Modification of lifestyle and nutrition interventions for management of early chronic kidney disease

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GUIDELINES

Dietary modification

Protein

a. **We suggest that patients with progressive chronic kidney disease (CKD) have individualised diet intervention involving an appropriately qualified dietitian (2C).**
b. **We recommend adults with early CKD consume a normal protein diet, consisting of 0.75 - 1.0 g/kg/day, with adequate energy. This is in line with the Recommended Daily Intake (RDI) for the general population (1C).**
c. **A low protein diet (≤0.6 g/kg/day) to slow down CKD progression is not recommended due to the risk of malnutrition (1C).**
d. **We suggest people with excess protein intakes reduce their intakes to the RDI levels as a high protein diet may accelerate renal function decline in mild renal insufficiency (2C).**

Salt

e. **We recommend that early CKD patients restrict their dietary sodium intake to 100 mmol/day (or 2.3 g sodium or 6 g salt per day) or less, as it reduces blood pressure and albuminuria in patients with CKD (1C).**
f. **We recommend that patients with CKD should not use salt substitutes that contain high amounts of potassium salts (1D).**

Phosphate

g. **We suggest that early CKD patients (stages 1-3) should not restrict dietary phosphate intake, as restriction of dietary phosphate does not influence renal or cardiovascular outcomes in these patients (2C).**

Potassium

h. **We suggest that early CKD patients with persistent hyperkalaemia restrict their dietary potassium intake with the assistance of an appropriately qualified dietitian (2D).**

Polyphenol-enriched diets

i. **We suggest that in early CKD patients with diabetic nephropathy, consumption of a carbohydrate-restricted, low-iron-available, polyphenol-enriched (CR-LIPE) diet may slow the progression of diabetic nephropathy (2C).**

Caloric restriction

j. **We recommend that overweight/obese patients with CKD should be prescribed caloric restriction under the management of an appropriately qualified dietitian. A reduction in weight can mean improvement of CKD (1C).**
k. **We suggest that, in the absence of specific recommendations for CKD, overweight or obese patients are encouraged to lose body fatness to aim for a Body Mass Index (BMI) closer to 18.5 – 24.9 kg/m^2 and waist circumference ≤102 cm for men and ≤88 cm for women (2C).**
   - **This is in line with the Dietary Guidelines for Australian Adults recommended by the NHMRC and Australian better health initiatives.**

Fruit and vegetables

l. **We suggest adults with early CKD consume a balanced diet rich in fruits and vegetables, as these appear to reduce blood pressure and have renoprotective effects comparable to sodium bicarbonate (2C).**

Mediterranean diet

m. We suggest adults with early CKD consume a Mediterranean style diet to reduce dyslipidemia and to protect against lipid peroxidation and inflammation (2C).

Dietary Fibre

n. We suggest adults with early CKD consume a diet rich in dietary fiber that is associated with reduced inflammation and mortality in patients with CKD (2D).

Lifestyle modification

Physical exercise

o. We suggest that patients with CKD be encouraged to undertake regular physical exercise that is appropriate for their physical ability and medical history (2B).

p. We suggest that, in the absence of specific exercise recommendations, patients are encouraged to include a minimum of 30 minutes of moderate physical activity each day in line with the Guidelines for Australian Adults recommended by the NHMRC (2C).

Smoking

q. We recommend that patients with CKD stop smoking to reduce their risk of CKD progression and cardiovascular risk (1C).

Alcohol

r. There is no specific evidence for alcohol consumption in patients with CKD. However, we suggest the recommendations made by the NHMRC Australian Guidelines to Reduce Health Risks from Drinking Alcohol be applied to patients with early CKD (2C).

Carbonated beverages

s. We suggest patients with CKD minimise their intake of cola beverages to a maximum of one glass (250ml) or less of cola per day (2C).

Fluid intake

t. We suggest that patients drink fluid in moderation. For most patients with early CKD, a daily fluid intake of 2-2.5 L (including the fluid content of foods) is sufficient; this might need to be varied according to individual circumstances (2C).

Note:

- **There is no convincing evidence to date that pushing oral fluid intake beyond this amount, except in states of excessive fluid loss (e.g. sweating or diarrhoea), is beneficial for long-term kidney health.**

UNGRADED SUGGESTIONS FOR CLINICAL CARE

There are no ungraded statements.

IMPLEMENTATION AND AUDIT

KCAT education programs for primary health care providers should incorporate the CARI Early CKD Lifestyle Modification and Nutritional Intervention recommendations. KHA and KCAT should commission audits of the awareness of each of the CARI Early CKD Lifestyle Modification and Nutritional Intervention recommendations amongst primary health care providers.

BACKGROUND

Important risk factors for chronic kidney disease (CKD) include diabetes mellitus, hypertension, obesity and smoking (reviewed in Early CKD Guideline 2). Modification of lifestyle habits (e.g. healthy diet, physical exercise, smoking cessation, moderate alcohol consumption and weight loss in obese people) may therefore be of value in retarding the progression of CKD. In addition, restriction of dietary protein [1] and augmentation of fluid intake [2] have been recommended as a treatment for retarding CKD progression for over 50 years. The objective of the current guideline is to evaluate the available clinical evidence pertaining to the effects of dietary interventions, smoking cessation, increased fluid intake, moderated alcohol consumption and physical exercise on the progression of CKD. The group also considered the recommendations in other guidelines and the evidence underpinning these recommendations.

The NHMRC Dietary Guidelines for Australian Adults are based on the best available scientific evidence to provide information for health professionals and the general population about healthy food choices, both quality and quantity (http://www.nhmrc.gov.au/guidelines/publications/n29-n30-n31-n32-n33-n34) (All levels of evidence). These guidelines encourage optimal eating to prevent under- or over- nutrition, inclusion of health promoting food components (e.g. phytochemicals and antioxidants), dietary patterns and healthy lifestyles that will minimize the risk of developing diet-related diseases such as coronary heart disease, vascular disease, obesity, diabetes, stroke, hypertension and cancer. Although these guidelines are not directly targeted to people with CKD, the recommendations are likely to help prevent or reduce risks and complications associated with CKD. The guidelines "Enjoy a wide variety of nutritious foods" and "Prevent weight gain: be physically active and eat according to your energy needs" and the sub-guidelines are known to be beneficial in the management of cardiovascular disease, hypertension and metabolic syndromes (all levels of evidence). Examples of the sub-guidelines are "Limit saturated fat and moderate total fat intake", "choose foods low in salt" and "Limit your alcohol intake if you choose to drink". While these guidelines may provide useful generalised information for patients with CKD, referral to an appropriately qualified dietitian for patients with progressive CKD for individualised diet prescription is recommended.

SEARCH STRATEGY

Databases searched: Text words for chronic kidney disease were combined with MeSH terms and text words for low protein diet, dietary protein restriction, protein intake, dietary intake, low calorie diet, caloric restriction, dietary intervention, exercise, physical activity, alcohol, fluid intake, potassium, hyperkalaemia, water intake, weight loss and weight reduction. The search was carried out in Medline (1966 – 3 August 2009). No language restrictions were placed on the search. The conference proceedings of the American Society of Nephrology from 1994-2008 were also searched for trials. An updated search was conducted in Medline (2010 – May 2012). Text words and MeSH terms used were the same as those from the previous search.

Date of search/es: 25 August 2010; May 2012

WHAT IS THE EVIDENCE?

1. Dietary protein restriction

The effect of dietary protein restriction on CKD progression has been discussed in detail in the CARI Guidelines on Prevention of Renal Failure Progression (http://www.cari.org.au/CKD_Prevent_List_Published/Dietary_protein_restriction.pdf) and will be only briefly discussed here. The relationship between dietary protein restriction and non-diabetic renal failure progression has been examined by 5 meta-analyses [3-7], 14 randomised controlled trials (RCTs) [8-21], 1 prospective double-blind cross-over study [22], 9 prospective non-randomised controlled trials [23-31] and 16 prospective non-controlled trials [32-48].

The largest and best-designed prospective, randomised controlled trial to date was the Modification of Diet in Renal Disease (MDRD) study [8]. Patients were included in the study if their GFR was 25-55 mL/min/1.73 m^2 (Study A) or 13-24 mL/min/1.73 m^2 (Study B), their mean arterial pressure was less than 125 mmHg and their dietary protein intake was greater than or equal to 0.9 g/kg body weight/day (Study A only). Patients with body weight extremes (<80% or >160% of standard body weight), "dubious" compliance, insulin-dependent diabetes mellitus or heavy proteinuria (>10 g/day) were excluded. Study A patients (n = 585) were randomly assigned (with adequate allocation concealment) to a usual protein diet (1.3 g protein/kg/day) or a low-protein diet (0.58 g/kg/day), while Study B patients (n = 255) were randomised to a low protein diet (0.58 g/kg/day) or a very low protein diet (0.28 g/kg/day). An open-label design was used. The groups were similar at the start of the trial. Only 3% of the patients had non-insulin-dependent diabetes mellitus and 24% of the patients had polycystic kidney disease. ACE inhibitors were permitted and used by 32-44% of patients in each of the randomisation groups. Mean follow-up was 2.2 years (range 0 to 3.7) and the drop-out rate was very low (Study A

1.9%, Study B 1.2%). Compliance was reasonable, but the actual dietary intakes of the normal and low protein groups were 1.1 and 0.7 g/kg/day, respectively. No significant differences in GFR decline, measured by ^{125}I-iothalamate clearance every 4 months, were found between the diet groups in either study. In Study A, a biphasic response of GFR to the low protein diet was noted, with a greater decline in the first 4 months (3.4 versus 1.8 mL/min/4 months), followed by a significantly slower rate of decline (2.8 versus 3.9 mL/min/year), which only resulted in a small absolute benefit of 1.1 mL/min/year. This effect of dietary intervention was unrelated to baseline glomerular filtration rate or urinary protein excretion. The time to occurrence of a rapid decline in GFR (>50% or ≥ 20 mL/min/1.73 m^2) or end-stage renal disease did not differ significantly between the diet groups in either study, although these were secondary end-points for which the study was not adequately powered. In Study A, the low protein diet group had significantly lower energy intakes (males -3.6 kcal/kg/day, females -2.8 kcal/kg/day), body weight (males -5.3 kg, females -2.9 kg) and biochemical nutritional markers (transferrin, percent body fat, biceps skinfold thickness, triceps skinfold thickness, subscapular skinfold thickness and arm muscle area were all 5-10% lower than in the usual protein group) [49]. A 15-20% decline in urinary creatinine excretion was also observed in the lower protein diet groups and was attributed to a reduction in dietary creatinine and creatinine intake. However, the significant reduction in arm muscle area also suggests that there was an additional component due to reduced skeletal muscle mass. The limitations of this study included: (a) overall GFR decline was relatively slow compared with that of other studies and roughly 25% of patients did not experience progressive renal function decline; (b) the study design may not have provided sufficient statistical power to find a positive result, particularly in view of the erratic GFR decline in Study A patients and the relatively high proportion of polycystic kidney disease patients (which may be less amenable to therapy); and, (c) the separation of GFR decline into 2 phases represented a post hoc analysis.

Apart from the Study A sub-group of the MDRD study, there have only been 4 small RCTs examining the effect of dietary protein restriction (0.6-0.8 g/kg/day) on CKD progression in adult patients with early (stages 2-3) CKD [18-21]. Three of these trials involved diabetic nephropathy (types 1 and 2 diabetes mellitus) [18-20] and 1 involved both diabetic and non-diabetic patients with stage 3 CKD [21]. Follow-up ranged from 1-4 years. Overall, none of the trials demonstrated a significant effect of dietary protein restriction on CKD progression, except in a subgroup of 89 patients with non-diabetic early CKD [21]. Several studies observed a significant decline in nutritional parameters [20, 21] and suboptimal compliance with protein-restricted diets [20].

Most of the other RCTs evaluating the impact of dietary protein restriction on CKD progression have predominantly involved patients with more advanced (stages 4 and 5) CKD. These trials have yielded conflicting findings ranging from no effect to a substantial effect of dietary protein restriction on CKD progression and have been the subject of 5 systematic reviews [3-7].

The most recent meta-analysis of the effects of dietary protein restriction on the rate of decline of kidney function in patients with diabetic and non-diabetic CKD was reported by Kasiske et al. [3]. The meta-analysis only considered published studies between 1980 and 1996 using Medline and bibliographies found in published reviews. The results of 13 randomised controlled trials (including 4 trials in purely diabetic populations) were pooled (n = 1919) and found that dietary protein restriction reduced the rate of decline in estimated GFR by a meagre 0.53 ml/min/year (95% CI 0.08 - 0.98 mL/min/year). The unweighted mean dietary protein content was 0.68±0.11 g/kg/day in the low protein groups and 1.01±0.32 g/kg/day in the control groups. Interestingly, the magnitude and variability of the treatment effects were inversely proportional to the size of the studies, indicating a possible publication bias in favour of low-protein diets. A weighted regression analysis of 13 RCTs compared with 11 other non-randomised trials demonstrated that the effect of dietary protein restriction was significantly less in the former and relatively greater among diabetic versus non-diabetic patients. The impact of restricted protein diets on nutrition was not considered in this meta-analysis, but is clearly crucial in view of the very modest beneficial effect on GFR decline.

A subsequently published Cochrane review of 9 RCTs and 3 before and after studies evaluating dietary protein restriction (0.7-1.1 g/kg/day) in diabetic CKD found no significant effect on GFR decline [7] .

The available RCTs and systematic reviews have frequently been limited by a number of weaknesses, including trial heterogeneity (CKD diagnosis, duration of intervention, level of protein restriction), suboptimal compliance with dietary protein restriction, failure to study GFR as an outcome measure,

exclusion of patients receiving ACE inhibitors, failure to analyse on an intention to treat basis, open label designs, suboptimal or uncertain sequence generation and allocation concealment, evidence of publication bias favouring low protein diets, failure to consider costs of implementation and monitoring of dietary protein restriction and failure to consider harms, such as malnutrition. For example, only 5 RCTs [8, 14, 20, 21, 50] have addressed the effect of restricted protein diets on nutrition and 4 have found statistically important reductions in nutritional parameters (the other observed neither a benefit nor adverse effect of dietary protein restriction). Another concern regarding dietary protein restriction in patients with chronic kidney disease is the spontaneous reduction in dietary protein intake with declining GFR. Ikizler et al. [51] noted that mean spontaneous dietary intakes averaged 1.1 g/kg/day for patients with creatinine clearances >50 mL/min, 0.85 g/kg/day at 25-50 mL/min, 0.70 g/kg/day at 10-25 mL/min and 0.54 g/kg/day <10 mL/min. These changes presumably reflect uraemic anorexia and raise questions regarding the safety of further restricting protein intake.

In the above mentioned RCTs examining the effects of dietary protein restriction in CKD, the levels of proteins used were "usual" ~ 1.0g/kg/day vs "low protein" ~ 0.6g/kg/day. There was little information in the literature to examine "free" or "high" protein intakes compared to the "usual" protein or low protein diets.

In a small RCT [21], 89 stage 3 (mean GFR ~ 45 mL/min/1.73m^2), non-diabetic CKD patients were randomised to receive a low-protein diet (0.6 g/kg/day) while the control group continued on with their usual free protein diet. The free protein diet group has 2.3 times higher protein intake than the study group (1.54± 0.39 Vs 0.67 ± 0.21 g/kg/day) and showed significant decline in renal function over 12 months (P < 0.01) with a mean decrease in GFR of 6.05 ± 1.23 vs 3.47 ± 0.26 mL/min/1.73 m2 (P < .001). Despite the significant decline in total energy intake in the study group, there was no significant change in serum albumin and pre-albumin, and signs of malnutrition were not observed. The authors commented the significant weight loss and BMI decline in the control group (25.1 ± 2.8 vs 23.9 ± 2.9 m/kg^2, P < 0 .05) could be beneficial to the cardiovascular pathology. A significant slowing of the progression of renal damage in the low protein diet group was concluded in this study (level II evidence) In this small sample size study, dietary components other than protein and phosphorous that may affect disease progression were not discussed e.g. energy, sodium, potassium and fat etc, therefore the claim of renal protective effect using a low protein diet compared to a free protein diet requires further testing.

In a prospective cohort study over 11 years, Knight et al. [52] examined the impact of protein intake on renal function decline in women with normal renal function (estimated GFR > or = 80 mL/min/1.73 m^2) or mild renal insufficiency(estimated GFR 55 to 80mL/min/1.73 m^2). It involved 1624 women enrolled in the Nurses' Health Study. Protein intake was measured near enrolment and repeated at the 4th year using a semi-quantitative food-frequency questionnaire. In multivariate linear regression analyses, in subjects with normal renal function, high protein intake was not significantly associated with change in estimated GFR. In subjects with early CKD, protein intake was significantly associated with a change in estimated GFR of -1.69 mL/min/1.73 m^2 (CI, -2.93 to -0.45 mL/min/1.73 m^2) per 10-g increase in protein intake. After measurement-error adjustment, the change in estimated GFR was -7.72 mL/min/1.73 m^2 (CI, -15.52 to 0.08 mL/min/1.73 m^2) per 10-g increase in protein intake, an association of borderline statistical significance. High intake of non-dairy animal protein in women with mild renal insufficiency was associated with a significantly greater change in estimated GFR (-1.21 mL/min/1.73 m^2 [CI, -2.34 to -0.33 mL/min/1.73 m^2] per 10-g increase in non-dairy animal protein intake). The authors concluded that high protein intake was not associated with renal function decline in women with normal renal function. However, high total protein intake, particularly high intake of non-dairy animal protein, may accelerate renal function decline in women with mild renal insufficiency (level III-2 evidence).

In a review article, Friedman [53] critically evaluated the possible effects on renal function using some of the common high-protein (HP) weight-loss diets. The American Recommended Daily Allowance (RDA) for protein is approximately 0.8g/kg/d. Typically, Americans consume approximately 1.2g/kg/d or 15% total energy. The author defined HP diet was > 1.5g/kg/d or > 25% total energy. The literature reported that HP consumption has been found, under various conditions, to lead to glomerular hyperfiltration and hyperaemia, acceleration of chronic kidney disease (CKD), increased proteinuria, diuresis, natriuresis, and kaliuresis with associated blood pressure changes, increased risk for nephrolithiasis, and various metabolic alterations. Although there was a dearth of evidence pertaining to HP diets in patients with CKD, it was concluded that, while there are no clear renal-related contraindications to HP diets in individuals with healthy kidney function, the theoretical risks should be

reviewed carefully with the patient with CKD as HP diets have the potential for significant harm in individuals with CKD. HP diets should therefore be avoided in CKD patients if possible.

In the 1995 National Nutrition Survey of the general population, Australians were found to consume more protein than they needed. Protein intakes were well above RDI levels for all age groups and genders (Dietary Guidelines for Australian Adults, Background Information page 6-7 (http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/n33.pdf, and http://www.abs.gov.au/ausstats/abs@.nsf/PrimaryMainFeatures/4802.0?OpenDocument).

In a cross-sectional study [54] of 113 Australian patients with CKD (serum creatinine 223.4 ±110.0 mmol/L), mean baseline protein intake was estimated to be 0.9 ± 0.3 g/kg/d, higher than RDI of 0.75 g/kg/d. After assessing the dietary reporting methods and errors, valid reporters showed higher protein intake of.1.2 ±0.3 g/kg/d

Nutritional status deteriorates as renal disease progresses. While malnutrition is common in CKD stages 4-5, observational studies suggested that it can occur as early as stages 3. Therefore close monitoring of nutritional status, including protein and energy intakes, is recommended [49]

To summarise, there is no convincing or conclusive evidence that long-term protein restriction delays the progression of CKD stages 1-5. The longest lasting, largest and best-designed RCT (MDRD study) argues against an important benefit. Five meta-analyses have demonstrated either no effect or a modest benefit of protein restricted diets, but 3 of these used an inappropriate outcome measure (renal survival), which did not allow distinction between delay of dialysis due to suppression of uraemic symptoms versus slowing of CKD progression. The 2 meta-analyses which used estimated GFR as an outcome measure found either no or only a very weak benefit of dietary protein restriction on CKD progression. There is also funnel plot evidence of possible publication bias favouring a beneficial effect of low protein diets. Any benefit of dietary protein restriction, if it exists at all, is likely to be offset by deleterious nutritional consequences, difficulties with achieving patient compliance, and the costs associated with implementation and patient monitoring.

Based on the current evidence, it is not possible to deduce the optimal levels of protein intake for patients with early CKD. In view of the complex physiology of protein metabolism in CKD, it is reasonable to recommend adults with early CKD, a diet with adequate energy and a normal protein near the RDI level of 0.75 - 1.0 g/kg/day.

2. Dietary sodium restriction

There have only been several, small, short-term (1-4 weeks) randomised, crossover studies evaluating the impact of dietary salt restriction on surrogate outcome measures (blood pressure and albuminuria) in diabetic patients with microalbuminuria[55, 56] or non-diabetic black hypertensive patients [57]. Vedovato et al. [55] reported body, 24-hour blood pressure and albuminuria in 41 type 2 diabetic patients (20 with microalbuminuria) who spent 2 consecutive 7-day periods on a high salt diet (250 mmol/day) or low salt diet (20 mmol/day). Switching from a low to high salt diet was associated with an increase in blood pressure (7.4±4.7 kg, p<0.001), body weight (1.9±0.4 kg, P < 0.05) and albuminuria (from 80[31-183] to 101 [27-965] µg/min only in patients with microalbuminuria). Similarly, Imanishi et al. [56] observed in 21 diabetic patients with albuminuria and normal serum creatinine concentrations that a sodium-restricted diet for 1 week was associated with reduced blood pressure and albuminuria. A randomised, double-blind, placebo-controlled trial of dietary salt restriction (169±73 vs 89±52 mmol/day approximately equivalent to 10 vs 5 g/day) was conducted in 40 non-diabetic, black hypertensive patients over for 4 weeks. Results demonstrated that salt restriction was associated with reduced blood pressure (159/100±13/8 vs 151/98±13/8, P < 0.01) and urine protein excretion (93±48 vs 75±30 mg/day, P < 0.008) [57]. Pimenta et al [58] conducted a prospective, randomised crossover trial of a low sodium diet (50 mmol/day) and a high sodium diet (250 mmol/day) over consecutive 7 day periods separated by a 2-week washout period in 12 patients with resistant hypertension. Dietary sodium restriction decreased mean office systolic BP by 22.7 mmHg and diastolic BP by 9.1 mmHg. Similarly, Todd et al [59] reported the results of a prospective, randomised crossover trial of 35 patients with hypertension randomly assigned to sequentially receive 1 of 3 interventions (sodium-free tomato juice, tomato juice containing 90 mmol Na, and tomato juice containing 140 mmol Na) for 4 weeks each, with

a 2 week washout period between interventions. Dietary sodium loading was associated with significant increases in the surrogate outcome measures of BP and pulse wave velocity. There are no longer-term RCTs examining the impact of dietary salt restriction in on kidney disease progression or other patient-level outcomes in CKD patients.

A systematic review of the evidence linking dietary salt intake and CKD progression [60] evaluated 3 randomised cross-over trials, 5 non-randomised crossover trials, 4 non-randomised comparative trials, 1 prospective observational cohort study, 1 retrospective observational cohort study and 1 cross-sectional study. Overall, the studies were mostly of poor quality and extremely heterogeneous. This limited the conclusions that could be drawn, although clear associations were identified between increasing salt intake and worsening blood pressure and albuminuria. However, limited and conflicting evidence was found pertaining to the effects of dietary salt consumption on CKD progression, especially over medium- to long-term follow-up.

In the Dietary Approaches to Stop Hypertension (DASH)-Sodium trial [61], 412 subjects were randomly allocated to either a typical US diet or the DASH diet (rich in vegetables, fruits, low-fat dairy products). Within each assigned diet, participants ate foods with high (150 mmol/day), intermediate (100 mmol/day) or low (50 mmol/day) levels of sodium for 30 consecutive days each, in random order. Reducing the sodium intake from high to intermediate to low was associated with respective, significant systolic blood pressure reductions of 2.1 mmHg and 6.7 mmHg in the control diet groups and 1.3 mmHg and 3 mmHg in the DASH diet group. At each sodium level, the DASH diet was associated with significantly lower systolic blood pressure. Patients with stage 1 hypertension who received the DASH diet with a low dietary sodium level had a mean systolic blood pressure that was 11.5 mmHg lower than those receiving the control diet at the highest sodium level. These results were limited by the short follow-up and the exclusion of patients with CKD. It should also be emphasised that the DASH diet has higher protein (1.4 g/kg/day), potassium (110-115 mmol/day) and phosphate (1.7 g/day) contents than would ordinarily be advisable for patients with stages 3-5 CKD (http://www.kidney.org/professionals/KDOQI/guidelines_bp/guide_6.htm).

Vogt et al [62] conducted a single centre, double-blind, randomized, placebo-controlled crossover trial to determine the separate and combined effects over consecutive 6 week periods, of a low-sodium diet (50 vs 200 mmol/day) and hydrochlorothiazide (HCT, 25 mg versus placebo) on proteinuria and BP in 34 non-diabetic CKD patients with moderate proteinuria (2-10 g/day, mean 3.8 g/day) and stable renal function (creatinine clearance >30 ml/min and <6 ml/min per yr decline). Proteinuria was reduced 22% by a low-sodium diet alone, 30% by losartan monotherapy, 55% by losartan plus a low-sodium diet, 56% by losartan plus HCT and 70% by all 3 interventions combined (all $P < 0.05$). BP showed a similar stepwise reduction with the various combinations of interventions. The investigators concluded that a low-sodium diet and a thiazide diuretic are equally effective in reducing proteinuria and BP when added to an ARB and the combination of a low-sodium diet, thiazide diuretic and angiotensin receptor blocker was a very effective strategy for reducing proteinuria and BP in patients with CKD. This study was limited by washout effects with the cross-over design, its single centre design, small sample size and a possible confounding effect of dietary salt restriction on lowering dietary protein intake.

Suckling et al [63] performed a Cochrane systematic review of 13 randomised controlled trials of salt reduction in 254 individuals with type 1 diabetes (n=75) and type 2 diabetes (n=158). Over a median trial period of 1 week, salt restriction was associated with reductions in systolic BP of -7.11 mmHg (95% CI -9.13 to -5.10) in type 1 diabetes mellitus and -6.90 mmHg (95% CI -9.84 to -3.95) in type 2 diabetes mellitus). The corresponding values for diastolic BP were -3.13 mmHg (95% CI -4.28 to -1.98) in type 1 diabetes mellitus and -2.87 mmHg (95% CI -4.39 to -1.35) in type 2 diabetes mellitus. The magnitude of BP reduction seemed to be greater in normotensive patients, possibly because of a greater magnitude of dietary sodium reduction. Pooled analysis of 10 studies (114 individuals) reporting changes in GFR did not find that salt restriction was associated with a significant change GFR (-1.92 mL/min, 95% CI -4.49 to 0.64). This review was limited by the short durations and significant heterogeneity of the studies. The effect of dietary salt restriction on patient-level outcomes was unable to be assessed.

To summarise, there are a number of short-term randomised controlled trials designed to determine the effectiveness and safety of dietary therapies to lower blood pressure in patients with CKD. Although

there is observational cohort and short-term randomised crossover study evidence linking dietary salt intake with blood pressure and degree of albuminuria, there is currently no clinical evidence that dietary salt restriction retards the progression of CKD.

3. Dietary phosphate restriction

There are no randomised controlled trials that have specifically addressed the issue of whether isolated phosphate restriction improves renal or cardiovascular outcomes in CKD.

Many of the protein restricted diets trialled in progressive CKD have additionally incorporated dietary phosphate restriction [8-10, 12-16, 22-28, 30-41, 43-45, 48, 64-74]. However, the specific role of phosphate restriction remains uncertain due to the conflicting findings of the studies and their often poor experimental design due to small numbers, short follow-up times, variable phosphate binder usage, different degrees of renal insufficiency, concomitant protein and caloric restrictions, and the inappropriate use of plasma creatinine or creatinine clearance as a GFR measure (as these are inaccurate and influenced by diet).

Barsotti et al. [70] performed a non-randomised study of a very-low-phosphate low-protein diet (6.5 mg/kg/day phosphate, 0.6 g/kg/day protein) versus a conventional low-phosphate low-protein diet (12 mg/kg/day phosphate, 0.6 g/kg/day protein) in 55 patients with non-diabetic CKD. It is not clear from the analysis whether the study was prospective or retrospective and whether the 2 groups were studied in parallel or sequentially. Both groups were followed initially on a free uncontrolled mixed diet for mean durations of 11.5 and 10.0 months, respectively. They were then switched to their special diets for average durations of 20.8 and 16.3 months, respectively. Serum phosphate significantly fell in the first group from 4.39 to 3.99 mg/dl and rose in the second group from 4.25 to 4.96 mg/dl. Urinary phosphate excretion differed between the 2 groups (362.3 versus 628.8 mg/day), but urinary urea excretion was comparable (7.62 versus 8.23 g/day) thereby indicating that protein intake was not significantly different. Despite comparable declines in creatinine clearance whilst on the free diet (-0.90±0.67 versus -0.79±0.53 mL/min/month), the patients who subsequently received a very low phosphate diet had a slower rate of renal functional deterioration compared with the other group (-0.07±0.38 versus -0.53±0.40 mL/min/month), although no comment was made as to whether the difference was statistically significant (in fact the difference did not appear to be significant based on calculations from the summary data). The limitations of the study are its small size, short follow-up time, inappropriate renal function measure, lack of randomisation and inappropriate statistical analysis (t-tests in the setting of repeated measures).
Dietary phosphate restriction to control hyperphosphataemia is usually not required in early (stages 1-3) CKD. In patients with stages 4-5 CKD, there are no RCTs examining the effects of dietary phosphate restriction on patient-level cardiovascular outcomes. Russo et al. [75] randomised 90 phosphate-binder-naive patients with CKD stages 3–5 who were not on dialysis to a low-phosphate diet alone or in combination with fixed doses of either calcium carbonate (2 g/d) or sevelamer hydrochloride (1600 mg/d) over a 2-year follow-up period. Final coronary artery calcification scores significantly increased in the group receiving phosphate-restricted diet alone, increased to a lesser extent in calcium carbonate-treated patients and did not change in sevelamer-treated patients. Thus, a low phosphate diet alone did not prevent CKD-associated progression of coronary artery calcification in patients not receiving dialysis. The main limitation of the study was that it was not adequately powered as an equivalence or non-inferiority study.

There has not been adequate study of the nutritional consequences of phosphate-restricted diets in CKD patients.

In summary, there has only been 1 non-randomised study of isolated dietary phosphate restriction versus a conventional low phosphate, low protein diet in 55 patients with non-diabetic CKD. No significant differences were found between the 2 groups, although the study was limited by a lack of statistical power, inappropriate statistical analysis, inadequate measurement of renal function and a lack of randomisation. There is therefore no evidence in early (stages 1-3) CKD that dietary protein restriction significantly influences cardiovascular or renal outcomes. In more advanced (stages 4-5 CKD), dietary phosphate restriction has not been found in one small RCT to prevent the progression of coronary artery calcification. There is no evidence that dietary protein restriction has a significant effect

on cardiovascular or renal outcomes. There has been inadequate study of the effects of phosphate restriction on nutrition in CKD patients.

4. Dietary potassium restriction

Hyperkalaemia is occasionally observed in patients with stage 3 CKD and more frequently observed in patients with stage 4-5 CKD. Although dietary potassium restriction is a standard recommendation for managing CKD patients with hyperkalaemia, there are no RCTs of dietary potassium restriction in CKD patients.

5. Polyphenol-enriched diets

Facchini and Saylor [76] conducted a prospective, open-label, RCT of a low-iron-available, polyphenol-enriched, 50% carbohydrate restricted (CR-LIPE) diet versus a standard, protein-restricted (0.8 g/kg/day) diet in 191 type 2 diabetic patients with various degrees of CKD (GFR 15-75 mL/min) or proteinuria (350-12000 mg/day). Over a mean follow-up period of 3.9±1.8 years, serum creatinine concentration doubled in 19 (21%) patients on CR-LIPE compared with 31 (39%) patients on the control diet ($P < 0.01$). Renal death occurred in 18 (20%) patients on CR-LIPE and 31 (39%) of controls ($P < 0.01$). The observed differences between the groups were independent of follow-up interval, sex, mean arterial blood pressure, glycated haemoglobin, initial renal dysfunction and angiotensin system inhibition. Drop-out rates were low in each group (CR-LIPE 9%, controls 13%). Dietary compliance was not assessed, but serum ferritin concentration did fall significantly in the CR-LIPE group (from 301±162 to 36±31 μg/L), while it was unchanged in control subjects. Despite the development of iron deficiency in a number of subjects in the CR-LIPE group, haemoglobin levels did not fall (141±21 versus 140±20 g/L). Body weight and serum albumin concentration also did not fall in the CR-LIPE patients. The principal limitations of the study were (a) its small size (potentially limiting the generalisability of these findings); (b) the lack of monitoring of dietary compliance; and, (c) the uncertainty regarding adequate concealment of randomisation allocation.

To summarise, 1 small RCT has demonstrated that a CR-LIPE diet is markedly more effective at retarding the progression of diabetic nephropathy than standard dietary protein restriction. These findings should be considered preliminary.

6. Dietary caloric restriction

In a single centre RCT [77], 30 overweight (BMI >27 kg/m^2) diabetic and non-diabetic CKD patients with proteinuria > 1g/d on at least 3 consecutive determinations over a 6-month period were randomly allocated in a 2:1 ratio to a low calorie (500 kcal restriction compared to usual diet), normoproteinic (1-1.2 g/kg/day) diet or a control diet (no recommendations made to modify diet except to provide a protein intake of 1-1.2 g/kg/day). During the 5-month period of the study, body weight decreased from 87.5±11.1 to 83.9±10.9 kg ($P < 0.01$) in the diet group, but increased significantly in the control group from 96.1±16.6 to 98.0±16.4 kg ($P < 0.05$). The primary outcome measure was proteinuria, which significantly decreased in the diet group from 2.8±1.4 to 1.9±1.4 g/day ($P < 0.005$) and tended to rise in the control group from 3.0±2.2 to 3.5±2.1 g/day (P = not significant). Creatinine clearance did not change significantly in the diet group, however it decreased significantly in the control group from 61.8±22.1 to 56±19.9 ml/min/1.73m^2 ($P < 0.05$). Blood pressure and creatinine clearance did not change significantly in either group. The major limitations of this study were its open-label design, small sample size, relatively short follow-up, use of a surrogate outcome (proteinuria), and exclusion of angiotensin converting enzyme inhibitors and angiotensin receptor blockers (therefore creating uncertainty as to whether the effects of caloric restriction are additive with those of calorie restriction).

Saiki et al. [78] reported a before and after prospective study of the safety and efficacy of a 4-week, low calorie (11-19 kcal/day), normal protein (0.9-1.2 g/kg/day) diet partly supplemented with formula in 22 patients with diabetic CKD, BMI > 25 kg/m^2, urinary albumin > 300 mg/day and serum creatinine < 265.2 μmol/L. Mean body weight decreased by 6.2±3.0 kg and was associated with a significant decrease in proteinuria (from 3.27±2.63 to 1.50±1.28 g/day, $P < 0.0001$) but no change in creatinine clearance (0.68±0.29 to 0.77±0.24 mL/sec/1.73 m^2). The main limitations of the study were its small sample size, short follow-up and pre-test/post-test design (raising the possibility of co-intervention bias).

Another before and after study of a hypocaloric dietary change from 1870 to 1410 kcal/day (without changes of protein:carbohydrate ratio) in 24 type 1 and 2 diabetic patients with obesity and CKD reported significant decreases in proteinuria (from 1280±511 to 623±307 mg/day, $P < 0.01$) and albuminuria (from 723±388 to 492±170 µg/min, $P < 0.01$) and significant improvements in estimated GFR (from 66±13 to 81±11 mL/min/1.73 m^2) and measured creatinine clearance (from 79±14 to 91±13 mL/min, $P < 0.01$) over 12 months [79]. The limitations of this study were its small sample size, short follow-up and pre-test/post-test design (raising the possibility of co-intervention bias).
Navaneethan et al. [80] conducted a systematic review of 11 observational studies and 2 RCTs of weight loss interventions (mostly hypocaloric diets) in CKD patients (mostly stage 1-3). Body mass index (BMI) decreased significantly (weighted mean difference [WMD] -3.67 kg/m^2, 95% CI -6.56 to -0.78) at the end of the study period with nonsurgical interventions. This was associated with a significant decrease in proteinuria (WMD -1.31 g/24 h; 95% CI -2.11 to -0.51) and systolic BP with no further decrease in GFR during a mean follow-up of 7.4 mo. In morbidly obese individuals (BMI >40 kg/m^2) with glomerular hyperfiltration (GFR >125 ml/min), surgical interventions decreased BMI, which resulted in a decrease in GFR (WMD -25.56 ml/min; 95% CI -36.23 to -14.89), albuminuria, and systolic BP. This meta-analysis was limited by poor study quality, a high degree of heterogeneity (I^2=75%), surrogate outcome measures (albuminuria), inadequate power to adequately evaluate patient-level outcomes, and short-term follow-up.

In summary, the limited available evidence suggests that caloric restriction leading to weight loss results in amelioration of CKD in overweight/obese individuals, as evidenced by diminished proteinuria and improved kidney function.

There are a limited number of small, short-term pre-/post-intervention studies which have demonstrated that gastric bypass surgery is associated with reductions in blood pressure and proteinuria/albuminuria in obese patients with early CKD due to diabetic nephropathy [81], focal segmental glomerulosclerosis [82-84] and stage 3 CKD due to various aetiologies [85, 86]. Navaneethan et al. [87] conducted a retrospective study of 25 patients with stage 3 CKD who had undergone bariatric surgery at a US university hospital. Their average BMI decreased from 49.8 kg/m^2 to 38.4 kg/m^2 ($P < 0.001$) at the end of 6 months to 34.5 kg/m^2 ($P < 0.001$) at the end of 12 months. The mean systolic blood pressure had decreased from 133±13 to 128±17 mm Hg at the end of 12 months. The mean GFR at 6 months of follow-up had improved to 56.6 mL/min/1.73 m^2 ($P < 0.001$) and to 61.6 mL/min/1.73 m^2 ($P < 0.001$) at 12 months. However, these benefits must be weighed against reports of an increased risk of CKD following bariatric surgery secondary to secondary hyperoxaluria and calcium oxalate nephrolithiasis [88-93] Gastric banding is not reported to be associated with an increased risk of kidney stones [94], but there is also no evidence yet that such surgery has an impact on CKD progression in patients with early CKD.

Afshinnia et al [95] reported the results of a meta-analysis of 522 subjects from 5 controlled and 8 uncontrolled trials published in English prior to June 2009 in which urinary protein was examined among obese or overweight adults before and after weight loss interventions including dietary restriction, exercise, anti-obesity medications and bariatric surgery. After excluding one study which greatly increased heterogeneity in the pooled analysis, weight loss interventions were associated with a decrease in proteinuria by 1.7 g (95% CI 0.7-2.6 g), a 55% decrease from baseline (95% CI 23%-87%), Heterogeneity testing demonstrated a moderate degree of heterogeneity (I^2 = 59.5%) that almost achieved statistical significance (p = 0.08). Meta-regression analysis suggested that this heterogeneity may have been partially explained by variation in baseline weight, weight loss and decline of mean arterial pressure among different studies. Weight loss interventions also decreased urinary albumin excretion by 14 mg (95% CI 11-17), representing a 52% decrease from baseline (95% CI 40%-64%). This finding was again associated with moderate heterogeneity (I^2 = 50.0%, p=0.051). Subsequent meta-regression analysis demonstrated that each 1 kg weight loss was associated with 110 mg (95% CI 60-160 mg, p<0.001) decrease in proteinuria and 1.1 mg (95% CI, 0.5 to 2.4 mg, $P = 0.011$) decrease in microalbuminuria. Surgical interventions decreased GFR or creatinine clearance by 23.7 mL/min (95% CI, 11.4 to 36.2), a 17% decrease from baseline (95% CI, 8% to 26%). Non-surgical interventions were not significantly associated with changes in GFR or creatinine clearance. The conclusions that could be drawn from this systematic review were limited by significant trial heterogeneity, generally poor trial quality, inclusion of non-randomized studies, inclusion of different populations at different stages of disease (both with and without CKD) and failure to account for the impact of weight on GFR estimating equations.

7. Physical exercise

Eidemak et al. [96] randomised 30 patients with stages 3-5 CKD (median GFR 25 mL/min/1.73 m^2, range 10-43) to physical training (30 minutes of bicycling daily or an equal amount of other physical activities) or to maintenance of usual lifestyle. Over a median follow-up time of 20 months, median maximal work capacity increased significantly in the exercise group, but not in the controls. However, no change in GFR decline was observed between the 2 groups. The chief limitation of the study was its lack of statistical power.

A small prospective, non-controlled study of 16 subjects with chronic kidney disease [97] showed no effect of endurance exercise training (cycle ergometer) on CKD progression, as determined by plasma creatinine. The major limitations of the study were its small numbers, short follow-up time, high drop-out rate (50%) and inappropriate measure of kidney function (plasma creatinine rather than estimated or measured GFR).

A subsequent RCT by the same group [98] randomly assigned 26 adults with moderate CKD (serum creatinine between 133 and 442 µmol/L) to a low protein diet (0.6 g/kg/day) plus resistance training (n = 14) or a low protein diet plus sham training for 12 weeks. GFR, as measured by iothalamate clearance, increased with resistance training and decreased with sham training (1.18 vs -1.62 mL/min, p=0.048). The limitations of this study include its small sample size, short duration (12 weeks) and questionable generalisability (requirement for exercise physiologist supervisor together with limited [9%] participation of eligible subjects). The risks of exercise in the CKD population, who are at significantly increased risks of cardiovascular events, have also not been adequately studied. In the RCT by Castaneda et al. [98], a preliminary screening treadmill stress test was performed on participants.

Castaneda et al [99] conducted a randomised controlled trial of 26 adults with CKD randomly allocated to resistance training (n=14) or a control group (n=12) for 12 weeks. The intervention group exhibited a significant increase in muscle strength (28±14% vs 13±22%, p=0.001). The major limitations of the study were its small numbers, short follow-up time, and use of a surrogate outcome measure.

Leehey et al [100] performed a randomized controlled feasibility study comparing thrice weekly aerobic exercise plus optimal medical management to medical management alone in patients with type 2 diabetes, obesity and stage 2-4 CKD over a 24 week period. There were no significant differences between the intervention and control groups with respect to BP, proteinuria, GFR, haemoglobin, glycated haemoglobin, serum lipids, C-reactive protein, caloric intake or body weight and composition. The major limitations of the study were its small numbers and short follow-up time,

In another trial, 23 patients with moderate-to-severe CKD were randomized to resistance training (n = 13) or attention-control (stretching and flexibility exercises, n = 10) for 12 weeks. It was observed that resistance training increased skeletal muscle mitochondrial DNA copy number on muscle biopsy, but did not affect GFR.[101] The major limitations of the study were its small numbers, short follow-up time, and use of a surrogate outcome measure of questionable clinical significance.

A recently published Cochrane review examined 1863 adults with CKD or kidney transplants from 45 randomized controlled trials examining any type of physical exercise intervention over a period of at least 8 weeks [102]..Of these 45 studies, 32 were able to be incorporated into meta-analysis. Physical exercise training decreased resting diastolic blood pressure by a mean level of 2.32 mmHg (95% CI 0.59-4.05 mmHg; 11 studies, 419 participants). However, moderate heterogeneity was identified (I^2 = 46%, p=0.05). Similar findings were observed for resting systolic blood pressure (5 studies, 211 participants; mean reduction 5.88 mmHg, 95% CI 1.42-10.34, p=0.01; I^2 =0%, p= 0.97). No significant effects of exercise were observed on serum lipids, inflammatory parameters, adverse events or mortality. CKD progression was not examined as an outcome parameter. Significant benefits of exercise training were found for aerobic capacity, walking capacity, heart rate, serum albumin and health-related quality of life. Assessment of trial quality suggested that the overall risk of bias was low in 17%, moderate in 33% and high in 49% of studies. The authors concluded that, “clinicians should inform adults with CKD that there is scientific evidence showing that by exercising regularly for > 30 minutes/session and three times/week they would improve their physical fitness, walking capacity, cardiovascular dimensions (e.g. blood pressure and heart rate), some nutritional parameters and

health-related quality of life." However, the strength of these conclusions was limited by moderate trial heterogeneity and generally poor quality trials with limited sample size.

To summarise, there have been several small, short duration RCTs of exercise training in patients with stages 3-5 CKD. Several studies showed no effect of exercise on CKD progression although 1 showed improvement in GFR with exercise. The results of these studies should be considered preliminary. Further RCTs are required to establish the safety and efficacy of exercise in patients with CKD with respect to renal and cardiovascular outcomes.

8. Smoking cessation

The effects of smoking cessation in patients with CKD have been previously reviewed in the CARI Guidelines on Renal Failure Progression (http://www.cari.org.au/CKD_Prevent_List_Published/Smoking.pdf).
Briefly, there are no RCTs. Numerous retrospective and prospective studies (some of which have included thousands of patients) have suggested that smoking is associated with renal failure progression in both diabetic and non-diabetic CKD [103-112]. Current smoking confers a greater risk than former smoking. Three small cohort studies suggest that cessation of smoking may ameliorate renal failure progression in diabetic and non-diabetic CKD [105, 108, 113].

There are no good quality data examining the effect of smoking cessation on cardiovascular events in people with CKD, although there is clear epidemiological evidence associating smoking with increased cardiovascular risk in the general population [114, 115].

9. Alcohol intake

Chronic alcohol consumption has been linked with hypertension [116, 117] and therefore indirectly with CKD. However, there is conflicting epidemiological evidence with some studies demonstrating that moderate-to-heavy alcohol consumption is an independent risk factor for CKD [118-120] and other studies demonstrating an inverse association between alcohol intake and CKD risk [121, 122]. In the AusDiab study [118], alcohol intake of ≥30 g/day was associated with an increased risk of albuminuria after adjustment for age, sex and baseline kidney function (OR = 1.59, 95% CI: 1.07–2.36), but a reduced risk of eGFR <60 mL/min/1.73 m^2 (OR = 0.59, 95% CI: 0.37–0.95), compared with consumption of <10 g/day. These studies are likely to be limited by selective reporting, under-reporting of heavy alcohol consumption, ascertainment bias, residual confounding and Neyman bias. At this point in time, it is difficult to draw conclusions regarding the impact of alcohol consumption on CKD progression. There are no intervention studies examining the impact of modification of alcohol intake on CKD progression.

10. Carbonated beverages

Soft-drink (especially cola) consumption has been associated with diabetes [123], hypertension [124] and kidney stones [125-127]. The relationship between imbibing cola beverages and the development of kidney stones has been attributed to urinary acidification by phosphoric acid [126, 128, 129]. In a case-control study involving 465 patients with newly diagnosed CKD and 467 community controls recruited in North Carolina between 1980 and 1982 [130], drinking 2 or more colas per day was associated with increased risk of CKD (adjusted odds ratio [OR] 2.3, 95% CI: 1.4–3.7). Results were the same for regular colas (OR 2.1, 95% CI 1.3–3.4) and artificially sweetened colas (OR 2.1, 95% CI: 0.7–2.5). Non-cola carbonated beverages were not associated with CKD (OR 0.94, 95% CI: 0.4 –2.2). The results of this study were potentially limited by self-reporting bias, lack of other dietary information, residual confounding and a high proportion of proxy responders.

Bomback et al [131] examined the relationship between soda consumption, hyperuricaemia and CKD in 15,745 participants, men and women aged 45–64 years, in the Atherosclerosis Risk In Communities Study (ARIC) who completed dietary questionnaires and serum urate and creatinine measurements. Over 9 years of follow-up, participants who drank more than one soda per day were not at increased risk of incident hyperuricaemia (adjusted OR 1.17, 95% CI 0.95–1.43, p=0.1) or incident CKD (OR 0.82, 95% CI 0.59–1.16, p=0.3).When the multivariable logistic models were stratified by uric acid levels, only

participants with serum urate levels ≥ 9.0 mg/dl had an increased risk of developing CKD if they drank more than one soda per day (OR 3.90, 95% CI 1.55–9.82) compared to participants with similar serum uric acid elevations who drank less than one soda per day. When diet soda was analysed on its own, drinking more than 1 diet soda per day was not associated with incident hyperuricaemia (OR 0.97, 95% CI 0.83–1.14), or incident CKD (OR 0.80, 95% CI 0.64–1.00) on multivariable logistic regression analysis. The limitations of this study included self-reporting bias, misclassification bias (due to limited creatinine measurements and very limited albuminuria measurements), performance bias (by virtue of enrolment in a community health study) and lack of data on medications affecting serum urate (eg diuretics) and creatinine (eg ACE inhibitors and ARBs).

11. Fluid intake

Drinking vigorous amounts of water has commonly been advocated in the popular press to enhance kidney health. “Drink at least 8 glasses of water a day” is a ubiquitous exhortation [2] and is often referred to the “8 x 8” rule (i.e. drink at least 8 glasses containing 8 ounces of water each day). There is no clinical evidence supporting this health advice, although a comprehensive review by Dr Heinz Valtin [2] attributes its origin to an unsubstantiated, seemingly casual remark in a book by Dr Fredrick Stare and Dr Margaret McWilliams in 1974 [132]. On the other hand, there are isolated case reports that drinking excessive amounts of water, particularly in the setting of reduced renal excretory ability (e.g. patients with CKD), may be associated with water intoxication, fluid overload and hyponatraemia [133, 134]. Moreover, imbibing large volumes of water may be associated with considerable inconvenience (from frequent urination) and expense (from paying for considerable volumes of bottled water).

Recently, Strippoli et al. [135] reported the findings of a prospective, observational cohort study, which examined the associations between CKD (defined on the basis of Cockcroft-Gault or MDRD eGFR) and the intake of fluid and nutrients (determined by food frequency questionnaires) in 2 cross-sections of older patients in the Blue Mountains at 2 different time periods (1992-1994 and 1997-2000). The study found that lower CKD prevalence was associated with higher intakes of fluid. The authors concluded that augmented fluid intake has the possibility to reduce CKD by approximately 50% and that a high fluid intake should be strongly encouraged. The results of this observational study are hypothesis-generating, but do not establish whether the association between fluid intake and CKD prevalence represent cause, consequence or confounding.

To summarise, there is only 1 observational cohort study to date that has identified an inverse association between fluid intake and CKD prevalence. In light of the extremely limited evidence underpinning augmented fluid intake as a therapeutic strategy for mitigating CKD risk and the potential for harm from excessive fluid intake, particularly in patients with more advanced CKD, clinicians should be circumspect about encouraging increased fluid intakes in CKD patients.

12. Nutritional management by dietitians

There is limited evidence pertaining to the impact of individualised dietary intervention by a qualified dietitian, on clinical outcomes in patients with CKD. Slinin et al [136] conducted a retrospective, observational cohort study of 156,440 CKD patients who commenced haemodialysis between 2005 and 2007 in the United States and for whom predialysis dietitian care was reported on the Centers for Medicare & Medicaid Services Medical Evidence Report. Overall, 88% of patients received no dietitian care, whilst 9% received dietitian care for 12 months or less, and 3% received dietitian care for more than 12 months before dialysis commencement. Predialysis dietitian care was independently associated with higher serum albumin concentrations, lower total cholesterol levels and, in patients receiving predialysis dietitian care for more than 12 months, higher weight at HD commencement. Using multivariable Cox proportional hazards model analysis, predialysis dietitian care was associated with reduced mortality in the first year of dialysis commencement (0-12 months care HR 0.95, 95% CI 0.91-0.99; >12 months care HR 0.85, 95% CI 0.79-0.91). This difference was no longer significant after adjustment for predialysis nephrology care. Using the propensity score method, predialysis dietitian care for more than 12 months, was associated with a lower first year mortality on haemodialysis in the second tertile of propensity score (HR 0.81, 95% CI 0.71-0.93, p = 0.002), but not in the first tertile (HR 1.16, 95% CI 0.44-3.09; p= 0.8) or third tertile (HR 0.93, 95% CI 0.86-1.01, p=0.1). Predialysis dietitian

care for less than 12 months was not associated with subsequent mortality on haemodialysis in any of the three propensity score strata. This study was potentially limited by indication bias with residual confounding, recall bias and ascertainment bias (18.6% of Medical Evidence Report Forms were missing).

Campbell et al [137] reported the results of a retrospective evaluation of the impact of initiating specific nutrition care guidelines for haemodialysis patients, as described in the Evidence-Based Practice Guidelines for the Nutritional Management of Chronic Kidney Disease [138], by renal dietitians every 6 months at a public tertiary teaching hospital and a private dialysis facility between 2004 and 2006. The key findings of the study were that implementation of standardized nutrition guidelines by renal dietitians was associated with a significant reduction in serum phosphate concentration ($p=0.004$), a decrease in the proportion of patients with malnutrition (subjective global assessment category B or C) from 14% to 3% ($p=0.06$), and improvements in both energy and protein intakes ($p<0.001$). The study was potentially limited by recall bias, cointervention bias, Neyman bias, use of surrogate outcome measures and lack of adjustment for comorbid illnesses.

13. Fruit and vegetables

In a 30 day intervention study in subjects with CKD stage 1 to 2 due to hypertensive nephropathy, Goraya et.al[139] compared the effects of daily oral sodium bicarbonate (NaHCO3) and the fruit and vegetables intake on 3 urinary markers, including Urinary albumin (Ualb), urinary N-acetyl b-D-glucosaminidase (UNAG), and transforming growth factor β (UTGFB). These are markers of progressive kidney injury and kidney tubulo-interstitial injury; in particular, UNAG and UTGFB reflected kidney injury by dietary acids in experimental model of CKD. The secondary outcomes were urine aldosterone (Ualdo) and urine endothelin (UET) excretions. The authors referred to the literature, which showed that neutralization of dietary acid with sodium bicarbonate decreased kidney injury and slowed the decline of the GFR. They hypothesised a similar alkali - inducing effects from fruit and vegetables consumption compared to the oral NaHCO3. Within each of the CKD stage 1 (n=79) and stage 2 (n=120) groups, there was a control or no intervention group, an oral NaHCO3 group (receiving 0.5 mEq/kg/day of HCO3) and a "fruit & vegetables" group (receiving added fruit and vegetables, especially the base-inducing types, in amounts calculated to reduce dietary acid by half). All patients had 6 months of antihypertensive control by angiotensin-converting enzyme inhibition before and during the study. In the CKD stage 1 study, there was no difference among the three groups. However, in the study with CKD stage 2, both interventions (NaHCO3 and fruit & vegetables diet) decreased the urinary markers of kidney injury to the same extent compared with controls. The authors concluded that fruit and vegetable consumption was comparable to sodium bicarbonate in reducing dietary acid and urinary markers of kidney injury in patients with moderately reduced eGFR due to hypertensive nephropathy.

The potent blood pressure lowering effect of fruit and vegetables was demonstrated in the Dietary Approaches to Stop Hypertension (DASH)[61] diet trial in hypertensive patients. Although subjects with renal insufficiency were excluded from the study, this dietary pattern clearly confirmed the blood pressure lowering effects from fruit and vegetables. In addition, the known benefit of fruit and vegetables on increased intake of antioxidant, vitamins and fibre and on cardiovascular health in the non–renal population further support the recommended inclusion of fruit and vegetables, as part of a healthy diet in patients with early CKD.

14. Mediterranean diet

In a small RCT with 40 subjects of CKD stages 1 to 3[140] the intervention group (n=20) received nutritional advice adapted to a Mediterranean diet (MD) compared to controls (n=20). Both groups followed the dietary recommendations by the K/DOQI guidelines for protein (0.75g/kg/IBW/d), energy (0.12MJ/kg/IBW/d) with fat and carbohydrates contributing to 35% and 55% total energy, respectively. The MD group have increased use of mono and polyunsaturated fats, dietary fibres, whole grains, fruit and vegetables and fish. Patients were assessed at baseline and after 30, 60 and 90 days for dietary intake and biomarkers. Compared to the control group, at various time points, the intervention group showed significant reduction in serum lipids such as triglycerides, total cholesterol (TC), LDL-

cholesterol, TC/HDL-C ratio; and increased in serum albumin, decreased in C reactive protein (CRP), fibrinogen and thiobarbituric acid reactive substances (TBARS). Renal function remained stable throughout the study. The results suggested the combination of K/DOQI nutritional recommendations for CKD and a Mediterranean diet reduced dyslipidemia and protected against lipid peroxidation and inflammation.

15. Dietary fibre

Krishnamurthy et.al[141] examined the associations between dietary fibre intake, elevated C-reactive protein, a marker of inflammation and all-cause mortality from the data base of the National Health and Nutrition Examination Survey III. In the entire cohort of 14,543 subjects, 5.8% had GFR less than 60ml/min/1.73m^2 (mean ~ 50ml/min) or CKD stages 3-5. The average fibre intake was 17 g/d, and was below the 20 – 30 g/d level recommended for the general population. Patients with CKD averaged 15g/d. The mortality rate was 54% in the CKD group after an average follow-up of 6.5 years and ~ 11.5% in the non-CKD group (GFR ~ 93 ml/min) with an average follow- up of 8.6 years. At baseline, CKD group had a higher prevalence of elevated serum CRP compared to the non-CKD group (44.5 vs. 24.5%, P<0.001). However, no data was available if any of these patients were on renal replacement therapy. In the entire cohort, intakes of total, insoluble, and soluble fibres were each inversely associated with elevated serum CRP and these demonstrated relationships were significantly stronger in those with CKD than those without CKD. In patients with CKD, but not those without CKD, dietary fibre intake was also associated with mortality risk. Each 10 g /d increase in intake was associated with an overall mortality hazard ratio of 0.83; 95% CI 0.73-0.94 for total fibre, 0.77; 95% CI 0.65-0.91 for insoluble fibre, and 0.67; 95% CI 0.42-1.04 for soluble fibre. The results of this study also suggested that CKD is a potential modifier of the beneficial effects of dietary fibre intake. However, the ideal levels of fibre intake cannot be confirmed from this study. One cannot conclude causation from this epidemiologic study nor infer such effects for the CKD stages 1-3 population. However, the results of this study and the known health benefits of dietary fibre in the general population may serve to encourage patients with early CKD to include an adequate fibre intake as part of healthy eating,

SUMMARY OF EVIDENCE

1. Dietary protein restriction

There is no convincing or conclusive evidence that long-term protein restriction delays the progression of CKD stages 1-5. The longest lasting, largest and best-designed RCT (MDRD study) argues against an important benefit. Five meta-analyses have demonstrated either no effect or a modest benefit of protein restricted diets, but 3 of these used an inappropriate outcome measure (renal survival), which did not allow distinction between delay of dialysis due to suppression of uraemic symptoms versus slowing of CKD progression. The 2 meta-analyses which used estimated GFR as an outcome measure found either no or only a very weak benefit of dietary protein restriction on CKD progression. There is also funnel plot evidence of possible publication bias favouring a beneficial effect of low protein diets. Any benefit of dietary protein restriction, if it exists at all, is likely to be offset by deleterious nutritional consequences, difficulties with achieving patient compliance, and the costs associated with implementation and patient monitoring.

Based on the current evidence, it is not possible to deduce the optimal levels of protein intake for patients with early CKD. In view of the complex physiology of protein metabolism in CKD, it is reasonable to recommend adults with early CKD, a diet with adequate energy and a normal protein near the RDI level of 0.75 - 1.0 g/kg/day.

2. Dietary sodium restriction

There are a number of short-term controlled trials of dietary sodium restriction in CKD patients, which have demonstrated clinically important reductions in BP and proteinuria. However, there are no trials extending beyond a few months and no trials which have been adequately powered to determine whether dietary salt restriction improves patient-level outcomes such as CKD progression or cardiovascular disease.

3. Dietary phosphate restriction

There has only been one non-randomised study of isolated dietary phosphate restriction versus a conventional low phosphate, low protein diet in 55 patients with non-diabetic CKD. No significant

differences were found between the 2 groups, although the study was limited by a lack of statistical power, inappropriate statistical analysis, inadequate measurement of renal function and a lack of randomisation. There is therefore no evidence in early (stages 1-3) CKD that dietary protein restriction significantly influences cardiovascular or renal outcomes. In more advanced (stages 4-5 CKD), dietary phosphate restriction has not been found in one small RCT to prevent the progression of coronary artery calcification. There is no evidence that dietary protein restriction has a significant effect on cardiovascular or renal outcomes. There has been inadequate study of the effects of phosphate restriction on nutrition in CKD patients.

4. Dietary potassium restriction

There are no RCTs of dietary potassium restriction in CKD patients.

5. Polyphenol-enriched diets

One small RCT has demonstrated that a CR-LIPE diet is markedly more effective at retarding the progression of diabetic nephropathy than standard dietary protein restriction. These findings should be considered preliminary.

6. Dietary caloric restriction

The limited available evidence suggests that caloric restriction leading to weight loss results in amelioration of CKD in overweight/obese individuals, as evidenced by diminished proteinuria and improved kidney function.

7. Physical exercise

There have been several small, short duration RCTs of exercise training in patients with stages 3-5 CKD. Several studies showed no effect of exercise on CKD progression although 1 showed improvement in GFR with exercise. The results of these studies should be considered preliminary. Further RCTs are required to establish the safety and efficacy of exercise in patients with CKD with respect to renal and cardiovascular outcomes.

8. Smoking cessation

There are no good quality data examining the effect of smoking cessation on cardiovascular events in people with CKD, although there is clear epidemiological evidence associating smoking with increased cardiovascular risk in the general population.

9. Alcohol intake

Studies on alcohol intake are likely to be limited by selective reporting, under-reporting of heavy alcohol consumption, ascertainment bias, residual confounding and Neyman bias. At this point in time, it is difficult to draw conclusions regarding the impact of alcohol consumption on CKD progression. There are no intervention studies examining the impact of modification of alcohol intake on CKD progression.

10. Carbonated beverages

There is one case-control study, which indicated that drinking two or more colas per day was associated with increased risk of CKD. These results were potentially limited by self-reporting bias, lack of other dietary information, residual confounding and a high proportion of proxy responders.

11. Fluid intake

There is only one observational cohort study to date that has identified an inverse association between fluid intake and CKD prevalence. In light of the extremely limited evidence underpinning augmented fluid intake as a therapeutic strategy for mitigating CKD risk and the potential for harm from excessive fluid intake, particularly in patients with more advanced CKD, clinicians should be circumspect about encouraging increased fluid intakes in CKD patients.

12. Nutritional management by dietitians

There is limited retrospective observational cohort evidence that nutritional interventions by renal dietitians result in improved nutritional surrogate outcomes in patients with CKD. Moreover, pre-dialysis dietitian care in patients with early CKD may be associated with improved survival following the commencement of dialysis. These results were limited by recall bias, ascertainment bias, selection bias and the possibility of residual confounding. There are no randomised controlled trials in patients with

early CKD evaluating the effect of dietitian care versus nutritional advice provided by a doctor on surrogate or patient-level outcomes.

13. Fruit and vegetables
The benefit of fruit and vegetables consumption to correct metabolic acidosis was observed in a small short-term controlled study in patients with stage 2 CKD. The implications for improvement in clinical outcomes cannot be deduced based on the improvement in the surrogate markers of kidney injury and metabolic acidosis. However, the results support the suggestion that people with early CKD should include adequate amounts of fruit and vegetables in their diet as part of healthy eating.

14 . Mediterranean diet
In one small RCT over 3 months, the K/DOQI nutrition recommendations adapted to a Mediterranean diet were shown to improve serum lipid profiles, markers of oxidative stress and inflammation in patients with CKD stages 1-3. The long-term compliance, safety and efficacy of this diet regimen with respect to improving clinical outcomes require further study.

15. Dietary fibre
There is limited evidence to support the benefit of dietary fibre in reducing inflammation (CRP) and mortality risk in the CKD population.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative: [142]
Dietary and other therapeutic lifestyle modifications are recommended as part of a comprehensive strategy to lower blood pressure and reduce CVD risk in CKD.

6.1 Dietary sodium intake of less than 2.4 g/d (less than 100 mmol/d) should be recommended in most adults with CKD and hypertension (A).
6.2 Other dietary recommendations for adults should be modified according to the stage of CKD (Table 83) (B).
6.3 Lifestyle modifications recommended for CVD risk reduction should be recommended as part of the treatment regimen (Table 84) (B).
6.4 Referral to a registered dietitian should be considered to help patients achieve dietary recommendations (C).

See (Figures 1 and 2)
Kidney Disease Outcomes Quality Initiative (Guideline 13): [143]
There is insufficient evidence to recommend for or against routine prescription of dietary protein restriction for slowing the progression of chronic kidney disease; individual decision-making is recommended, after discussion of risks and benefits (R).

There is insufficient evidence to recommend lipid-lowering therapy for the purpose of slowing the progression of chronic kidney disease (R).

Dietitians Association of Australia: Evidence based practice guidelines for the nutritional management of chronic kidney disease (Figures 3 to 8) [138]
http://daa.asn.au/for-health-professionals/daa-endorsed-practice-guidelines-and-practice-recommendations/

Australian Government - Department of Health and Ageing: National Physical Activity Guidelines for Adults [144]
1. Think of movement as an opportunity, not an inconvenience
- Where any form of movement is seen as an opportunity for improving health, not as a time-wasting inconvenience.

2. Be active every day in as many ways as you can.
- Make a habit of walking or cycling instead of using the car, or do things yourself instead of using labour-saving machines

3. Put together at least 30minutes of moderate to vigorous physical activity on most, preferably all days.

- You can accumulate your 30 minutes (or more) throughout the day by combining a few shorter sessions of activity of around 10 to 15 minutes each.

4. If you can, enjoy some regular vigorous activity for extra health and fitness.

This guideline does not replace guidelines 1 to 3. Rather, it adds an extra level for those who are able, and wish to achieve greater health and fitness benefits

UK Renal Association: No recommendation.

Canadian Society of Nephrology: [145]

Smoking cessation

Smoking cessation should be encouraged to reduce the risk of developing chronic kidney disease and end-stage renal disease, and to reduce the risk of cardiovascular disease (grade D).

Weight reduction

Obese (BMI > 30.0 kg/m2) and overweight (BMI 25.0–29.9 kg/m2) people should be encouraged to reduce their BMI to lower their risk of chronic kidney disease and end-stage renal disease (grade D). Maintenance of a health body weight (BMI 18.5–24.9 kg/m2; waist circumference < 102 cm for men, < 88 cm for women) is recommended to prevent hypertension (grade C) or to reduce blood pressure in those with hypertension (grade B). All overweight people with hypertension should be advised to lose weight (grade B).

Dietary protein control

A protein-controlled diet (0.80–1.0 g/kg/d) is recommended for adults with chronic kidney disease (grade D). Dietary protein restriction of < 0.70 g/kg/day should include careful monitoring of clinical and biochemical markers of nutritional deficiencies (grade D).

Alcohol intake

To reduce blood pressure, alcohol consumption in both normotensive and hypertensive people should be in accordance with Canadian guidelines for low-risk drinking. Healthy adults should limit alcohol consumption to 2 drinks or less per day, and consumption should not exceed 14 standard drinks per week for men and 9 standard drinks per week for women (grade B).

Exercise

People without hypertension (to reduce the possibility of becoming hypertensive) or those with hypertension (to lower their blood pressure) should be encouraged to accumulate 30–60 minutes of moderate-intensity dynamic exercise (walking, jogging, cycling or swimming) 4–7 days per week (grade D). Higher intensities of exercise are no more effective.

Dietary salt intake

To prevent hypertension, a dietary sodium intake of < 100 mmol/day is recommended, in addition to a well-balanced diet (grade B). Patients with hypertension should limit their dietary sodium intake to 65–100 mmol/day (grade B).

European Best Practice Guidelines: No recommendation.

International Guidelines:

National Institute for Clinical Excellence (NICE) [146]

R35 Encourage people with CKD to take exercise, achieve a healthy weight and stop smoking.

R36 Where the clinician in discussion with the patient has decided that dietary intervention to influence progression of CKD is indicated, an appropriately trained professional should discuss the risks and benefits of dietary protein restriction, with particular reference to slowing down the progression of disease versus protein-calorie malnutrition.

R37 Where dietary intervention is agreed this should occur within the context of education, detailed dietary assessment and supervision to ensure malnutrition is prevented.

R38 Offer dietary advice to people with progressive CKD concerning potassium, phosphate, protein, calorie and salt intake when indicated.

Scottish Intercollegiate Guidelines Network (SIGN): [147]

3.7.1 Dietary protein restrictions (<0.8 g/kg/day) are not recommended in patients with early stages of CKD (stages 1-3) (A). In stage 4 CKD, high protein intake (> 1.0 g/kg/day) is not recommended. No evidence was identified to show that phosphate restriction affects the progression of CKD.

3.7.2 For patients with stage 1-4 CKD and hypertension a reduction in sodium <2.4 g/day or <100 mmol/day which is equivalent to <6 g of salt) is recommended as part of a comprehensive

strategy to lower blood pressure and reduce cardiovascular risk (B). Salt substitutes that contain high amounts of potassium salts should not be used in patients with CKD.

3.7.3 In the absence of other recognised medical causes, patients with CKD and consistently raised potassium levels should be managed with the involvement of an appropriately qualified dietitian.

3.8.2 People with CKD who smoke should be advised to stop and referred to an NHS smoking cessation service if they are motivated to quit.

People with CKD with a waist circumference ≥94 cm in men or ≥80 cm in women should be considered for weight management with the involvement of an appropriately qualified dietitian. People with CKD should be encouraged to take regular exercise.

3.10.1 If patients experience a reduction in exercise capacity which impacts on their daily life, they should have access to an appropriately qualified physiotherapist

3.10.5 Nutritional status (height, weight, body mass index and percentage weight loss should be monitored in all patients with CKD stages 3 or higher (D). Patients exhibiting signs of malnutrition (body mass index <20kg/m2 or >30kg/m2 or unintentional weight loss of >10% in six months) should be referred to an appropriately qualified dietitian.

Canadian Hypertension Education Program Recommendations 2010: [148]

For lifestyle modifications to prevent and treat hypertension:

- restrict dietary sodium to 1500 mg (65 mmol) per day in adults 50 years of age or younger, to 1300 mg (57 mmol) per day in adults 51 to 70 years of age, and to 1200 mg (52 mmol) per day in adults older than 70 years of age
- perform 30 min to 60 min of moderate aerobic exercise four to seven days per week; maintain a healthy body weight (body mass index 18.5 kg/m(2) to 24.9 kg/m(2)) and waist circumference (less than 102 cm for men and less than 88 cm for women)
- limit alcohol consumption to no more than 14 standard drinks per week for men or nine standard drinks per week for women
- follow a diet that emphasizes fruits, vegetables and low-fat dairy products, dietary and soluble fibre, whole grains and protein from plant sources, that is low in saturated fat and cholesterol; and consider stress management in selected individuals with hypertension

For the pharmacological management of hypertension treatment thresholds and targets should be predicated on the patient's global atherosclerotic risk, target organ damage and comorbid conditions. Blood pressure should be decreased to less than 140/90 mmHg in all patients, and to less than 130/80 mmHg in patients with diabetes mellitus or chronic kidney disease. Most patients will require more than one agent to achieve these target blood pressures. Antihypertensive therapy should be considered in all adult patients regardless of age (caution should be exercised in elderly patients who are frail). For adults without compelling indications for other agents, considerations for initial therapy should include thiazide diuretics, angiotensin- converting enzyme (ACE) inhibitors (in patients who are not black), long-acting calcium channel blockers (CCBs), angiotensin receptor blockers (ARBs) or beta-blockers (in those younger than 60 years of age). A combination of two first-line agents may also be considered as initial treatment of hypertension if systolic blood pressure is 20 mmHg above target or if diastolic blood pressure is 10 mmHg above target. The combination of ACE inhibitors and ARBs should not be used, unless compelling indications are present to suggest consideration of dual therapy. Agents appropriate for first-line therapy for isolated systolic hypertension include thiazide diuretics, long-acting dihydropyridine CCBs or ARBs. In patients with coronary artery disease, ACE inhibitors, ARBs or beta-blockers are recommended as first-line therapy; in patients with cerebrovascular disease, an ACE inhibitor/diuretic combination is preferred; in patients with proteinuric non-diabetic chronic kidney disease, ACE inhibitors or ARBs (if intolerant to ACE inhibitors) are recommended; and in patients with diabetes mellitus, ACE inhibitors or ARBs (or, in patients without albuminuria, thiazides or dihydropyridine CCBs) are appropriate first-line therapies. In selected high-risk patients in whom combination therapy is being considered, an ACE inhibitor plus a long-acting dihydropyridine CCB is preferable to an ACE inhibitor plus a thiazide diuretic. All hypertensive patients with dyslipidemia should be treated using the thresholds, targets and agents outlined in the Canadian lipid treatment guidelines. Selected patients with hypertension who do not achieve thresholds for statin therapy, but who are otherwise at high risk for cardiovascular events, should nonetheless receive statin therapy. Once blood pressure is controlled, low-dose acetylsalicylic acid therapy should be considered.

SUGGESTIONS FOR FUTURE RESEARCH

1. An RCT of different levels of fluid intake (<3 L/day vs > 3L/day) on CKD progression in patients with stage 1-3 CKD.
2. A study of the impact of moderation of alcohol intake on CKD progression in patients with stage 1-4 CKD).
3. A long-term RCT evaluating the effect of exercise on CKD progression in patients with stage 1-3 CKD.
4. An RCT evaluating the effect of dietary salt restriction on CKD progression in patients with stage 1-3 CKD.
5. An RCT evaluating the effect of bariatric surgery (gastric banding) versus non-surgical intervention on CKD progression in patients with stage 1-3 CKD.
6. A long - term RCT evaluating the effect of healthy eating as per Australian dietary guidelines on CKD progression in adult patients with stage 1-3 CKD. This includes the optimal levels of energy, nutrients (protein, sodium, fat), dietary patterns (fruit and vegetables) and healthy lifestyle (30 min/day) moderate physical activity.
7. An RCT investigating CR-LIPE diets that includes larger sample size and monitors for dietary compliance.
8. A large RCT investigating the effects of exercise on CKD progression, cardiovascular structure and function, body composition, bone mineral metabolism, compliance and safety profile. Methods to optimise adherence for CKD patients should also be evaluated.

CONFLICT OF INTEREST

Maria Chan has no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

David Johnson has a level II b. conflict of interest for receiving speaker honoraria and advisor's fees from several companies related to anaemia, CKD-MBD, hypertension and cardiovascular disease between 2008 and 2012.

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APPENDICES

Table 1. Characteristics of included studies

Study ID	N	Study design	Participants	Follow up	Comments and results
1. Dietary protein restriction					
Klahr et al. (1994) [8]	585 = Study A 255 = Study B	RCT	Patients with low eGFR and aged 18 to 70 years were included in the study. Study A eGFR 25 – 55 mL/min/1.73m^2 and Study B 13 – 24 mL/min/1.73m^2. Patients had to have mean arterial pressure of < 125 mmHg and dietary protein intake ≥ 0.9 g/kg body weight / day	2.2 years	• Study A: patients divided into four groups, combining usual protein and low protein diets with usual and low mean arterial pressure. • Study B: patients were also divided into four groups, combining low protein and very low protein diets with usual and low mean arterial pressure • Study A: the mean decline in the glomerular filtration rate did not differ significantly between the diet groups or between the blood-pressure groups. Although there was a greater decline in the low protein group compared to the usual protein group in the first four months (3.4 vs 1.8 ml/min/4 months). Followed by a slower rate of decline (2.8 vs 3.9 ml/min/year) respectively • Study B: the very-low protein group had a marginally slower decline in the glomerular filtration rate than did the low-protein group (P = 0.07) • In both study groups, patients in the low-blood pressure group had a significantly slower rate of decline in the glomerular filtration rate.
Kopple et al (1997) [49]	585 = Study A 255 = Study B	RCT	Participants in Study A were randomised to usual-protein or low-protein diet. Participants in Study B were randomised to low-protein or very-low-protein diet.	2.2 years	• Study A: the low-protein diet group had significantly lower: energy intakes (males -3.6 kcal/kg/day, females -2.8 kcal/kg/day); body weight (males -5.3kg, females -2.9 kg) and biochemical and nutritional markers • Study B: both men and women had significantly lower mean values for: protein and energy intake, serum transferrin, body weight, percent body fat, arm muscle area and urine creatinine excretion compared to men and women in Study A • Urine creatinine excretion declined approximately 15% to 20% from baseline. In Study A the decline was significantly faster in the low-protein diet group as compared to the usual-protein diet group, both during (P < 0.001) and after (P = 0.013) the first four months of follow-up. In Study B the decline was significantly faster in the very-low-protein diet group as compared to the low-protein diet group during the first four months of follow-up (P < 0.001) but significantly slower after (P < 0.001) the first four months. • Rates of death, hospitalisations and stop points were low and there were no significant differences between diet groups in either study
Hansen et al (2002) [18]	82	RCT	Patients 18 to 60 years old with type I diabetes and diabetic	4 years	• Usual-protein group consumed 1.02 g/kg/day (95% CI: 0.95-1.10) as compared with 0.89 (95%CI: 0.83-0.95) in the low-protein diet group (P =

			nephropathy, were randomised into two groups low-protein diet and a usual-protein diet. 41 = usual-protein diet 41 = low-protein diet		0.005) • Mean declines in GFR in the usual-protein compared with the low-protein diet group were 3.9 mL/min/year (95% CI: 2.7-5.2) and 3.8 (95% CI: 2.8-4.8) respectively. • ESRD or death occurred in 27% of patients on the usual-protein diet compared to 10% on a low-protein diet (log-rank test; P = 0.042) • The adjusted relative risk of ESRD or death was 0.23 (95% CI: 0.07-0.72; P = 0.01)) for patients assigned to a low-protein diet
Pijls et al (2002) [19]	160	RCT	Patients ≤ 79 years of age, with type 2 diabetes mellitus ± microalbuminuria. 63 = experimental group 68 = control group	2.3 years	• At six months, protein intake differed only by 0.08 g/kg/day between the study groups. The difference eventually disappeared. • GFR rate decreased in the experimental group at a 1.6 ± 2.2 mL/min/1.73m2/y lower rate than in the control group (P = 0.5) • Comparison of patients in the experimental group with a decrease in protein intake of at least 0.2g/kg/day, compared with no decrease, showed a small and insignificant effect on GFR • Long-term prevention or delay of renal damage in patients with type 2 diabetes, protein restriction is neither feasible nor efficacious.
Meloni et al (2002) [20]	69	RCT	Nephrology outpatients between 35 and 73 years old. Affected by overt diabetic nephropathy and hypertension. Patients were randomised into two groups: a low-protein diet and a free diet intake	1 year	• There was no significant difference in the decline of glomerular filtration rate between the two groups. • Serum pre-albumin concentration decreased significantly in the low-protein diet group after 9 months, whereas serum albumin decreased after 12 months. • Dietary protein restriction does not seem to delay the progression of renal disease in patients with overt diabetic nephropathy, but it may induce malnutrition. Mean body weight in the low-protein group was 63.4 ± 8.8 kg compared with 60.8 ± 7.3 kg after 12 months; P <0.01.
Meloni et al (2004) [21]	169	RCT	Nephrology outpatients 29 to 73 years old. 89 patients had chronic renal failure, 80 patients had overt diabetic nephropathy. Patients were divided into two groups to receive a low-protein or a free-protein diet	1 year	• There was no significant difference in renal function between the treated and non-treated diabetic patients: mean GFR decline, 5.78 ± 1.5 mL/min/1.73m^2 compared with 6.03 ± 1.3 mL/min/1.73m^2 (P = NS) respectively • Non-diabetic treated patients showed a lower decrease in renal function compared to the non-treated group: GFR 3.47 ± 0.26 mL/min/1.73m^2 compared with 6.05 ± 1.23 mL/min/1.73m^2 (P < 0.001) respectively. • The mean body weight and obesity index decreased significantly in the treated diabetic and non-diabetic patients compared to non-treated patients.
Kasiske et al (1998) [3]	13 RCT n = 1,919 11 non-RCT n = 2,248	Meta-analysis	Effects of dietary protein restriction on the rate of decline of kidney function in patients with diabetic and non-diabetic CKD	N/A	• Dietary protein restriction reduced the rate of decline in eGFR by only 0.53 mL/min/yr (95%CI: 0.08 to 0.98) • The effect of dietary protein restriction was less in randomized vs nonrandomized trials (regression coefficient, -5.2 mL/min/yr; 95% CI: -7.8 to 2.5) and relatively greater among diabetic versus non-diabetic patients

					(5.4 mL/min/yr; 95% CI: 0.3 to 10.5, P < 0.05) • With each additional year of follow-up, there was a trend toward a greater effect (2.1 mL/min/yr; 95% CI: -0.05 to 4.2, P = NS) • Although dietary protein restriction retards the rate of renal function decline, the effect was relatively weak. Also the number of diabetic patients studied was small and the duration of follow-up was short in most trials
Robertson et al (2007) [7]	12 studies	Cochrane review	Nine RCTs and three before and after studies were included	N/A	• The relative risk (RR) of ESRD or death was 0.23 (95%CI: 0.07 to 0.72) for patients assigned to a low protein diet (LPD) • There was a non-significant reduction in the decline of glomerular filtration rate (GFR) of 0.1mL/min/month (95%CI: -0.1 to 0.3) in patients with type 1 diabetes in the LPD group • For type 2 diabetes, one trail showed a small insignificant improvement in the rate of decline of GFR in the LPD group, a second found similar decline in both the intervention and control groups. • One study detected malnutrition in the LPD group
Ikizler et al (1995) [51]	90	Cohort	Patients with chronic renal failure monitored in the Renal Clinic at Vanderbilt University Medical Center	16.5 ± 11.8 months	• The mean dietary protein intake (DPI) was 1.01 ± 0.21 g/kg/day for patients with creatinine clearance (CrCl) > 50 mL/min • DPI decreased to 0.85 ± 0.23 g/kg/day for patients with CrCl 25 – 50 mL/min. • DPI further decreased to 0.70 ± 0.17 g/kg/day for patients with CrCl 10 – 25 mL/min • DPI decreased to 0.54 ± 0.16 g/kg/day for patients with CrCl < 10 mL/min. • This trend was statistically significant (P < 0.001) • A similar trend was seen for serum cholesterol, transferring and total creatinine excretion (all P < 0.01). • Progression of renal failure is associated with a spontaneous decrease in DPI, especially bellow a CrCl of 25 mL/min. • Most nutritional indices in CRF patients worsen as CrCl and DPI decrease.
Knight et al (2003) [52]	1,624	Cohort	Subgroup of women enrolled in the Nurses' Health Study, 42 to 68 years of age.	11 years	• Women with normal renal function (eGFR ≥ 80 mL/min/1.73m2) did not have a significant high protein intake. The change in eGFR was 0.25 mL/min/1.73m2 (95%CI: -0.78 to 1.28) per 10 gram increase in protein intake • In women with mild renal insufficiency (eGFR 55 to 80 mL/min/1.73m2), protein intake was significantly associated with a change in eGFR of -1.69 mL/min/1.73 m2 (95%CI: -2.93 to -0.45) per 10g increase in protein intake. After adjustment of measurement error, the change in eGFR was -7.72 mL/min/1.73m2 (95%CI: -15.52 to 0.08 mL/min/1.73 m2) per 10g increase in protein intake. • High intake of non-dairy animal protein in women with mild renal insufficiency was associated with a significantly greater change in eGFR -1.21 mL/min/1.73m2 (95% CI: -2.34 to -0.33) per 10g increase in non-dairy animal protein intake.

2. Dietary sodium restriction					
Suckling et al (2010) [63]	13 RCTs N=254	Systematic review	Adults (18 years or older) with type 1 or type 2 diabetes. Studies where interventions of low salt were compared to high salt intake.	1 week (mean)	• BP was reduced in both type 1 and type 2 diabetes. • In 56 individuals with type 1 diabetes, salt restriction reduced systolic BP (SBP) by 7.11 mmHg (95%CI: 5.10 to 9.13; P<0.00001) and diastolic BP (DBP) by 3.13 mmHg (95%CI: 1.98 to 4.28; P<0.00001) • In 56 individuals with type 2 diabetes, salt restriction also reduced SBP by 6.90 mmHg (95%CI: 3.95 to 9.84; P<0.00001) and DBP by 2.87 mmHg (95%CI: 1.35 to 4.39; P=0.0002) • There was a non-significant change in GFR of -1.92 mL/min (95%CI: -4.49 to 0.64; P=0.14) • There was a median reduction in urinary sodium of 203 mmol/24 hr in type 1 diabetes and 125 mmol/24hr in type 2 diabetes.
Todd et al (2010) [59]	35	Randomised crossover	Hypertensive participants aged between 20 and 65 years old. All were assigned to low-sodium diet (60 mmol/L) during run-in and then assigned to consume 500 mL of tomato juice A) with 0 mmol Na; B) with 90 mmol Na; or C) with 140 mmol Na. [Total dietary sodium for: A=60mmol/d; B=150mmol/d; C=200mmol/d] Single centre, New Zealand	18 weeks	• There was a mean increase in pulse wave velocity (PWV) of 0.39 m/s (95%CI: 0.18-0.60; P≤0.001) in intervention B compared to intervention A. As well as an increase of 0.35 m/s (95%CI: 0.13-0.57; P≤0.01) in intervention C compared to intervention A. • There was a non-significant decrease of PWV of 0.04 m/s (95%CI: 0.18-0.26) in intervention C compared to intervention B. • For systolic BP - there was a 4.4 mmHg (95%CI: 1.7-7.1; P≤0.01) mean increase in intervention B compared to A; 5.8 mmHg (95%CI: 2.9-8.6; P≤0.001) mean increase in intervention C compared to A; and a non-significant increase of 1.4 mmHg (95%CI:-1.5 to 4.2) in intervention C compared to B. • For diastolic BP – there were significant increases of 2.5 mmHg (95%CI: 0.8-4.2; P≤0.01) and 3.4 mmHg (95%CI: 1.7-5.2; P≤0.001) in interventions B and C respectively, compared to intervention A. There was a non-significant increase of 0.9 mmHg (95%CI: -0.8 to 2.7) in intervention C compared to intervention B.
Pimenta et al (2009) [58]	12	Randomised crossover	Adult patients with resistant hypertension. Randomised to receive a low salt diet (50mmol/24hrs/7days) or a high salt diet (250mmol/24hrs/7days), separated by a 2-week washout period. Single centre, USA.	4 weeks	• Low-salt diet – mean urinary sodium excretion was 46.1 ± 26.8 compared to 252 ± 64.6 mmol/24hrs during the high-salt diet. • Mean office systolic BP was reduced by 22.7mmHg (95%CI: 11.8 - 33.5; P=0.0008) and diastolic BP decreased by 9.1 mmHg (95%CI: 3.1-15.1; P=0.0065) when low-salt was compared to high-salt diet • When compared to high-salt diet, low-salt diet also reduced ambulatory BP: - daytime systolic by 20.7 mmHg (95%CI: 12.4-29.1; P=0.0002) - daytime diastolic by 9.6 mmHg (95%CI: 5.3-14.0; P=0.0005) - night time systolic by 20.3 mmHg (95%CI: 8.3-32.3;P=0.0034) - night time diastolic by 9.9 mmHg (95%CI: 4.8-15.0; P=0.0013) - 24-hour systolic by 20.1 mmHg (95%CI: 12.1-28.1; P=0.0002) - 24-hour diastolic by 9.8 mmHg (95%CI: 5.8-13.8; P=0.0002)
Vogt et al (2008) [62]	34	Randomised cross-over	Patients with stable proteinuria and stable renal function, between	36 weeks	• For all interventions, there was a significant reduction in the proteinuria level when compared to baseline (placebo-HS). Proteinuria decreased by:

		controlled trial	18 and 70 years of age. Patients were randomised to either: Placebo; Losartan (100 mg once daily); or Losartan +HCT (100/25 mg) (hydrochlorothiazide) as well as either a low-sodium (LS) diet (50 mmol sodium/d) or high-sodium (HS) diet (200mmol sodium/d)		22% on the placebo-LS intervention; 30% on Losartan-HS; 55% Losartan-LS; 56% Losartan+HCT-HS; and 70% Losartan+HCT-L; (P<0.05 for all interventions) • BP also decreased in response to the various interventions, however the greatest reduction occurred when all interventions were combined Losartan+HCT-LS
Vedovato et al (2004) [55]	41	Randomised crossover	Type 2 diabetics with and without micro-albuminuria. Recruited from the Diabetes Clinics at the Padova University Hospital and the Bergamo Hospital. Participants were given a low-Na+ (25 mmol) diet and a high-Na+ (250 mmol) diet. [20 participants had microalbuminuria and 21 didn't]	14 days	• Switching from low to high-Na+ diet caused an increase in: blood pressure (7.4 ± 4.7 mmHg; P < 0.001); body weight (1.9 ± 0.4 Kg; P < 0.05) and albuminuria [from 80 (31-183) μg/min to 101(27 – 965) μg/min; P < 0.01) in patients with microalbuminuria. • No changes occurred in patients without microalbuminuria. • Patients with microalbuminuria also had: greater intraglomerular pressure (44 ± 1 mmHg vs 36 ± 1; P <0.001); reduced insulin sensitivity (5.16 ± 49 vs 7.36 ± 0.63 mg/kg/min; P = 0.007) • High salt intake increases blood pressure and albuminuria in Type 2 diabetic patients with microalbuminuria.
Imanishi (2001) [56]	32	Randomised crossover	Type 2 diabetic inpatients at Osaka City General Hospital. 11 patients had normoalbuminuria, 12 had microalbuminuria and 9 had macroalbuminuria. Patients were given a normal-Na+ (~200 mmol/day) diet and a restricted-Na+ (~80 mmol/day) diet.	14 days	• The median sensitivity index and the mean blood pressure were higher in micro- and macroalbuminuric patients than in normoalbuminuric patients. • Urinary albumin was correlated with the sodium sensitivity index but not with blood pressure. • In patients with albuminuria, sodium restriction compared with ordinary sodium intake, decreased albuminuria 36.6 mg/day (95% CI: 23.5-56.5) vs 48.6 (95% CI: 32.3-68.7) mmHg P < 0.02 and decreased blood pressure: systolic BP 125 ± 5 mmHg vs 136 ± 9 mmHg (P < 0.001), diastolic BP 74 ± 3 mmHg vs 80 ± 5 mmHg (P = 0.0021)
Swift et al (2005) [57]	47 (40 completed the study)	Randomised crossover	Black (African or African-Caribbean) non-diabetic hypertensive participants. Participants were randomised to slow sodium tablets or placebo	8 weeks	• Urinary sodium excretion decreased from 167±73 to 89±52 mmol/24 hrs (P < 0.001) on slow sodium (10 g salt/day) compared to placebo (5 g salt/day) tablets • Blood pressure dropped from 159/101±13/8 to 151/98±13/8 mmHg (P < 0.01) • Protein excretion decreased from 93±48 mg to 75±30 mg per 24 hrs (P < 0.008) • The mean urine protein to creatinine ratio decreased from 6.6±3.2 to 5.7±2.2 mg/mmol (P = 0.03) • There was no significant relationship between the change in urine protein excretion and the change in systolic BP (r = 0.07; P=0.70) or change in diastolic BP (r-0.19; P = 0.26) with salt reduction. • There was a significant correlation between the change in urinary protein excretion and the change in urine sodium excretion (r = 0.53; P = 0.001) • It is recommended that all black individuals with raised blood pressure

					reduce their salt intake to ≤ 5 g per day
Jones-Burton et al (2006) [60]	16 studies	Systematic review	Search was conducted from January 1st 1966 to 31st August, 2004	N/A	• Study methodologies were extremely heterogeneous • Conclusions include: variations in salt consumption are directly correlated with albuminuria; increase in salt intake is associated with worsening albuminuria and with an acute increase in glomerular filtration rate; reduction in salt consumption may slow the rate of renal function loss • There was no evidence of a detrimental effect of reduced salt intake • Dietary salt restriction should be considered in patients with chronic kidney disease
Sacks et al (2001) [61]	412	RCT	Participants ≥22 years old, with blood pressure > 120/80 mmHg. Participants were assigned to either a control diet or the DASH diet. Diets were prepared at three sodium levels: high (150 mmol/day), intermediate (100 mmol/day) and low (50 mmol/day). (September 1997 to November 1999, Multicentre, USA)	90 days	• Reduction in sodium intake from high to intermediate level, reduced the systolic blood pressure by 2.1 mmHg (P < 0.001) during the control diet and by 1.3 mmHg (P = 0.03) during the DASH diet. • Reducing the sodium intake from intermediate to low level caused further reductions in systolic BP of 4.6 mmHg (P < 0.001) for the control diet and 1.7 mmHg (P < 0.01) for the DASH diet. • As compared with the control diet with a high sodium level, the DASH diet with a low sodium level led to a mean systolic blood pressure that was 7.1 mmHg lower in participants without hypertension, and 11.5 mmHg lower in participants with hypertension • The reduction of sodium intake and the DASH diet, both lower blood pressure considerably, with greater effects in combination than individually.
3. Dietary phosphate restriction					
Barsotti et al (1984) [70]	55	Cohort	Patients with renal failure, aged between 25 and 77 years old. Patients were given a diet low in phosphate and nitrogen (LPLND) (Group 1: 6.5 mg/kg/day) or a conventional diet (CLND) higher in phosphate and low in nitrogen (Group 2: 12 mg/kg/day)	12.4 months	• In both groups, the rate of decline of creatinine clearance decreased when patients changed from a free mixed diet to the controlled diet, especially with the lower phosphate group • Patients in the higher phosphate diet (Group 2) had higher mean levels of serum phosphate (4.96±0.77) mg/100ml compared with the low phosphorus diet (3.99±0.65) mg/100 ml (P < 0.005); higher urinary output of phosphate per unit of creatinine clearance (628.8±116.7) mg/24 hr compared to (362.3±89.5) mg/24hr; as well as elevated mean levels of serum iPTH (0.65±0.92) ng/100ml compared to (0.18±0.25) ng/100ml. • Patients in Group 1 had a slower rate of renal functional deterioration compared with Group 2 patients (-0.07±0.38 vs -0.53±0.40 ml/min/month)
Russo et al (2007) [75]	90	RCT	Participants > 18 years old, with stage 3 – 5 chronic kidney disease. Patients assigned to three groups: low-phosphate diet alone; low-phosphate diet + calcium carbonate; low-phosphate diet +	2 years	• The total calcium score (TCS) increased significantly in patients on the low-phosphorus diet alone, to a lesser extent in calcium carbonate-treated patients, and not at all in sevelamer-treated patients. • The final TCS was significantly greater than the initial TCS in controls (369 ±115 [mean±s.e.] vs 547 ± 175; P < 0.001) and in calcium-treated subjects (340 ±38 vs 473 ± 69; P < 0.001); however the final TCS was not significantly different from the initial TCS in subjects receiving sevelamer

			sevelamer		(415 ± 153 vs 453 ± 127; NS) • Annualised progression of TCS was 205 ±82 in controls, 178 ±40 in calcium carbonate patients, and 36 ±32 in sevelamer patients. • Progression of coronary calcification paralleled that of the calcium score. • Sevelamer should not be restricted to dialysis patients
5. Polyphenol-enriched diets					
Facchini & Saylor (2003) [76]	191	RCT	Participants with Type 2 diabetes were randomised to either a carbohydrate-restricted, low-iron-available, polyphenol-enriched (CR-LIPE) diet or standard protein restriction	3.9 ± 1.8 years	• Serum creatinine doubled in 19 (21%) participants in the CR-LIPE diet and in 31 (39%) of control subjects (P < 0.01) • RRT or death occurred in 18 (20%) of patients on the CR=LIPE diet and in 31 (39%) of control patients (P < 0.01) • CR-LIPE was 40 – 50% more effective than standard protein restriction in improving renal and overall survival rates
6. Dietary caloric restriction					
Morales et al (2003) [77]	30	RCT	Obese patients with either diabetic or non-diabetic proteinuric nephropathy. Patients were assigned to either a low-calorie normoproteinic diet or maintain their usual dietary intake	5 months	• There was a significant decrease in body weight and BMI in patients in the diet group, but a significant increase for patients in the control group (P < 0.05, between-group comparison) • Proteinuria decreased in the diet group by 31.2% ± 37% (from protein of 2.8 ± 1.4 to 1.9 ± 1.4 g/24hr; P < 0.005), but it tended to increase in the control group (3.0 ± 2.2 to 3.5 ± 2.1 g/24 hr; P = NS) • Serum triglyceride levels remained stable in the diet group and tended to increase in the control group (between-group comparison, P < 0.05) • Changes in renal function did not differ significantly between the groups, but there was a significant worsening in the control group (from 61.8 ± 22.1 to 56 ± 19.9 mL/min/1.73m^2; P < 0.05)
Saiki et al (2005) [78]	22	Cohort	Obese patients with diabetic nephropathy. Patients put on a low-calorie, normal-protein diet supplemented with formula diet	4 weeks	• Mean body weight decreased by 6.2±3.0 kg. • There was a significant decrease in 1. systolic blood pressure (from 126.5±14.2 to 119.0±13.0 mmHg; P < 0.05) 2. serum creatinine (from 172.4±57.5 to 130.8±46.9 µmol/l; P < 0.0001) 3. blood urea nitrogen (from 11.5±5.8 to 9.9±5.8 mmol/L; P < 0.005) 4. urinary protein (from 3.27±2.63 to 1.50±1.28 g/day; P < 0.0001) • There was no significant change in creatinine clearance (0.68±0.29 to 0.77±0.24 mL/sec/1.73m^2; P = NS) • Changes in serum creatinine and in urinary protein, correlated with changes in body weight (r = 0.62 and 0.49, respectively) and changes in visceral fat area (r = 0.58 and 0.58, respectively)
Solerte et al (1989) [79]	24	Cohort	Obese patients with Type 1 and Type 2 diabetes and with overt nephropathy. Participants had their diet changed to a hypocaloric	1 year	• There was a significant reduction in: body weight (BMI from 33±1.6 to 26±1.8 kg/m^2; P < 0.001) and blood pressure levels (P < 0.002) • There was a significant decrease of proteinuria (from 1280±511 to 623±307 mg/day; P < 0.01) and albuminuria (from 723±388 to 492±170 µg/min; P <

			diet		0.01) • An improvement of GFR (from 66±13 to 81±11 mL/min/1.73m^2; P < 0.01) and creatinine clearance (from 79±14 to 91±13 mL/min; P < 0.01) were evident at the end of the study
Navaneethan et al (2009) [80]	13 studies	Systematic review	Searched studies that examined various surgical and nonsurgical interventions (diet, exercise, and/or anti-obesity agents) in adult patients with CKD	N/A	• In studies with non-surgical interventions, the body mass index (BMI) decreased significantly (weighted mean difference [WMD] -3.67 kg/m2; 95% CI: -6.56 to -0.78) • Decrease in BMI was associated with a significant decrease in proteinuria (WMD -1.31g/day; 95% CI: -2.11 to -0.51) and systolic BP with no further decrease in GFR during a mean follow-up of 7.4 months. • In morbidly obese individuals (BMI >40 kg/m^2) with glomerular hyper filtration (GFR >125 mL/min), surgical interventions decreased BMI, which caused a decrease in GFR (WMD -25.56 mL/min; 95% CI: -36.23 to -14.89), albuminuria and systolic BP
Navaneethan & Yehnert (2009) [87]	25	Cohort	Patients with stage 3 CKD (GFR 30 – 59 mL/min/1.73m^2) who had undergone bariatric surgery	2 years	• Body mass index (BMI) decreased (from 49.8±7.5 to 34.5±5.9 kg/m^2; P < 0.001) • Systolic blood pressure decreased from 133±13 to 128±17 mmHg; P < 0.01) • Mean GFR improved from 47.9±10.2 to 61.6±16.7 mL/min/1.73m^2, (P < 0.001)
Afshinnia et al (2010)[95]	5 RCTs 8 non-RCTs (n=522)	Systematic review	Studies looking at urinary protein among obese or overweight adults before and after weight loss interventions.	NA	• Weight loss interventions were associated with decreased proteinuria by 1.7g (95%CI: 0.7-2.6g; P<0.05), 55% decrease from baseline (95%CI: 23% to 87%); and decreased microalbuminuria by 14mg (95%CI: 11-17mg, P<0.05), 52% decrease from baseline (95%CI: 40% to 64%) • Meta-regression analysis showed that each 1kg weight loss was associated with a decrease in proteinuria of 110mg (95%CI: 60-160mg; P<0.001), representing a 4% decrease (95%CI: 2% to 5%); and 1.1mg (95%CI: 0.5-2.4mg; P=0.01) decrease in microalbuminuria, also a 4% decrease from baseline (95%CI: 2% to 9%) • Surgical interventions decreased GFR or creatinine clearance by 23.7ml/min (95%CI: 11.4-36.2), a 17% decrease from baseline (95%CI: 8% to 26%) • There was significant trial heterogeneity.
7. Physical exercise					
Balakrishnan et al (2010) [101]	23	RCT	Adult patients with CKD stages 3 and 4 were randomised to either a resistance exercise training or attention-control group. All participants followed a low-protein diet (0.6 g/kg/d). single centre,	12 weeks	• Skeletal muscle mitochondrial DNA copy number increased in the intervention group: median (IQR) 13,125 (9904) at baseline and 14,099 (10,725) at 12 weeks; whereas it decreased in the attention-control group from 14, 762 (8577) to 12,094 (6884) at 12 weeks. • The mean difference in mtDNA copy number were +1306 (13,306), P=0.22 and -3,747 (15,467), P=0.04 in the intervention and control groups, respectively.

Leehey et al (2009) [100]	13	RCT (pilot)	Adult patients with obesity (BMI >30), type II diabetes and stage 2-4 CKD with persistent proteinuria. Participants were randomised to an exercise or control group. Single centre, USA	24 weeks	• There were no differences in proteinuria, BP, GFR, haemoglobin, HbA1c, serum lipids, or C-reactive protein between the two groups.
Castaneda et al (2004) [99]	26	RCT	Adults older than 50 years of age with moderately severe chronic kidney disease (median GFR 27.5 mL/min/1.73m2), not on dialysis. Participants were randomised to a low-protein diet alone (0.6 g/kg/day - control) or to a low-protein diet plus resistance training (experimental)	12 weeks	• Serum C-reactive protein levels decreased in subjects undergoing resistance training (-1.7mg/L) compared with controls (1.5mg/L; P=0.05) • Serum interleukin-6 levels were also reduced in the resistance training group compared to the control group (-4.2 vs 2.3 pg/mL; P=0.01), respectively. • Muscle strength increased in the intervention group compared to the control (28% ± 14% vs -13% ± 22%; P=0.001), respectively. • Type I and type II muscle fibre cross-sectional areas increased in the intervention group compared to the control group: type I (24% ± 31% vs -14% ± 34%), type II (22% ± 41% vs -13%±18%), P<0.05.
Castaneda et al (2001) [98]	26	RCT	Patients > 50 years old, with moderate renal insufficiency, were assigned to a low-protein diet plus resistance training or a low-protein diet plus sham exercise. (Boston, Massachusetts)	12 weeks	• Total body potassium and type I and II muscle-fibre cross-sectional areas increased in patients in the resistance-training group by a (mean±S.D) 4±8%, 24±31%, 22±29% respectively, compared to those with the sham exercise. • Improvement in muscle strength was significantly greater with resistance training (32±14%) than without (-13±20%), P < 0.001 • GFR increased with resistance training and decreased with sham exercise (1.18 vs -1.62 mL/min/1.73m2; P = 0.048)
Eidemak et al (1997) [96]	30	RCT	Non-diabetic patients with moderate progressive chronic renal failure, were assigned to an exercise routine or to control	20 months	• Median maximal work capacity increased significantly in the exercise group but not in the control group • The median loss of GFR was -0.27 (0.57 to -1.31) mL/min/month (P = NS) in the exercise group, and -0.28 (0.18 to -0.93) mL/min/month (P = NS) in the control group • Thus physical exercise had no effect on progression of renal disease
Boyce et al (1997) [97]	16	Cohort	Participants with chronic renal failure not yet on dialysis underwent exercise training	4	• Exercise training improved aerobic capacity, muscular strength and blood pressure • Resting systolic and diastolic blood pressures decreased significantly from baseline (BL) after the exercise training (ET) (146 ±15.7 / 87 ± 9 mmHg to 124 ± 17.5/78 ± 9.5 mmHg, P<0.02) but increased significantly after detraining (DT) (139 ± 14.7 mmHg and 87 ± 9.9 mmHg, P < 0.01) • GFR (measured by creatinine clearance) continued to decrease from 25.3 ± 12.0 mL/min at baseline to 21.8 mL/min after exercise training
Heiwe et al (2011)[102]	45 studies (32 in meta-analysis)	Systematic review	Included RCTs recruiting adults with CKD or kidney transplant recipients undergoing physical exercise intervention for	NA	• Regular exercise significantly improved: physical fitness standard mean difference (SMD) -0.56 (95%CI: -0.70 to -0.42; P<0.00001) 24 studies n=847; walking capacity SMD -0.36 (95%CI: -0.65 to -0.06; P=0.02) 7 studies n=191; resting diastolic blood pressure MD 2.32 mmHg (95%CI: 0.59 to 4.05; P=0.009) 11 studies, n=419; resting systolic blood pressure

					MD 6.08 mmHg (95%CI: 2.15 to 10.12) 9 studies, n=347; heart rate MD 6 bpm (95%CI: 10 to 2; P=0.002) 11 studies, n=229; nutritional parameters and health-related quality of life also improved. • 17%, 33% and 49% of studies had low, moderate and high risk of bias, respectively.
9. Alcohol intake					
White et al (2009) [118]	6,259	Longitudinal survey	Participants were ≥ 25 years of age without a history of alcohol dependence.	5 years	• Heavy alcohol intake ≥ 30 g/day was associated with an increased risk of albuminuria after adjustment for age, sex and baseline kidney function (OR = 1.59, 95% CI: 1.07-2.36). However, it reduced the risk of de novo eGFR< 60mL/min/1.73m2 (OR = 0.59, 95% CI: 0.37-0.95) compared to alcohol consumption <10 g/day. • Moderate-heavy alcohol consumption may be an important modifiable risk factor for albuminuria in the general population. •
10. Carbonated beverages					
Saldana et al (2007) [130]	932	Cohort	Participants > 30 years old with newly diagnosed chronic kidney disease and community controls. (North Carolina 1980 – 1982)	2 years	• Drinking 2 or more colas per day was associated with increased risk of CKD (adj odds ratio, 2.3; 95% CI: 1.4 to 3.7) • Results were the same for regular colas and artificially sweetened colas (2.1; 95% CI: 1.3-3.4) and (2.1; 95% CI: 0.7- 6.3) respectively • Non-cola carbonated beverages, were not associated with CKD (0.94; 95% CI: 0.4-2.2)
Bomback et al (2010)[131]	15,745	Cross-sectional	Patients taking part in the Atherosclerosis Risk in Communities Study completed a questionnaire and serum urate and creatinine were measured. Multicentre, USA	3 and 9 years	• Drinking more than one sugar-sweetened soda per day was not associated with increased risk of incident hyperuricaemia OR 1.17 (95%CI: 0.95 to 1.43; P=0.1;) nor was it associated with an increased risk of developing kidney disease. OR 0.82 (95%CI: 0.59 to 1.16; P=0.3) • The odds of hyperuricaemia significantly rose with increasing soda intake. • The odds ratio for CKD increased significantly among those who drank >1 soda per day, OR 1.50 (95%CI:0.95 to 2.37; P=0.08) and had hyperuricaemia compared to those without hyperuricaemia OR 0.76 (95%CI: 0.23 to 2.45; P=0.6) • Only participants with uric acid levels of ≥9.0 mg/dl at the first visit, showed an increased odds of developing CKD if they drank >1 soda/day, OR 3.90 (95%CI: 1.55 to 9.82)
11. Fluid intake					
Strippoli et al (2010) [135]	7,162	Validated two cross-sectional studies	Participants > 50 years old, living in the Blue Mountains region, Australia.	N/A	• CKD was present in 12.4-23.5% of men and in 14.9-28.7% of women. • Participants who drank more than 3.2 L/day had a significantly lower risk of CKD (OR 0.5; 95% CI: 0.32-0.77; P for trend = 0.003)
12. Nutritional management by dietitians					
Slinin et al (2011) [136]	156,440	Retrospective cohort analysis	Patients (> 20 years of age) who commenced haemodialysis between June 2005 and May 2007 and who received	2 yrs	• 88% of patients received no pre-dialysis dietitian care; 9% received it for ≤12months; and 3% received it for >12months before commencing dialysis. • 97% of patients who received >12months of predialysis dietitian care also received >12months nephrologist care.

			predialysis dietitian care as reported on the Centers for Medicare & Medicaid Services Medical Evidence Report. USA		• Pre-dialysis dietitian care was associated independently with higher albumin (P<0.001) and lower total cholesterol levels (P=0.002) at dialysis therapy start. • Pre-dialysis dietitian care for 0 – 12 months was associated with lower weight (P<0.001) and BMI (P=0.04); pre-dialysis dietitian care for >12months was associated with higher weight (P=0.005), but not BMI (P=0.2). • In the second tertile of propensity scores, there was a 19% relative risk reduction for death in patients with >12months of dietitian care (Hazard ratio [HR] 0.81; 95%CI: 0.71 to 0.93; P=0.002) compared to no dietitian care. This was not evident in the first or third tertiles: (HR 1.16; 95%CI: 0.44 to 3.09; P=0.8) and (HR 0.93; 95%CI: 0.86 to 1.01; P=0.1), respectively. • Predialysis dietitian care for <12 months was not associated with mortality in any of the 3 propensity score strata.
Campbell et al (2009) [137]	65	Retrospective observational study	Adult patients on maintenance haemodialysis. A dietary interview was conducted every 6 months and outcomes assessed annually. Multicentre, Australia.	2 yrs	• The proportion of patients with malnutrition decreased from 14% at baseline to 3% (P=0.06) after 2 years. • There was a significant decrease in serum phosphate, mean (SD) 1.8±0.5 mmol/L to 1.5±0.5 mmol/L, P=0.004 • The proportion of patients with ideal protein and energy intake increased from 30% to 48% (P=0.02) and 10% to 20% respectively (P=0.001)
13. Fruit and vegetables					
Goraya et al (2012)[139]	199 (n=79, CKD 1; n=120, CKD 2)	Non-randomised controlled trial	Adult patients with stage 1 and 2 CKD due to hypertensive nephropathy. Each group of patients (CKD1 and CKD 2) were divided into three groups: time control, sodium-bicarbonate ($NaHCO_3$) and fruit and vegetables (F+V). Single centre, Texas, USA	30 days	• Net urinary albumin (Ualb) did not differ significantly amongst the three groups in the CKD 1 group (P = 0.201). • There were significant reduction in the Ualb level for CKD 2 $NaHCO_3$ group (-14.4 ± 22.2 mg/g Cr, P<0.001) and CKD 2 F+V group (-34.3 ± 46.9 mg/g Cr, P<0.001) each compared to the control group at zero time. • The urine N-acetyl β-D-glucosaminidase (UNAG) excretion levels pre-and-post intervention were not different in the CKD 1 group (P=0.99). However in the CKD 2 groups, the UNAG level increased in the time-control group (0.062 ± 0.136 U/g Cr, P = 0.006), but significantly decreased in both the CKD 2 $NaHCO_3$ and F=V groups (-0.088 ± 0.134 U/g Cr, P<0.001) and (-0.08 ± 0.08 U/g Cr. P<0.01) respectively.
14. Mediterranean diet					
Mekki et al (2010)[140]	40 (n=20, intervention; n=20, control)	RCT	Adult patients with chronic renal failure (eGFR 60-89 mL/min) and dyslipidaemia. Patients were randomised into two groups: Intervention – KDOQI nutritional advice + Mediterranean Diet Control – KDOQI nutritional advice only. Single centre, Algeria	3 months	• The triglyceride level decreased by 26% in the intervention group compared to the control group at 90 days (T3), and by 9% compared to baseline (P<0.05) • Total cholesterol (TC) decreased by 14% at 60 days (T2) and by 35% at T3, in the intervention group compared to the control (P<0.05). TC levels were lower than at baseline (P<0.05) • Low-density lipoprotein-cholesterol were also lower in the intervention group compared to the control at T2 and T3 (P<0.05). The T3 values were significantly lower than at baseline (P<0.01) • TC/High-density lipoprotein-cholesterol ratio was reduced at T1 (30 days), T2 and T3 in the intervention group versus control (P<0.05)
15. Dietary fibre					

Krishnamurthy et al (2012)[141]	14,543	Analysis of cross sectional survey	Dietary fibre data from adult participants in the National Health and Nutrition Examination Survey III	NA	• For every 10 g/gay increase in total fibre intake, the odds of elevated serum C-reactive protein levels decreased by 11% in those without and by 38% in those with kidney disease. • For each 10 g/day of fibre the odds ratio for serum CRP was: OR 0.88 (95%CI: 0.81 – 0.96, for total fibre); OR 0.86 (0.77 – 0.96, for insoluble fibre); and OR 0.69 (95%CI: 0.54 – 0.87, for soluble fibre) for the entire cohort. This association was stronger in participants with kidney disease than those without (interaction p-values: 0.002 for total fibre, 0.008 for soluble fibre and 0.005 for insoluble fibre. • Total and insoluble fibre intake were inversely associated to mortality in those with kidney disease; P=0.006 (total fibre), P=0.004 (insoluble fibre) and P=0.09 (soluble fibre). This association was not evident in the non-CKD group. • For each 10 g/day increase of fibre, the hazard ratio for mortality was: HR 0.83 (95%CI: 0.73 – 0.94, for total fibre); HR 0.77 (95%CI: 0.65 – 0.91, for insoluble fibre); and HR 0.67 (95%CI: 0.42 – 1.04, for soluble fibre)

Table 1a. Characteristics of included randomised trials

Study ID (author, year)	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Follow up (months)	Comments
Dietary protein restriction								
Klahr et al. (1994) [8] and Kopple et al (1997) [49]	585 = Study A 255 = Study B	Randomised controlled clinical trial	15 centres, US	Patients with eGFR 25 to 55 ml/min/1.73m^2 were assigned to Study A and patients with eGFR 13 to 24 ml/min/1.73m^2 were assigned to Study B	Study A Low-protein diet Study B Very-low-protein diet	Study A Usual-protein diet Study B Low-protein diet	26.4	
Hansen et al (2002) [18]	82	Randomised controlled clinical trial	Single centre, Denmark	Participants with type I diabetes	Low-protein diet	Usual-protein diet	48	
Piljs et al (2002) [19]	160	Randomised controlled clinical trial	Single centre, Amsterdam	Participants with type 2 diabetes	Protein-restricted diet	Usual protein guidelines for diabetics	28	
Meloni et al (2002) [20]	69	Randomised controlled clinical trial	Single centre, Italy	Participants with type 1 and 2 diabetes affected with diabetic nephropathy and hypertension	Low-protein diet	Free-protein diet	12	
Meloni et al (2004) [21]	169	Randomised controlled clinical trial	Single centre, Italy	Patients with non-diabetic nephropathy and patients with diabetic nephropathy [89 diabetic & 80 non-diabetic patients]	Low-protein diet	Free-protein diet	12	4 arm study, diabetic and non-diabetic patients were randomised to low-protein and free-protein diet
Dietary sodium restriction								
Swift et al (2005) [57]	47	Randomised cross-over trial	Single centre, UK	Non-diabetic black hypertensive patients	Slow-sodium tablets	Placebo	1	
Sacks et al (2001) [61]	412	Randomised controlled clinical trial	Multicentre, US	African-American participants with and without hypertension (systolic BP 120 – 159 mmHg & diastolic 80 – 95 mmHg))	DASH (dietary approaches to stop hypertension) diet	Control diet (typical of intake in the US)	3	Within each diet participants ate foods with high, moderate and low sodium levels
Dietary phosphate restriction								
Russo et al (2007) [75]	90	Randomised controlled clinical trial	Single centre, Italy	Participants with stage 3-5 chronic kidney disease diagnosed with coronary artery calcification	Low-phosphorus diet with either calcium carbonate or sevelamer	Low-phosphorus diet	24	3 arm study

Polyphenol-enriched diets								
Facchini & Saylor (2003) [76]	191	Randomised controlled clinical trial	Single centre, US	Type 2 diabetic patients	CR-LIPE (carbohydrate-restricted low-iron-available polyphenol-enriched diet	Standard protein restriction	46.8	
Dietary caloric restriction								
Morales et al (2003) [77]	30	Randomised controlled clinical trial	Single centre, Spain	Overweight patients with diabetic and non-diabetic nephropathy	Low-calorie normal protein diet	Usual dietary intake	5	
Physical exercise								
Eidemak et al (1997) [96]	30	Randomised controlled clinical trial	Single centre, Denmark	Participants with moderate progressive chronic renal failure	Exercise training	No exercise training	20	
Castaneda et al (2001) [98]	26	Randomised controlled clinical trial	Single centre, US	Participants with moderate chronic renal failure	Low-protein diet + resistance training	Low-protein diet + sham exercises	3	

Table 2a. Methodological quality of randomised trials

Study ID (author, year)	Method of allocation concealment *	Blinding			Intention-to-treat analysis †	Loss to follow up (%)	Comments ‡
		(participants)	(investigators)	(outcome assessors)			
Dietary protein restriction							
Klahr et al. (1994) [8] and Kopple et al (1997) [49]	Not specified	No	No	No	Yes	Unclear	–
Hansen et al (2002) [18]	Not specified	No	No	No	Yes	No	_
Piljs et al (2002) [19]	Third party	No	Yes	Yes	No	18.1	_
Meloni et al (2002) [20]	Not specified	No	No	No	Yes	Unclear	_
Meloni et al (2004) [21]	Not specified	No	No	No	Yes	Unclear	_
Dietary sodium restriction							
Swift et al (2005) [57]	Not specified	Yes	Yes	No	No	13	_
Sacks et al (2001) [61]	Not specified	No	No	Yes	Yes	Unclear	_
Dietary phosphate restriction							
Russo et al (2007) [75]	Not specified	No	No	No	No	6.7	_
Polyphenol-enriched diets							
Facchini & Saylor (2003) [76]	Not specified	No	Yes	No	No	11	_
Dietary caloric restriction							
Morales et al (2003) [77]	Not specified	No	No	No	Yes	No	_
Physical exercise							
Eidemak et al (1997) [96]	Not specified	No	No	No	Yes	Unclear	_
Castaneda et al (2001) [98]	Not specified	No	No	Yes	Yes	No	_

* Choose between: central; third party (e.g. pharmacy); sequentially labelled opaque sealed envelopes; alternation; not specified.
† Choose between: yes; no; unclear.
‡ Quality score – "How successfully do you think the study minimised bias?" Choose between: very well (+); okay (Ø); poorly (–).

Table 3a. Results and quality rating for dichotomous outcomes

Outcomes	Study ID (author, year)	Intervention group (no. of patients with events/no. of patients exposed)	Control group (no. of patients with events/no. of patients exposed)	Relative risk (RR) [95% CI]	Risk difference (RD) [95% CI]	Importance**
Dietary protein restriction						
Death	Kopple et al (1997) [49]	Study A = 2/291	Study A = 9/294	0.22 (0.05, 1.03)	-0.02 (-0.05, -0.00)	Critical
		Study B = 4/126	Study B = 1/129	4.10 (0.46, 36.14)	0.02 (-0.01, 0.06)	
	Hansen et al (2002) [18]	2 / 41	7 / 41	0.29 (0.06, 1.29)	-0.12 (-0.25, 0.01)	
ESRD	Hansen et al (2002) [18]	2 / 41	4 / 41	0.50 (0.10, 2.58)	-0.05 (-0.16, 0.06)	Important
Polyphenol-enriched diets						
Death	Facchini & Saylor (2003) [76]	8 / 91	14 / 79	0.5 (0.22, 1.12)	-0.09 (-0.19, 0.01)	Critical
ESRD	Facchini & Saylor (2003) [76]	10 / 91	17 / 79	0.51 (0.25, 1.05)	-0.11 (-0.22, 0.01)	Important

- Methodological quality, consistency across studies and directness of the evidence (generalisability/applicability).

****** The GRADE system uses the following 3 categories to rank the importance of end points:

- critical for decision making
- important but not critical for decision making
- not important for decision making (of lower importance to patients)

*NA = not available

Table 3b. Results and quality rating for continuous outcomes

Outcomes	Study ID (author, year)	Intervention group (mean [SD])	Control group (mean [SD])	Difference in means (95% CI)	Importance**
Dietary protein restriction					
Urine creatinine excretion	Kopple et al (1997) [49]	Study A (men) 1479 (261)	Study A (men) 1698 (316)	Study A (men) -219.0 (-279.29, -158.71)	Important
		Study A (women) 970 (173)	Study A (women) 1108 (231)	Study A (women) -138.0 (-192.33, -83.67)	
		Study B (men) 1185 (244)	Study B (men) 1307 (261)	Study B (men) 148.0 (66.64, 229.36)	
		Study B (women) 789 (165)	Study B (women) 912 (153)	Study B (women) -123.0 (-184.44, -61.56)	
Decline in eGFR (mL/min/1.73m^2)	Pijls et al (2002) [19]	4.8 (12)	6.4 (14)	-1.60 (-6.06, 2.86)	Important
	Meloni et al (2002) [20]	6.15 (1.61)	6.26 (1.84)	-0.11 (-0.93, 0.71)	
	Meloni et al (2004) [21]	Diabetic 5.78 (1.5)	Diabetic 6.03 (1.3)	Diabetic -0.25 (-0.87, 0.37)	
		Non-diabetic 3.47 (0.26)	Non-diabetic 6.05 (1.23)	Non-diabetic -2.58(-2.95, -2.21)	
Dietary sodium restriction					
Urinary sodium excretion (mmol/24hr)	Swift et al (2005) [57]	167 (73)	89 (52)	78.0 (50.22, 105.78)	Important
Urine protein excretion (mg/24hr)	Swift et al (2005) [57]	93 (48)	75 (30)	18.0 (0.46, 35.54)	Important
Systolic blood pressure (mmHg)	Swift et al (2005) [57]	159 (13)	151 (13)	8.0 (2.30, 13.70)	Important
	Sacks et al (2001) [61]	*NA	NA	NA	
Diastolic blood pressure (mmHg)	Swift et al (2005) [57]	101 (8)	98 (8)	3.0 (-0.51, 6.51)	important
	Sacks et al (2001) [61]	*NA	NA	NA	
Dietary phosphate restriction					
Total calcium scores	Russo et al (2007) [75]	*NA	NA	NA	Not important
Dietary caloric restriction					
Creatinine clearance (mL/min/1.73m2)	Morales et al (2003) [77]	67 (34.1)	56 (19.9)	11.00 (-8.38, 30.38)	Important
Proteinuria (g/24hr)	Morales et al (2003) [77]	1.9 (1.4)	3.5 (2.1)	-1.60 (-3.04, -0.16)	Important
Physical exercise					
GFR (ml/min/1.73m^2)	Eidemak et al (1997) [96]	*NA	NA	NA	Important
	Castaneda et al (2001) [98]	*NA	NA	NA	

- Methodological quality, consistency across studies and directness of the evidence (generalisability/applicability).

** The GRADE system uses the following 3 categories to rank the importance of end points:

- critical for decision making
- important but not critical for decision making
- not important for decision making (of lower importance to patients)

*NA = not available

Figure 1

Table 83. Macronutrient Composition and Mineral Content of the Dietary Approaches to Stop Hypertension (DASH) Diet Recommended by JNC 7, with Modification for Stages 3-4 of CKD

Nutrient	Stage of CKD	
	Stages 1-4	
Sodium (g/d)*	<2.4	
Total Fat (% of calories)	<30	
Saturated Fat (% of calories)	<10	
Cholesterol (mg/d)	<200	
Carbohydrate (% of calories)**	50-60	
	Stages 1-2	Stages 3-4
Protein (g/kg/d, % of calories)	1.4 (~18)	0.6-0.8 (~10)
Phosphorus (g/d)	1.7	0.8-1.0
Potassium (g/d)	>4	2-4

*Not recommended for patients with "salt-wasting."
**Adjust so total calories from protein, fat and carbohydrate is 100%.

National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. Am J Kidney Dis. 2004; 43 (suppl1): S1-290

Figure 2

Table 84. Other Lifestyle Modifications Recommended by JNC 7

Lifestyle Component	Recommendation
Weight maintenance if BMI <25 kg/m^2	Balanced diet to maintain desirable body weight
Weight loss if overweight or obese (BMI ≥25 kg/m^2)	Calorie restricted, balanced diet
Exercise and physical activity	Moderate intensity for 30 minutes/day, most days of the week
Moderation of alcohol intake	≤2 drinks/day (men) ≤1 drink/day (women)
Smoking cessation	Counseling, nicotine supplementation

National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. Am J Kidney Dis. 2004; 43 (suppl1): S1-290

Figure 3

Table 2. Stages of chronic kidney disease

Stage	*Description*	*GFR (mL/min/1.73 m^2)*
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

Figure 4

Table 3. Summary of recommendations for the nutritional management of chronic kidney disease

CKD	*Stage 3 (GFR 30–59)*[4]
Point of referral	GFR <60 mL/min[2,4]
Time for consultation	45–60 mins[9]
Biochemistry and clinical	Alb[4], K^+[9], PO_4,[9] Cr,[9] bld glucose & HbA_{1c} (for persons with diabetes),[9] PTH,[8] BP,[9] lipids,[2] GFR,[9] Hb,[9] medications inc supplements[9]
Nutrition assessment	Dry wt,[2,4] BMI,[2]%IBW/SGA,[4] diet assessment/nPNA,[2,4] activity level and limitations[9]
Nutrition intervention	
Energy	Ideal for age, gender, BMI and phys activity level[2]
Protein	0.75–1.0 g/kg IBW/day[2]
Sodium	<100 mmol if hypertensive and CKD is progressive[2]
Potassium	Not usually restricted, If K^+ >6.0 limit intake[6] to 1 mmol/kg IBW/day

CKD	*Stage 3 (GFR 30–59)*[4]
Phosphate	If >1.49 mmol/L (or >target PTH) restrict to 800–1000 mg/day (adj for protein) &/or binders[8]
Fluid	Individualised based on CKD, oedema and hypertension[2]
Nutrition counselling	Adequate protein and energy,[2,4] bld glucose control in DM,[4] fluid and Na control in HT,[4] lipid[2] & weight[4] control, meal plan,[9] self monitoring,[9] physical activity[17]
Review & frequency of follow up	Dry wt & BMI monthly,[2] 20–30 min[9] r/v every 6–12 months if no evidence of malnutrition, more frequently if malnourished[4]

%IBW, percent ideal body weight; Alb, albumin; BMI, body mass index; BP, blood pressure; $CaxPO_4$, calcium phosphate ratio; Cr, creatinine; DEXA, dual xray absorptiometry; DM, diabetes mellitus; g, gram; Hb, haemoglobin; HbA_{1c}, glycosylated haemoglobin; HD, haemodialysis; HT, hypertension; K, potassium; kg, kilogram; kJ, kilojoules; Kt/V, dialysis adequacy; L, litre; mg, milligram; mL, millilitre; mmol, millimole; Na, sodium; NPNA, normalised protein nitrogen appearance; PD, peritoneal dialysis; PDUO, previous day's urine output; PO_4, phosphate; PTH, parathyroid hormone; SGA, subjective global assessment; TBN, total body nitrogen.

Figure 5

Criteria for Referral to Dietitian

Clinical question

At what level of Glomerular Filtration Rate (GFR) should patients be referred to the dietitian in order to maximise nutritional intervention opportunities?

Evidence statement	*Level of evidence*
CKD Stages 3 and 4	
CKD Stage 3 (GFR 30–59 mL/min)	Level IV[2]
CKD Stage 4 (GFR 15–29 mL/min)	Level III[4]
Protein energy malnutrition increases with deteriorating kidney function and is associated with adverse outcomes	Level III-2[4]
Low protein and calorie intake is an important cause of poor nutritional status	Level III-3[4]
CKD Stage 5	
CKD Stage 5 (GFR <15 mL/min)	Level I[2]
For patients undergoing haemodialysis and peritoneal dialysis, nutritional status should be routinely assessed at commencement of dialysis and at regular intervals thereafter	Level III[3]

Figure 6

Nutrition Assessment

Clinical question

Which specific measures best reflect nutrition status or change in nutritional status in CKD?

Evidence statement	*Level of evidence*
CKD Stages 3 and 4	
Maintained percent (%) oedema-free (dry) actual body weight reflects optimal nutritional status.	Level II[2]
Body Mass Index (BMI) = 18.5–25, reflects optimal nutritional status.	Level IV[3]
Subjective global assessment (SGA) and percentage ideal body weight (BMI) reflect change in nutritional status.	Level IV[3]
Total body nitrogen, dual X-ray absorptiometry (DEXA) or bioelectrical impedance (BIA) reflect long-term nutritional adequacy.	Level IV[2]
CKD Stage 5	
Maintained percent (%) oedema-free (dry) actual body weight reflect optimal nutritional status.	Level II[2]
Body Mass Index (BMI) = 23–26, reflects optimal nutritional status.	Level II[2]
SGA maintained or improved reflects nutritional status.	Level III-3[2]
Nutritional status of patients on peritoneal dialysis should be monitored by methods appropriate to assess total body stores and detect early signs of malnutrition, such as normalised protein nitrogen appearance (nPNA) >0.9, total body nitrogen (TBN) and DEXA within the normal range.	Level IV[2,3]

Figure 7

Nutrition Prescription/Intervention

Clinical question

What are the goals of nutrition intervention for CKD?

Evidence statement	*Level of evidence*
Achieve and maintain desirable weight and adequate nutritional status.	Level III-2[11]
Optimise status of comorbidities, blood glucose control in diabetes and fluid and sodium control in hypertension, phosphate control in hyperparathyroidism, lipid control and weight management.	Level III-2[4]
Normalise or stabilise biochemical markers, such as a normalised protein appearance (nPNA) ≥0.8 g/day in haemodialysis.	Level III-2[4]
Normalise or stabilise biochemical markers, such as a nPNA >0.9 g/day in peritoneal dialysis.	Opinion[4]
Maintain skeletal muscle stores and strength, using subjective global assessment (SGA), TBN and DEXA.	Opinion[4]

Clinical question

What are the prescriptions for appropriate nutritional intervention(s) to optimise nutritional status in CKD and prevent malnutrition?

Evidence statement	*Level of evidence*
CKD Stage 3	
Energy. Ideal kilojoule/calorie energy intake determined for age, gender and BMI and level of physical activity needs to be determined.	Opinion[2]
A nutritionally balanced diet with adequate energy intake to maintain a healthy weight needs to be prescribed.	
Protein. A level of protein of 0.75–1.0 g/ideal body weight (IBW)/day is recommended.	Level I[2]

Figure 8

Implementation and Management

Clinical question

What are effective methods of implementation to achieve positive outcomes in CKD?

Evidence statement	*Level of evidence*
EDUCATION	
CKD Stage 3	
Patients with decreased dietary intake or malnutrition need dietary modification, counselling and specialised nutrition therapy.	Level IV[4]
For patients with poorly controlled comorbidities, refer to medical specialist.	Opinion ANZRGT

Source for Figures 3 to 8:

Ash S, Campbell K, MacLaughlin H et al. Evidence based practice guidelines for the nutritional management of chronic kidney disease. *Nutrition & Dietetics*. 2006; **63**:S33-S45.
http://daa.asn.au/for-health-professionals/daa-endorsed-practice-guidelines-and-practice-recommendations/