremic retention solutes have gained more attention recently due to the fact that several groups have demonstrated direct associations with overall mortality and CVD in end-stage renal disease, as well as in CKD.[8,62–64] Specifically, these include p-cresol and indoxyl sulfates, which originate from bacterial protein fermentation in the large intestine.[11] Both have also individually been associated with progression of CKD.[10,65] Meijers *et al.*[8] demonstrated in addition to a significant reduction in serum urea, that serum p-cresol sulfate concentrations were significantly reduced by 20% in HD patients given oligofructose-enriched inulin for 4 weeks. In addition, Meyer *et al.*[66] have discussed how dietary fiber may be associated with reducing protein fermentation and thus reducing production of p-cresols and indoxyls as well as amines. A recent meta-analysis of the effect of pre- and probiotics on p-cresol and indoxyl sulfate levels in mostly healthy individuals demonstrated a significant reduction overall.[67] Therefore, dietary fiber supplementation may also act to affect multiple uremic retention solutes to improve CKD, however, further studies are warranted to support these potential effects.

Limitations of our analyses include the small number, small sample sizes (only one trial had >20 participants), short follow-up (median follow-up was only 4.5 weeks) and low quality ($<15\%$ were of high quality) of the available trials. Other limitations include the lack of description of trial characteristics, including the stage of CKD, the degree of renal impairment (baseline estimated glomerular filtration rate), fiber intake at baseline, body weight and body mass index. Thus, future high-quality, randomized controlled trials in a CKD population with larger sample sizes and longer follow-up are warranted.

The strengths of our analyses include that the median fiber dose used in the available trials was ~27g/day, which is in keeping with that recommended for adults, and all trials were controlled for dietary protein and had a crossover design, which minimizes the effects of confounders.

Practical implications

With regard to the feasibility in the CKD population, achieving higher fiber intakes remains a concern because of increased potassium and phosphorus levels, which can potentially have deleterious effects in CKD.[68,69] However, there are options for this group to increase their fiber intakes through low potassium and phosphorus fruits and vegetables and possibly fiber supplements without added phosphorus or potassium. In addition, the bioavailability of phosphorus and potassium in high-fiber foods is lower compared with other phosphorus and potassium foods, especially processed foods.

Although the present meta-analysis demonstrates significant reductions in the classical biomarkers of uremia, serum urea and creatinine, with increasing intake of dietary fiber, we are unsure whether this affects actual renal function. The search criteria employed in the current meta-analysis allowed for the capture of all clinical feeding trials using dietary fiber in a population with impaired renal function and highlighted the lack of literature, especially on other biomarkers of renal function, including serum calcium and potassium, urinary markers and glomerular filtration rate. For example, among the identified studies, only one had reported results for glomerular filtration rate. Therefore, an important implication of the current meta-analysis is that future studies evaluating the impact of dietary fiber supplements on kidney function should rely on 'creatinine-free' indices of renal function (for example, using cystatin C) or on actually measured glomerular filtration rate.

Overall, these results are important for patients, physicians and clinicians as they highlight the potential multifactorial benefits of consuming dietary fiber in the CKD population in which intakes are currently low.

CONCLUSION

Pooled analyses of controlled feeding trials show that dietary fiber supplementation in the diet of those with CKD leads to a reduction in serum urea and creatinine as clinical biomarkers of renal function and in a dose-dependent manner for serum creatinine.

CONFLICT OF INTEREST

LC works as a casual Clinical Research Coordinator at GI Laboratories, Toronto, Canada. LC and AM have received research support from the Canadian Institutes of Health Research (CIHR). JLS has received research support from the CIHR, Calorie Control Council, The Coca-Cola Company (investigator initiated, unrestricted grant), Pulse Canada and The International Tree Nut Council Nutrition Research & Education Foundation. He has received travel funding, speaker fees and/or honoraria from the American Heart Association (AHA), American Society for Nutrition (ASN), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH), Canadian Diabetes Association (CDA), Canadian Nutrition Society (CNS), Calorie Control Council, Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD), International Life Sciences Institute (ILSI) North America, International Life Sciences Institute (ILSI) Brazil, Abbott Laboratories, Pulse Canada, Dr. Pepper Snapple Group and The Coca-Cola Company. He is on the Clinical Practice Guidelines Expert Committee for Nutrition Therapy of both the Canadian Diabetes Association (CDA) and European Association for the study of Diabetes (EASD), as well as being on the American Society for Nutrition (ASN) writing panel for a scientific statement on the metabolic and nutritional effects of fructose, sucrose and high-fructose corn syrup. He is an unpaid scientific advisor for the International Life Science Institute (ILSI) North America, Food, Nutrition and Safety Program (FNSP). His wife is an employee of Unilever Canada. DJAJ holds an unrestricted grant from the Coca-Cola Company and has served on the scientific advisory board for or received research support, consultant fees or honoraria from Barilla, Solae, Unilever, Hain Celestial, Loblaws Supermarkets, Sanitarium Company, Herbalife International, Pacific Health Laboratories Inc, Metagenics/MetaProteomics, Bayer Consumer Care, Oldways Preservation Trust, The International Tree Nut Council Nutrition Research & Education, The Peanut Institute, Procter and Gamble Technical Centre Limited, Griffin Hospital for the development of the NuVal System, Pepsi Company, Soy Advisory Board of Dean Foods, Alpro Soy Foundation, Nutritional Fundamentals for Health, Pacific Health Laboratories, Kellogg's, Quaker Oats, The Coca-Cola Sugar Advisory Board, Agrifoods and Agriculture Canada (AAFC), Canadian Agriculture Policy Institute (CAPI), Abbott Laboratories, the Almond Board of California, the California Strawberry Commission, Orafti, the Canola and Flax Councils of Canada, Pulse Canada and the Saskatchewan Pulse Growers. DJAJ also holds additional grant support from the Canadian Institutes of Health Research, Canadian Foundation for Innovation, Ontario Research Fund and Advanced Foods and Material Network. DJAJ's spouse is a vice president and director of research at GI Laboratories (Toronto, Ontario, Canada). PBD declares no conflict of interest.

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LC and PBD designed the research. LC and AM conducted the research. LC and AM analyzed the data. LC and PBD wrote the paper. LC, AM, JLS, DJAJ and PBD were responsible for critical revision of the manuscript. PBD had primary responsibility for final content. All authors read and approved the final manuscript.

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