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Dietary patterns for adults with chronic kidney disease

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Dietary patterns for adults with chronic kidney disease (Protocol)

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TABLE OF CONTENTS

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

This review will evaluate the benefits and harms of dietary patterns among adults with CKD (any stage including people with end-stage kidney disease (ESKD) treated with dialysis, transplantation or supportive care).

BACKGROUND

Description of the condition

Chronic kidney disease (CKD) is a disorder resulting from structural changes to the kidney (cysts, loss of tissue, or masses) and/or urinary tract leading to changes in the composition of the urine and/or reduced kidney function. The kidney is a target organ injured in diseases primary to the kidney (such as glomerulonephritis or polycystic kidney disease) and secondary diseases (including cardiovascular disease, metabolic syndrome, diabetes (predominantly type 2), obesity, and arterial hypertension). Secondary causes of kidney failure now dominate the global epidemiology of kidney disease - diabetes and hypertension are the leading causes of CKD in middle and higher income countries worldwide, accounting for approximately 35% and 25% of kidney disease (Jha 2013). Kidney tissue in systemic diseases is injured by accelerated vascular damage, glomerular hypertension, and increased cellular glycosylation and oxidation.

Overall, CKD affects an estimated 10% to 15% of people around the world (Chadban 2003; Singh 2009; Zhang 2012) and leads to poorer health outcomes for affected individuals and communities. Among people who have moderate to severe CKD, early death and cardiovascular complications are two to three times more likely than for people without kidney disease and quality of life is reduced (Go 2004; Hemmelgarn 2010; Wyld 2012).

Description of the intervention

Dietary patterns (dietary intake of whole foods rather than single dietary nutrients, such as sodium or protein) may play an important and complex role in the aetiology and progression of CKD, in part through modification of systemic disease processes affecting kidney function (arterial hypertension, tissue glycosylation, glomerular injury, and macrovascular and microvascular diseases) and in part through altering the risks of non-communicable diseases such as diabetes that play such an important role in the prevalence of kidney disease in developed and developing nations. Individual dietary components may influence blood lipid levels, oxidative stress, insulin sensitivity, blood pressure, systemic inflammatory responses, pro fibrotic processes, thrombosis risk, and endothelial function to modify clinical outcomes (Abiemo 2012; Nakayama 1996; Peters 2000; Stamler 1996; van Dijk 2012).

While the exact mechanisms through which dietary patterns might act to prevent or slow CKD progression are likely to be multifactorial, there is emerging evidence showing the impact of dietary modification on risk factors for kidney injury. In recent Cochrane reviews of dietary advice in broader populations - predominantly by reduction of salt and fat intake and increases in fruit, vegetables, and fibre intake - dietary changes reduced arterial blood pressure by 2.61 mm Hg on average, as well as serum cholesterol and sodium excretion (Hartley 2013; Rees 2013a; Rees 2013b). Combined dietary and exercise interventions among people at risk of diabetes reduce weight and body mass and have modest effects on blood lipids and blood pressure, while altered carbohydrate or energy intake plus exercise improves glycaemic control in people with type 2 diabetes (Nield 2008; Orozco 2008). Intensive advice and support to reduce salt intake may have small and unsustained effects on blood pressure (Adler 2014) of uncertain clinical importance.

Although numerous randomised controlled trials (RCTs) in people with CKD have evaluated single nutrient management (such as protein intake), there is relatively less information about the impact of dietary patterns that consider whole food modification - for example, Mediterranean Diet or Dietary Approaches to Stop Hypertension (DASH) - on clinical outcomes in people with CKD. Clinical studies in this area have been largely restricted to modifying protein, sodium, and phosphorus dietary intake as well as antioxidant supplementation (Fouque 2009; Jun 2012; Liu 2015; McMahon 2015). Among people with CKD, lowered dietary salt intake reduced blood pressure and the amount of protein excreted by the kidney (an indicator of cardiovascular risk) (McMahon 2015), although there was no high-quality evidence this translated to slower kidney disease progression or fewer cardiovascular complications. Although dietary interventions in the setting of CKD have commonly focused on protein restriction as a mechanism to slow kidney failure, there is limited evidence that this dietary strategy is effective and safe and the impact of different protein sources on clinical outcomes is poorly understood (Robertson 2007).

Why it is important to do this review

Global clinical guidelines recommend dietary strategies in the management of CKD (KDIGO 2012). Specifically, guidelines include suggestions to lower protein intake with appropriate education and avoid high protein intake for people at risk of kidney disease progression, lower salt intake and increase physical activity (aiming for at least 30 minutes, 5 times/week). Guidelines recommend that people with CKD receive dietary advice and information in the context of an education program that is tailored to the severity of their CKD and the need to modify salt, phosphate, potassium, and protein intake. Given these guidelines, up to date evidence of the benefits and harms of dietary management is needed to inform practice and policy.

In addition, patients, caregivers and health professionals consider the effects of dietary management as important and a priority treatment uncertainty in CKD (Manns 2014). When speaking about dietary strategies, some patients experience dietary restrictions as an intense and unremitting burden (Palmer 2015), while at the same time offering them greater self-efficacy in the management of their CKD. In general, patients value better understanding of the role of lifestyle management as a research priority (Tong 2015). Dietary management is therefore an important potential intervention for improving clinical outcomes in CKD that aligns with patient priorities.

O B J E C T I V E S

This review will evaluate the benefits and harms of dietary patterns among adults with CKD (any stage including people with end-stage kidney disease (ESKD) treated with dialysis, transplantation or supportive care).

M E T H O D S

Criteria for considering studies for this review

Types of studies

We will include RCTs and quasi-RCTs (in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth, or other predictable methods) measuring the effect of dietary patterns in adults with CKD.

Types of participants

Inclusion criteria

Adults with any stage of CKD (any structural kidney or urine abnormality with or without reduced glomerular filtration rate below 60 mL/min/1.73 m² as defined by the Kidney Disease: Improving Global Outcomes (KDIGO 2012)) including people with ESKD treated with dialysis, kidney transplantation or supportive care.

Exclusion criteria

Pregnant women and children younger than 18 years.

Types of interventions

Inclusion criteria

We will evaluate the following dietary patterns (including dietary advice or lifestyle management) compared with any other dietary pattern or standard care (including lifestyle advice).

- Dietary patterns (e.g. DASH diet; Mediterranean diet, American Heart Association diet)
- Nutritional counselling and education about food-based dietary interventions
- Lifestyle advice about dietary intake

We will include studies evaluating treatment for at least one month and studies in which concomitant *non-randomised* interventions such as antihypertensive medication, sodium restriction, or other co-interventions including supplements were used during the study period (e.g. specific blood pressure targets), providing that these interventions were administered to all treatment groups. These means we will include studies of dietary patterns regardless of whether other dietary modifications such as salt or phosphorus dietary intake were adjusted. We will not include differing levels of energy intake as interventions in the review.

Exclusion criteria

We will exclude dietary management interventions that are "single-nutrient" or nutrient-focused interventions (including supplementation). This will include the following dietary management interventions.

- Dietary management of specific dietary factors including sodium, phosphorus, and protein (as these are evaluated in other Cochrane reviews (Fouque 2009; Jun 2012; Liu 2015; McMahon 2015)
- Probiotics
- Parenteral, intra-dialysate or intra-peritoneal dietary supplementation
- Implementation strategies for dietary or lifestyle management

Types of outcome measures

We will categorise outcomes according to length of follow up (< 6 months and ≥ 6 months). We will extract and analyse data for shorter (< 6 months) and longer (≥ 6 months) term outcomes separately.

Primary outcomes

1. All-cause mortality
2. Major adverse cardiovascular events (as defined by study investigators)
3. Health-related quality of life (as defined and measured by investigators)

Secondary outcomes

1. Withdrawal from dietary intervention
2. Cause-specific death (cardiovascular mortality, sudden death, infection-related mortality)
3. Progression to ESKD (as defined by the investigators including estimated glomerular filtration rate below 15 mL/min/1.73 m² or requiring treatment with long-term dialysis or kidney transplantation)
4. Participant adherence to intervention
5. Myocardial infarction
6. Kidney function measures (creatinine clearance or estimated glomerular filtration rate, doubling of serum creatinine, serum creatinine)
7. Serum lipids (total cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides)
8. Blood pressure
9. Blood glucose control (glycated haemoglobin; fasting plasma glucose)
10. Global measures of nutritional status (body mass index; body weight; waist circumference; subjective global assessment; malnutrition screening tool; mini nutritional assessment; skin-fold measurements; bioelectrical impedance analysis; albumin; prealbumin)

Search methods for identification of studies

Electronic searches

We will search the Cochrane Kidney and Transplant Specialised Register through contact with the Trials Search Co-ordinator using search terms relevant to this review. The Specialised Register contains studies identified from several sources.

1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP

3. Handsearching of kidney-related journals and the proceedings of major kidney conferences

4. Searching of the current year of EMBASE OVID SP

5. Weekly current awareness alerts for selected kidney journals

6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Studies contained in the Specialised Register are identified through search strategies for CENTRAL, MEDLINE, and EMBASE based on the scope of Cochrane Kidney and Transplant. Details of these strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the Specialised Register section of information about Cochrane Kidney and Transplant.

See Appendix 1 for search terms used in strategies for this review.

Data collection and analysis

Selection of studies

The search strategy will be used to obtain titles and abstracts of studies that might have been relevant to the review. The titles and abstracts will be screened independently by at least two authors, who will discard studies that are not eligible; however, studies and reviews that might include relevant data or information on studies will be retained initially. Two authors will independently assess retrieved abstracts and, if necessary the full text, of these studies to determine which studies satisfied the inclusion criteria. Any uncertainties about study eligibility will be discussed between authors and if necessary with a third author.

Data extraction and management

Data extraction will be carried out independently by two authors using pre-specified standard data extraction forms. Studies reported in non-English language journals will be electronically translated before assessment. Where more than one publication of one study exists, study reports will be grouped together and the publication with the most complete data will be used in the analyses. Where relevant outcomes are only published in earlier publications of the study, these data will used. Any discrepancy between published versions will be evaluated and highlighted.

Assessment of risk of bias in included studies

The following reporting items will be independently assessed by two authors using the risk of bias assessment tool (Higgins 2011) (see Appendix 2):
- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study?
  - Participants and personnel (performance bias)
  - Outcome assessors (detection bias)
- Were incomplete outcome data adequately addressed (attrition bias)?
- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias

Measures of treatment effect

For dichotomous outcomes (total and cause-specific mortality, myocardial infarction, progression to ESKD, doubling of serum creatinine, participant adherence, withdrawal from intervention), the treatment effects of dietary management will be expressed as a risk ratio (RR) together with 95% confidence intervals (CI). Where continuous scales of measurement are used to assess the effects of dietary management (health-related quality of life, blood pressure, lipids (total cholesterol, LDL cholesterol, triglycerides), kidney function (serum creatinine, creatinine clearance, glomerular filtration rate), body composition (weight, waist circumference, body mass index)), the mean difference (MD) between treatment groups will be used, or the standardised mean difference (SMD) if different measurement scales have been reported. We will evaluate mean end of treatment values for continuous outcomes together with the reported standard deviation in meta-analyses for these continuous outcomes.

Unit of analysis issues

Studies with non-standard designs will be analysed in this review including cross-over RCTs, studies with more than two interventions, and cluster RCTs. We will use recommended methods for data extraction and analysis described by the Cochrane Collaboration (Higgins 2011).

Cross-over studies

Cross-over studies will be included in this meta-analysis. However, as carry-over of the dietary intervention given in the first period is likely to persist into subsequent treatment periods due to behaviour modification, we will only include data for end points reported during the first period of study in studies in which the order of receiving treatments was randomised.

Studies with more than two interventions

Studies with multiple intervention groups will be included. When a study was a 'multi-arm' study, and all treatment arms provided data for eligible interventions, the study will be described and included in the systematic review. If there are adequate data from the study, then treatment arms relevant to the treatment comparisons of interest will be included in applicable meta-analyses.

Cluster randomised studies

We will include data from cluster RCTs in meta-analyses according to recommendations from the "Cochrane Handbook for Systematic Reviews of Interventions", namely that the effective sample size for each data point is divided by a quantity called the design effect calculated as 1 + (M - 1) ICC, where M is the average cluster size and ICC is the intra-cluster correlation coefficient (Higgins 2011). A common design effect will be assumed across intervention groups. The intra-cluster coefficient (ICC) is seldom available in published reports. We will therefore adopt a common approach to use external estimates obtained from similar studies. For dichotomous outcomes, both the number of participants and the number experiencing the event will be divided by the design effect. For continuous data, only the sample size will be divided by the design effect with means and standard deviations remaining unchanged. However, as resulting data for dichotomous outcomes must be rounded to whole numbers for entry into RevMan, this approach will be considered unsuitable for studies with a small sample size (e.g. fewer than 50 participants overall).

We will consider the following potential sources of bias in available cluster RCTs.

1. Recruitment bias
2. Baseline imbalance
3. Loss of clusters; and
4. Incorrect analyses.

Dealing with missing data

Any further information required from the original author will requested by electronic mail and any relevant information obtained in this manner will be included in the review. Evaluation of important numerical data such as screened, randomised patients as well as intention-to-treat, as-treated and per-protocol population will be carefully performed. Attrition rates, for example drop-outs, losses to follow-up and withdrawals will be investigated. Issues of missing data and imputation methods (for example, last-observation-carried-forward) will be critically appraised (Higgins 2011).

Assessment of heterogeneity

Statistical heterogeneity in treatment effects among studies will be analysed using a Chi² test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I² test (Higgins 2003). We will consider I² values of 25%, 50% and 75% as corresponding to low, medium and high levels of heterogeneity, respectively.

Assessment of reporting biases

If possible, funnel plots will be used to assess for the potential existence of small study bias for the outcome of all-cause mortality. In any analysis including data from 10 or more studies and without evidence of statistically important heterogeneity, we will construct funnel plots for the log risk ratio in individual studies plotted against the SE of the risk ratio to assess for plot asymmetry.

Data synthesis

We will group studies by dietary patterns into similar interventions (e.g. low-fat; Mediterranean; high fibre; increased fruits and vegetables). Treatment estimates for the specified will be summarised within groups of dietary patterns and treatment effects will be summarised using random-effects meta-analysis. Effects will be reported as the relative risk (RR) and 95% confidence interval (CI) for binary outcomes and mean difference (MD) and 95% CI for continuous outcomes.

We will summarise information for outcomes in which meta-analysis is not possible due to insufficient observations using narrative tables. Narrative outcome reporting will particularly include health-related quality of life domains described in the studies and nutrition assessments. The dietary interventions and associated implementation strategies will be described using the "Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide" (Hoffmann 2014) and tabulated in the review.

Subgroup analysis and investigation of heterogeneity

Subgroup and univariate meta-regression analysis will be used to explore possible sources of heterogeneity (e.g. intervention duration, baseline nutritional status, baseline serum cholesterol or phosphorus level, blood pressure, stage of CKD, study risk of bias (allocation concealment), date of publication, sample size). We will explore the following pre-specified study-level covariate as potential sources of heterogeneity: mean study age, mean proportion of men, stage of CKD (CKD not treated with dialysis or transplantation, CKD treated with dialysis, CKD treated with transplantation), energy intake, study-level mean blood pressure or cholesterol at baseline, proportion with diabetes, adequacy of allocation concealment, sample size, and duration of follow up (< 12 months versus ≥ 12 months).

Sensitivity analysis

Where sufficient extractable data are available, we will perform sensitivity analyses in order to explore the influence of the following factors on effect size.

• Repeating the analysis excluding unpublished studies
• Repeating the analysis taking account of risk of bias, as specified above
• Repeating the analysis excluding any very long or large studies to establish how much they dominated the results
• Repeating the analysis excluding studies using the following filters: diagnostic criteria, language of publication, source of funding (industry versus other), and country.

'Summary of findings' tables

We will present the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of the available data for the main outcomes (Schunemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach (GRADE 2008). The GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schunemann 2011b).

REFERENCES

Additional references

Abiemo 2012

Abiemo EE, Alonso A, Nettleton JA, Steffen LM, Bertoni AG, Jain A, et al. Relationships of the Mediterranean dietary pattern with insulin resistance and diabetes incidence in the Multi-Ethnic Study of Atherosclerosis (MESA). *British Journal of Nutrition* 2013;**109**(8):1490–7. MEDLINE: 22932232

Adler 2014

Adler AJ, Taylor F, Martin N, Gottlieb S, Taylor RS, Ebrahim S. Reduced dietary salt for the prevention of cardiovascular disease. *Cochrane Database of Systematic Reviews* 2014, Issue 12. DOI: 10.1002/14651858.CD009217.pub3

Chadban 2003

Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Welborn TA, Zimmet PZ, et al. Prevalence of kidney damage in Australian adults: The AusDiab kidney study. *Journal of the American Society of Nephrology* 2003;**14**(7 Suppl 2):S131–8. MEDLINE: 12819318

Fouque 2009

Fouque D, Laville M. Low protein diets for chronic kidney disease in non diabetic adults. *Cochrane Database of Systematic Reviews* 2009, Issue 3. DOI: 10.1002/14651858.CD001892.pub3

Go 2004

Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *The New England journal of medicine* 2004;**351**(13):1296–305. MEDLINE: 15385656

GRADE 2008

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**(7650):924–6. MEDLINE: 18436948

Hartley 2013

Hartley L, Igbinedion E, Holmes J, Flowers N, Thorogood M, Clarke A, et al. Increased consumption of fruit and vegetables for the primary prevention of cardiovascular diseases. *Cochrane Database of Systematic Reviews* 2013, Issue 6. DOI: 10.1002/14651858.CD009874.pub2

Hemmelgarn 2010

Hemmelgarn BR, Manns BJ, Lloyd A, James MT, Klarenbach S, Quinn RR, et al. Relation between kidney function, proteinuria, and adverse outcomes. *JAMA* 2010;**303**(5):423–9. MEDLINE: 20124537

Higgins 2003

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557–60. MEDLINE: 12958120

Higgins 2011

Higgins JP, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Hoffmann 2014

Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;**348**:g1687. MEDLINE: 24609605

Jha 2013

Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives.[Erratum appears in Lancet. 2013 Jul 20;382 (9888):208]. *Lancet* 20;**382**(9888):260–72. MEDLINE: 23727169

Jun 2012

Jun M, Venkataraman V, Razavian M, Cooper B, Zoungas S, Ninomiya T, et al. Antioxidants for chronic kidney disease. *Cochrane Database of Systematic Reviews* 2012, Issue 10. DOI: 10.1002/14651858.CD008176.pub2

KDIGO 2012

Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney International - Supplement* 2013;**3**(1):1–150. [EMBASE: 2014145464]

Liu 2015

Liu Z, Su G, Guo X, Wu Y, Liu X, Zou C, et al. Dietary interventions for mineral and bone disorder in people with chronic kidney disease. *Cochrane Database of Systematic Reviews* 2015, Issue 9. DOI: 10.1002/14651858.CD010350.pub2

Manns 2014

Manns B, Hemmelgarn B, Lillie E, Dip SC, Cyr A, Gladish M, et al. Setting research priorities for patients on or nearing dialysis. *Clinical Journal of The American Society of Nephrology: CJASN* 2014;**9**(10):1813–21. MEDLINE: 24832095

McMahon 2015

McMahon EJ, Campbell KL, Bauer JD, Mudge DW. Altered dietary salt intake for people with chronic kidney disease. *Cochrane Database of Systematic Reviews* 2015, Issue 2. DOI: 10.1002/14651858.CD010070.pub2

Nakayama 1996

Nakayama M, Okuda S, Tamaki K, Fujishima M. Short- or long-term effects of a low-protein diet on fibronectin and transforming growth factor-beta synthesis in Adriamycin-induced nephropathy. *Journal of Laboratory & Clinical Medicine* 1996;**127**(1):29–39. MEDLINE: 8592094

Nield 2008

Nield L, Summerbell CD, Hooper L, Whittaker V, Moore H. Dietary advice for the prevention of type 2 diabetes mellitus in adults. *Cochrane Database of Systematic Reviews* 2008, Issue 3. DOI: 10.1002/14651858.CD005102.pub2

Orozco 2008

Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roque I Figuls M, Richter B, et al. Exercise or exercise and diet for preventing type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews* 2008, Issue 3. DOI: 10.1002/14651858.CD003054.pub3

Palmer 2015

Palmer SC, Hanson CS, Craig JC, Strippoli GF, Ruospo M, Campbell K, et al. Dietary and fluid restrictions in CKD: A thematic synthesis of patient views from qualitative studies. *American Journal of Kidney Diseases* 2015;**65**(4):559–73. MEDLINE: 25453993

Peters 2000

Peters H, Border WA, Noble NA. Angiotensin II blockade and low-protein diet produce additive therapeutic effects in experimental glomerulonephritis. *Kidney International* 2000;**57**(4):1493–501. MEDLINE: 10760085

Rees 2013a

Rees K, Dyakova M, Wilson N, Ward K, Thorogood M, Brunner E. Dietary advice for reducing cardiovascular risk. *Cochrane Database of Systematic Reviews* 2013, Issue 12. DOI: 10.1002/14651858.CD002128.pub5

Rees 2013b

Rees K, Hartley L, Flowers N, Clarke A, Hooper L, Thorogood M, et al. 'Mediterranean' dietary pattern for the primary prevention of cardiovascular disease. *Cochrane Database of Systematic Reviews* 2013, Issue 8. DOI: 10.1002/14651858.CD009825.pub2

Robertson 2007

Robertson LM, Waugh N, Robertson A. Protein restriction for diabetic renal disease. *Cochrane Database of Systematic Reviews* 2007, Issue 4. DOI: 10.1002/14651858.CD002181.pub2

Schunemann 2011a

Schünemann HJ, Oxman AD, Higgins JP, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JP, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Schunemann 2011b

Schünemann HJ, Oxman AD, Higgins JP, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Singh 2009

Singh NP, Ingle GK, Saini VK, Jami A, Beniwal P, Lal M, 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 Nephrology 2009; Vol. 10:4. MEDLINE: 19220921

Stamler 1996

Stamler J, Caggiula A, Grandits G A, Kjelsberg M, Cutler JA. Relationship to blood pressure of combinations of dietary macronutrients. Findings of the Multiple Risk Factor Intervention Trial (MRFIT). *Circulation* 1996;**94** (10):2417–23. MEDLINE: 8921782

Tong 2015

Tong A, Crowe S, Chando S, Cass A, Chadban SJ, Chapman JR, et al. Research priorities in chronic kidney disease for Australia: Report of a conference. *American Journal of Kidney Diseases* 2015;**66**(2):212–22. DOI: 10.1053/j.ajkd.2015.02.341

van Dijk 2012

van Dijk SJ, Feskens EJ, Bos MB, de Groot LC, de Vries JH, Muller M, et al. Consumption of a high monounsaturated fat diet reduces oxidative phosphorylation gene expression in peripheral blood mononuclear cells of abdominally overweight men and women. *Journal of Nutrition* 2012;**142** (7):1219–25. MEDLINE: 22623392

Wyld 2012

Wyld M, Morton RL, Hayen A, Howard K, Webster AC. A systematic review and meta-analysis of utility-based quality of life in chronic kidney disease treatments. *PLoS Medicine* 2012;**9**(9):e1001307. MEDLINE: 22984353

Zhang 2012

Zhang L, Wang F, Wang L, Wang W, Liu B, Liu J, et al. Prevalence of chronic kidney disease in China: a cross-sectional survey.[Erratum appears in Lancet. 2012 Aug 18;380(9842):650]. *Lancet* 2012;**379**(9818):815–22. MEDLINE: 22386035

* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	1. MeSH descriptor: [Diet] explode all trees 2. MeSH descriptor: [Diet Therapy] explode all trees 3. MeSH descriptor: [Dietary Carbohydrates] explode all trees 4. MeSH descriptor: [Calcium, Dietary] this term only 5. MeSH descriptor: [Potassium, Dietary] this term only 6. MeSH descriptor: [Dietary Fats] explode all trees 7. MeSH descriptor: [Dietary Fiber] explode all trees 8. MeSH descriptor: [Dietary Proteins] explode all trees 9. MeSH descriptor: [Dietary Supplements] this term only 10. MeSH descriptor: [Micronutrients] explode all trees 11. MeSH descriptor: [Nutritional Requirements] explode all trees 12. MeSH descriptor: [Nutritional Status] this term only 13. MeSH descriptor: [Nutrition Therapy] this term only 14. MeSH descriptor: [Keto Acids] explode all trees 15. MeSH descriptor: [Amino Acids, Essential] explode all trees 16. MeSH descriptor: [Folic Acid] this term only 17. MeSH descriptor: [Patient Education as Topic] this term only 18. diet$ or nutrition$:ti,ab,kw (Word variations have been searched) 19. {and #17-#18} 20. (diet* or nutrition*) and (protein or fat or cholesterol or omega-3* or carbohydrates or glyc?emic index or fibre or fiber or folate or folic acid):ti,ab,kw (Word variations have been searched) 21. (diet* or nutrition*) and (mediterranean or vegetarian or DASH or macrobiotic):ti,ab,kw (Word variations have been searched) 22. (diet* or nutrition*) and (phosphorus or calcium or potassium or micronutrient* or vitamin*):ti,ab,kw (Word variations have been searched) 23. (diet* or nutrition*) and (supplement* or amino acid* or keto acid*):ti,ab,kw (Word variations have been searched) 24. (diet$ or nutrition*) and (advice* or education* or counselling):ti,ab,kw (Word variations have been searched)

	25. {or #1-#16, #19-#24}
	26. MeSH descriptor: [Kidney Diseases] explode all trees
	27. MeSH descriptor: [Renal Replacement Therapy] explode all trees
	28. MeSH descriptor: [Renal Insufficiency] explode all trees
	29. MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees
	30. dialysis:ti,ab,kw (Word variations have been searched)
	31. hemodialysis or haemodialysis:ti,ab,kw (Word variations have been searched)
	32. hemofiltration or haemofiltration:ti,ab,kw (Word variations have been searched)
	33. hemodiafiltration or haemodiafiltration:ti,ab,kw (Word variations have been searched)
	34. kidney disease* or renal disease* or kidney failure or renal failure:ti,ab,kw (Word variations have been searched)
	35. ESRF or ESKF or ESRD or ESKD:ti,ab,kw (Word variations have been searched)
	36. CKF or CKD or CRF or CRD:ti,ab,kw (Word variations have been searched)
	37. CAPD or CCPD or APD:ti,ab,kw (Word variations have been searched)
	38. predialysis or pre-dialysis:ti,ab,kw (Word variations have been searched)
	39. MeSH descriptor: [Diabetic Nephropathies] this term only
	40. diabetic kidney disease*:ti,ab,kw (Word variations have been searched)
	41. diabetic nephropath*:ti,ab,kw (Word variations have been searched)
	42. {or #26-#41}
	43. {and #25, #42}
MEDLINE	1. Diet/
	2. Diet Therapy/
	3. Caloric Restriction/
	4. Diabetic Diet/
	5. Diet, Carbohydrate-Restricted/
	6. Diet, Fat-Restricted/
	7. Diet, Gluten-free/
	8. Diet, Macrobiotic/
	9. Diet, High-Fat/
	10. Diet, Mediterranean/
	11. Diet, Paleolithic/
	12. Diet, Protein-Restricted/
	13. Diet, Reducing/
	14. Diet, Sodium-Restricted/
	15. Diet, Vegetarian/
	16. Diet, Atherogenic/
	17. Diet Fads/
	18. Diet, Cariogenic/
	19. Diet, Western/
	20. exp Dietary Carbohydrates/
	21. Calcium, Dietary/
	22. Potassium, Dietary/
	23. exp Dietary Fats/
	24. exp Dietary Fiber/
	25. exp Dietary Proteins/
	26. Dietary Supplements/
	27. exp Micronutrients/
	28. exp Nutritional Requirements/
	29. Nutritional Status/

	30. Nutrition Therapy/ 31. Energy Intake/ 32. Fasting/ 33. ketogenic diet/ 34. Portion Size/ or Serving Size/ 35. exp Keto Acids/ 36. exp Amino Acids, Essential/ 37. exp Amino Acids/ 38. Folic Acid/ 39. Patient Education as Topic/ 40. (diet$ and (mediterranean or vegetarian or DASH)).tw. 41. (diet$ and (supplement$ or amino acid$ or amino acids or keto acid$)).tw. 42. ((diet$ or nutrition$) and (advice$ or education$ or counselling)).tw. 43. or/1-42 44. Kidney Diseases/ 45. exp Renal Replacement Therapy/ 46. Renal Insufficiency/ 47. exp Renal Insufficiency, Chronic/ 48. dialysis.tw. 49. (hemodialysis or haemodialysis).tw. 50. (hemofiltration or haemofiltration).tw. 51. (hemodiafiltration or haemodiafiltration).tw. 52. (kidney disease* or renal disease* or kidney failure or renal failure).tw. 53. (ESRF or ESKF or ESRD or ESKD).tw. 54. (CKF or CKD or CRF or CRD).tw. 55. (CAPD or CCPD or APD).tw. 56. (predialysis or pre-dialysis).tw. 57. or/44-56 58. Diabetic Nephropathies/ 59. diabetic nephropath$.tw. 60. diabetic kidney$.tw. 61. or/58-60 62. Diabetes Mellitus/ 63. exp diabetes mellitus, type 1/ 64. exp diabetes mellitus, type 2/ 65. or/62-64 66. proteinuria/ or albuminuria/ 67. proteinuria$ or albuminuria$ or microalbuminuria$ or macroalbuminuria$).tw. 68. or/66-67 69. and/65,68 70. or/61,69 71. or/57,70 72. and/43,70
EMBASE	1. nutritional counseling/ 2. nutrition education/ 3. nutritional health/ 4. nutritional assessment/ 5. nutrition/ 6. exp diet/

7. exp diet therapy/
8. exp dietary intake/
9. exp diet restriction/
10. or/1-9
11. exp renal replacement therapy/
12. kidney disease/
13. chronic kidney disease/
14. kidney failure/
15. chronic kidney failure/
16. mild renal impairment/
17. stage 1 kidney disease/
18. moderate renal impairment/
19. severe renal impairment/
20. end stage renal disease/
21. renal replacement therapy-dependent renal disease/
22. kidney transplantation/
23. (hemodialysis or haemodialysis).tw.
24. (hemofiltration or haemofiltration).tw.
25. (hemodiafiltration or haemodiafiltration).tw.
26. dialysis.tw.
27. (CAPD or CCPD or APD).tw.
28. (kidney disease* or renal disease* or kidney failure or renal failure).tw
29. (CKF or CKD or CRF or CRD).tw.
30. (ESRF or ESKF or ESRD or ESKD).tw.
31. (predialysis or pre-dialysis).tw.
32. ((kidney or renal) adj (transplant* or graft* or allograft*)).tw
33. Diabetic Nephropathies/
34. diabetic nephropath$.tw.
35. diabetic kidney disease$.tw.
36. or/11-35
37. and/10,36

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	*Low risk of bias:* Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random)
	High risk of bias: Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory

(Continued)

	test or a series of tests; by availability of the intervention
	Unclear: Insufficient information about the sequence generation process to permit judgement
Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	*Low risk of bias:* Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes)
	High risk of bias: Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure
	Unclear: Randomisation stated but no information on method used is available
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	*Low risk of bias*: No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken
	High risk of bias: No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding
	Unclear: Insufficient information to permit judgement
Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors	*Low risk of bias:* No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken
	High risk of bias: No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding
	Unclear: Insufficient information to permit judgement

Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data	*Low risk of bias:* No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods
	High risk of bias: Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation
	Unclear: Insufficient information to permit judgement
Selective reporting Reporting bias due to selective outcome reporting	*Low risk of bias:* The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)
	High risk of bias: Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study
	Unclear: Insufficient information to permit judgement

(Continued)

Other bias Bias due to problems not covered elsewhere in the table	*Low risk of bias:* The study appears to be free of other sources of bias.
	High risk of bias: Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem
	Unclear: Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias

CONTRIBUTIONS OF AUTHORS

1. Draft the protocol: SP, GS, KC, JC, AT

2. Study selection: SP, BS, MR

3. Extract data from studies: SP, JM

4. Enter data into RevMan: SP, JM

5. Carry out the analysis: SP, JM

6. Interpret the analysis: All authors

7. Draft the final review: All authors

8. Disagreement resolution: GS

9. Update the review: SP, GS

DECLARATIONS OF INTEREST

- Suetonia C Palmer: none known

- Allison Tong: none known

- Katrina L Campbell: none known

- Jonathan C Craig: none known

- David W Johnson: is a consultant for Baxter Healthcare Pty Ltd and has previously received research funds from this company. He has also received speaker's honoraria and research grants from Fresenius Medical Care and is a current recipient of a Queensland Government Health Research Fellowship

- Bernadet Sutanto: none known

- Marinella Ruospo: none known

- Giovanni FM Strippoli: none known