National Institute for Health and Care Excellence

Draft for consultation

RRT and conservative management

Evidence review for dietary management and fluid restriction

NICE guideline

Intervention evidence review

April 2018

Draft for Consultation

This evidence review was developed by the National Guideline Centre

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ISBN

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1 Dietary management and fluid restriction

1.1 Review question: What is the clinical and cost effectiveness of dietary management and fluid restriction for RRT or conservative management?

1.2 Introduction

Diet and fluid management is an integral part of renal services as people with CKD may accumulate certain substances in their blood (such as salt, water, potassium and phosphate) and these can cause symptoms or complications. Dietary modifications and a fluid allowance can represent a considerable burden on people receiving RRT or conservative management. There is existing NICE guidance about dietary management for people with CKD prior to initiating renal replacement therapy and exclusively for phosphate management for people with stage 4 and 5 CKD (CG157). Recommendations are needed on this topic to address variations in dietary management currently provided indifferent renal services. Fluid restriction 'allowance' is routinely suggested to patients but it can be difficult to adhere to advice as intake limits are often quite stringent. Recommendations are needed on this topic to confirm the importance of tight fluid control, if supported by evidence.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Children, young people and adults undergoing RRT or conservative management Children and young people (0 to 18) being prepared for RRT or conservative management
Interventions	• Diet management (as a minimum including assessment and general dietary advice aimed at ≥1 of sodium, potassium or protein) • Fluid restriction (including advice) • Usual care/sham
Comparisons	Diet management vs usual care/sham Fluid restriction vs usual care/sham Combined diet and fluid management vs usual care/sham
Outcomes	Critical • Patient, family/carer health-related quality of life (continuous) • Mortality (dichotomous and time to event) • Time to failure of RRT form (time to event) Important • Hospitalisation (rates or continuous) • Subjective global assessment or malnutrition universal screen tool (continuous) • Interdialytic weight gain (continuous) • Symptom scores and functional measures (including grip strength, continuous)

	• Psychological distress and mental wellbeing (continuous)
	• Blood pressure (continuous)
	• Patient, family and carer experience of care (continuous)
	• Growth (continuous)
	• Adherence to information (dichotomous)
	• Adverse events
	  ○ Infections (dichotomous)
	  ○ Acute transplant rejection episodes (dichotomous)

Study design	RCTs will be prioritised. If insufficient evidence is found for any specified comparisons non-randomised studies will be considered but only if outcomes are adjusted for the following key confounders: • Age • Health at baseline • Co-morbidities • Ethnicity

The aim of this review was to compare the general approaches of dietary management vs usual care and fluid restriction vs usual care. Studies looking exclusively at specific supplementation interventions were not included as this was not considered to reflect general dietary management. A minimum study duration of 1 month was included in order to insure the outcomes reflected the impact of the interventions.

1.4 Clinical evidence

1.4.1 Included studies

Eight studies were included in the review;[21, 22, 42, 43, 62, 71, 75, 79] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary tables below (Table 3, Table 4, Table 5 and Table 6)

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix F.

1.4.2 Excluded studies

See the excluded studies list in appendix I.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
De Vries 2016[21]	Dietary management - sodium restriction, individualised dietary counselling from physician, target of 50mmol/d with 24hr urine sample at midpoint for monitoring, 6 weeks	Adults aged over 18 (mean 58) Transplant recipients, BP >120/80 but <180/100 (mean 138/95) Netherlands	Blood pressure At end of intervention	Crossover study

Study	Intervention and comparison	Population	Outcomes	Comments
	Usual care, normal diet aimed at 150mmol/d, 6 weeks n = 23			
Ebrahimi 2016[22]	Combined diet and fluid intervention – in person education sessions, twice a week for 12 weeks, focus on diet, limits in fluid intake, supported by pamphlets, 12 weeks Usual care, nil else specified, 12 weeks n = 99	Adults aged over 18 (mean 51) Haemodialysis Iran	Quality of life At end of intervention	
Kauric-Klein 2012[42]	Combined diet and fluid intervention – 2 BP education sessions with nurses, weekly monitoring, aim for fluid (<1500ml/d or <2.5kg IDWG) and sodium restriction (<2g/d), 16 weeks Usual care, BP monitoring and medication adjustment by health care professonals (HCPs) in unit as required, 16 weeks n = 118	Adults aged over 18 (mean 56-63) Haemodialysis, hypertensive (>150/90) USA	Interdialytic weight gain Blood pressure At end of intervention	Cluster randomised, six units
Keven 2006[43]	Dietary management – sodium restriction, 80-100mmol/d target, seen by dietician at 4, 8 and 12 weeks, 12 weeks Usual care, nil else specified, 12 weeks	Adults aged over 18 (mean 40-43) Transplant recipients, receiving antihypertensive medication Turkey	Blood pressure At end of intervention	

Study	Intervention and comparison	Population	Outcomes	Comments
	n = 32			
Molaison 2003[62]	Fluid restriction – regular group meetings with dieticians + written material to increase adherence to fluid restriction, aimed at 1000ml/d of fluid intake, 12 weeks Usual care, involving dieticians, nurses and technicians, nil else specified, 12 weeks n = 314	Adults aged over 18 (mean 53, SD 15) Dialysis USA	Interdialytic weight gain At end of intervention	Cluster randomised, ten units
Rodrigues Telini 2014[71]	Dietary management – sodium restriction, reduction of 2g from their usual diet, monitored by nutritionist, 16 weeks Usual care, monitored by nutritionist, nil else specified, 16 weeks n = 39	Adults aged over 18 (mean 56-60) Dialysis, raised inflammatory markers Brazil	Blood pressure At end of intervention	
Sharp 2005[75]	Fluid restriction – education and CBT based intervention to improve adherence to restriction, weekly hour long group sessions facilitated by trainee clinical psychologist, 4 weeks Usual care, nil else specified, 4 weeks n = 46	Adults aged over 18 (mean 54, SD 12) Haemodialysis, history of poor fluid restriction adherence UK	Quality of life Interdialytic weight gain At end of intervention	Elements of CBT to intervention, Glasgow University Liquid intake Program
Tsay 2003[79]	Combined diet and fluid intervention – self-efficacy education with nurse specialists, wide ranging but	Adults aged over 18 (mean 58, SD 12) Haemodialysis	Interdialytic weight gain At end of follow-up	Followed up for 5 months after 1 month intervention

Study	Intervention and comparison	Population	Outcomes	Comments
	focus on diet and fluid with realistic goal setting, three sessions a week each lasting one hour, facilitated by nurse nephrology specialists, 4 weeks Usual care, nil else specified, 4 weeks n = 64	Taiwan		

See appendix D for full evidence tables.

No RCTs or NRS were available for children under the age of 18 or for adults over the age of 70. No RCTs or NRS were available in the population of people who had opted for conservative management.

8 RCTs were included. 2 RCTs compared dietary management with usual care for transplant recipients. 1 RCT compared dietary management with usual care for people on dialysis. 2 RCTs compared fluid restriction with usual care for people on dialysis. 3 RCTs compared a combination of dietary management and fluid restriction with usual care for people on dialysis. In the majority of the RCTs the dietary management was either only general advice or focused on sodium restriction.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: dietary management vs usual care, transplant population, >18 to 70

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Dietary management (95% CI)
Systolic blood pressure (6-12w)	76 (2 studies) 6-12 weeks	LOW[1,2] due to risk of bias, imprecision		The mean systolic blood pressure (6-12w) in the control groups was 136 mmHg	The mean systolic blood pressure (6-12w) in the intervention groups was 13.26 lower (18.96 to 7.55 lower)
Diastolic blood pressure (6-12w)	76 (2 studies) 6-12 weeks	LOW[1,2] due to risk of bias, imprecision		The mean diastolic blood pressure (6-12w) in the control groups was 83 mmHg	The mean diastolic blood pressure (6-12w) in the intervention groups was 7.34 lower (11.18 to 3.5 lower)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 4: Clinical evidence summary: dietary management vs usual care, dialysis population, >18 to 70

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Dietary management (95% CI)
Systolic blood pressure (16 weeks)	39 (1 study) 16 weeks	VERY LOW[1,2] due to risk of bias, imprecision		The mean systolic blood pressure (16 weeks) in the control groups was 149 mmHg	The mean systolic blood pressure (16 weeks) in the intervention groups was 1.72 lower (13.97 lower to 10.53 higher)
Diastolic blood pressure (16 weeks)	39 (1 study) 16 weeks	VERY LOW[1,2] due to risk of bias,		The mean diastolic blood pressure (16 weeks) in the control groups was 84 mmHg	The mean diastolic blood pressure (16 weeks) in the intervention groups was 3.78 higher

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Dietary management (95% CI)
		imprecision			(7.96 lower to 15.52 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

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2 **Table 5: Clinical evidence summary: fluid restriction vs usual care, dialysis population, >18 to 70**

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Fluid restriction (95% CI)
QoL (SF-36, physical, 0-100, higher is better, 4 weeks)	56 (1 study) 4 weeks	VERY LOW[1,2] due to risk of bias, imprecision			The mean qol (sf-36, physical, 0-100, higher is better, 4 weeks) in the intervention groups was 7.28 higher (5.2 lower to 19.76 higher)
QoL (SF-36, mental, 0-100, higher is better, 4 weeks)	56 (1 study) 4 weeks	LOW[1] due to risk of bias			The mean qol (sf-36, mental, 0-100, higher is better, 4 weeks) in the intervention groups was 12.64 higher (5.59 to 19.69 higher)
Interdialytic weight gain (kg, 4-12 weeks)	370 (2 studies) 4-12 weeks	VERY LOW[1,2] due to risk of bias, imprecision			The mean interdialytic weight gain (kg, 4-12 weeks) in the intervention groups was 0.19 lower (0.42 lower to 0.04 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 6: Clinical evidence summary: combined dietary management and fluid restriction vs usual care, dialysis population, >18 to 70

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Usual care	Risk difference with Combined diet and fluid management (95% CI)
QoL (KDQOL, 0-100, higher is better, 12w)	99 (1 study) 12 weeks	MODERATE[1] due to risk of bias		The mean qol (kdqol, 0-100, higher is better, 12w) in the control groups was 58.8	The mean qol (kdqol, 0-100, higher is better, 12w) in the intervention groups was 8.6 higher (6.2 to 11 higher)
Interdialytic weight gain (kg, 16-24w)	182 (2 studies) 16-24 weeks	LOW[1,2] due to risk of bias, imprecision		The mean interdialytic weight gain (kg, 16w) in the control groups was 2.5 kg	The mean interdialytic weight gain (kg, 16w) in the intervention groups was 0.39 lower (0.67 to 0.11 lower)
Systolic blood pressure (16w)	118 (1 study) 16 weeks	LOW[1,2] due to risk of bias, imprecision		The mean systolic blood pressure (16w) in the control groups was 160 mmHg	The mean systolic blood pressure (16w) in the intervention groups was 6.5 lower (11.39 to 1.61 lower)
Diastolic blood pressure (16w)	118 (1 study) 16 weeks	MODERATE[1] due to risk of bias		The mean diastolic blood pressure (16w) in the control groups was -3.1 mmHg (change score)	The mean diastolic blood pressure (16w) in the intervention groups was 0.8 lower (4.34 lower to 2.74 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were included.

1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

1.5.3 Summary of studies included in the economic evidence review

None.

1.5.4 Unit costs

Relevant unit costs were provided to the committee to aid consideration of cost effectiveness. Dietician costs are included in Table 7 below.

Table 7: UK costs of hospital based scientific and professional staff: dieticians

Dietician	Cost per working hour[(a)]	Cost per patient contact hour[(b)]
Band 2	£24	£32
Band 3	£27	£36
Band 4	£30	£40
Band 5	£33	£44
Band 6	£44	£59
Band 7	£54	£72
Band 8a	£63	£84
Band 8b	£76	£101

(a) PSSRU. Unit Costs of Health and Social Care 2016.[19] Includes wages, salary on-costs, overheads (management, admin and estates staff, and non-staff) and capital overheads. Qualification costs are not included.

(b) Calculated using a ratio of direct hours : indirect hours of 1:0.33. Data regarding this was not reported in the PSSRU Unit Costs of Health and Social Care 2016 and so this is based on data reported in the 2010 report for a hospital based dietician.[18]

The interventions in the included clinical studies vary considerably. See Appendix D: Clinical evidence tables for details of the interventions.

1.6 Resource impact

The recommendations made based on this review (see section 1.8) are not expected to have a substantial impact on resources.

1.7 Evidence statements

1.7.1 Clinical evidence statements

1.7.1.1 Dietary management vs usual care, transplant population

- No evidence was identified for mortality or quality of life
- Clinically important benefit of dietary management was found for both systolic and diastolic blood pressure (low quality, 2 studies)

1.7.1.2 Dietary management vs usual care, dialysis population

- No evidence was identified for mortality or quality of life
- No clinically important difference with dietary management for both systolic and diastolic blood pressure (very low quality, 1 study)

1.7.1.3 Fluid restriction vs usual care, dialysis population

- No evidence was identified for mortality
- Clinically important benefit of fluid restriction for quality of life (physical and mental, low quality, 1 study)
- No clinically important difference with fluid restriction for interdialytic weight gain (very low quality, 2 studies)

1.7.1.4 Combined dietary management and fluid restriction vs usual care, dialysis population

- No evidence was identified for mortality
- Clinically important benefit with combined dietary management and fluid restriction for quality of life (moderate quality, 1 study)
- No clinically important difference with combined dietary management and fluid restriction for both interdialytic weight gain (low quality, 2 studies), systolic and diastolic blood pressure (low-moderate quality, 1 study)

1.7.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.8 Recommendations

I1. Offer a full dietary assessment by a specialist renal dietitian to people starting dialysis or conservative management. This should include:

- fluid intake
- sodium
- potassium
- phosphate
- protein
- calories
- micronutrients.

I2. After transplantation, offer dietary advice from a healthcare professional with training and skills in this area.

I3 Re-assess dietary management and fluid allowance when:

- a person's circumstances change (for example, when switching RRT modality), or
- biochemical measures indicate, or
- the person (or, where appropriate, their family members or carers) asks.

I4. Provide individualised information, advice and ongoing support on dietary management and fluid allowance to the person and their family members or carers (as appropriate). The information should be in an accessible format and be sensitive to the person's cultural needs and beliefs.

I5. Follow the recommendations on dietary management and phosphate binders in NICE's guideline on chronic kidney disease (stage 4 or 5): management of hyperphosphataemia.

1.9 Rationale and impact

1.9.1 Why the committee made the recommendations

Limited evidence, including in people with a transplant, indicated that people receiving RRT or conservative management may benefit from dietary and/or fluid management. The committee agreed that current practice is for people receiving dialysis or conservative management to have an assessment by a specialist dietitian. NICE's guideline on managing hyperphosphataemia in chronic kidney disease recommends assessment by a specialist

renal dietitian for those at risk of hyperphosphataemia which would include these populations. They also considered it current practice for dietary advice to be given after transplantation although who provided this advice varied and may not be a specialist renal dietician. The committee noted that there is some variation in how long people have to wait for this assessment and variation in ongoing management. The committee agreed that dietary advice is important for people with a transplant, particularly straight after the surgery. This was supported by the evidence. The committee noted the importance of the person giving dietary advice having specialist knowledge of dietary requirements in transplant patients. However, the evidence was too limited to recommend that dietary advice should routinely be from a specialist renal dietitian for this group given it would be a change in practice in many areas that could result in a substantial resource impact. The committee agreed that following initial assessment further dietary assessment would be determined by specific circumstances or indicators and made a recommendation summarising what these would be. They highlighted that there is variation in the level of dietitian input available in renal centres which may impact how quickly people can access services or the level of input following initial assessment; however, the evidence was not considered sufficient to make specific recommendations to address this.

The committee agreed that involving family members and carers in discussions was important for improving adherence to dietary management and fluid allowance. There was no evidence on the benefits or harms of a low protein diet so the committee was not able to make a recommendation on this. The committee agreed that dietary management and fluid assessment should not be a 'one-step' process and that people's needs should be reviewed when circumstances change (for example, when switching RRT modalities) or when biochemical measures indicate.

1.9.2 Impact of the recommendations on practice

The recommendations made reflect current practice and are not expected to result in a substantial resource impact to the NHS in England.

1.10 Interpreting the evidence

1.10.1 The outcomes that matter most

The committee considered the outcomes of quality of life, mortality and time to failure of RRT form to be critical. The committee considered the outcomes of hospitalisation, SGA/MUST, IDWG, symptom scores/functional measures, psychological distress/mental wellbeing, blood pressure, experience of care, growth, adherence to information and adverse events to be important.

1.10.2 The quality of the evidence

The committee noted that it is difficult at this stage in service provision to get ethical approval for a trial that compares dietary management with no dietary management. Therefore in the review the majority of usual care arms are likely to involve some element of dietary management, which is likely to lessen the observed impact of the intervention. The intervention arms were also very variable in terms of the level of resource use involved and some were quite intensive.

The committee noted that the only outcomes with any evidence identified in this review were quality of life, blood pressure, IDWG. There was no evidence on mortality, time to failure of modality, hospitalisation, SGA/MUST, symptom scores/functional measures, psychological distress/mental wellbeing, experience of care, growth, adherence or adverse events.

The evidence identified in the review ranged from moderate to very low quality, with the majority of the evidence being either low or very low quality. Most outcomes were downgraded for imprecision as the included trials were generally small. The studies were generally relatively short in follow-up (mostly less than 12 weeks in duration).

While the included studies met the protocol, few were designed to address the key question for the guideline – what is the clinical and cost effectiveness of providing dietary or fluid management, but instead were focused on specific interventions within the umbrella terms of dietary or fluid management.

1.10.3 Benefits and harms

Clinically important benefits from dietary management (focused on sodium) were seen on blood pressure in the transplant population, from a fluid allowance on quality of life in the dialysis population and from a combination of dietary management and a fluid allowance on quality of life in the dialysis population. There were also a number of outcomes for which no clinically important difference was observed. No outcomes demonstrated a clinically important harm of a fluid allowance or dietary management.

The committee noted that there was benefit for dietary management in the transplant population in terms of blood pressure reduction and highlighted that this could be important in maintaining the longevity of the transplant as well as having more general cardiovascular benefits. However, the duration of follow-up was relatively short. The committee discussed how current practice is variable and that people with transplants generally receive less dietary management than people on dialysis. However, information from a survey of renal dieticians showed that most units do provide cover for transplant patients even if the level of input varies. Given the available evidence, the committee agreed it was important for the transplant population to be included in these recommendations.

The committee agreed that the recommendations were relevant for both adults and children. Although there was no evidence identified in children, the committee consensus was that appropriate dietary management and fluid assessment were important parts of the care of children undergoing RRT.

Recommendations were weakly supported by the available evidence and supported by the pre-existing guidance on hyperphosphataemia and the committee's consensus.

1.10.4 Cost effectiveness and resource use

No published economic evaluations were included.

Providing dietary assessment and advice, and monitoring patients, will involve resource use due to the health care professional time involved. The committee noted that typically this would currently involve an initial assessment with a dietician and advice for people starting RRT or conservative management, and then if problems were detected, for example through routine monitoring of blood tests, then they may be referred back for further assessment. The committee noted that while the principle of what happens is the same across the country how services are organised can ultimately impact how quickly a patient can be seen by a dietician.

NICE's guideline on managing hyperphosphataemia in chronic kidney disease recommends assessment by a specialist renal dietitian for those at risk of hyperphosphataemia which would include these populations.

It was considered current practice for dietary advice to be given after transplantation although who provided this advice varied and may not be a specialist renal dietician. The committee noted that there is some variation in how long people have to wait for this assessment and variation in ongoing management. The committee agreed that dietary

advice is still important for people with a transplant, particularly straight after the surgery. The committee noted the importance of the person giving dietary advice having specialist knowledge of dietary requirements in transplant patients. However, the evidence was too limited to recommend that dietary advice should routinely be from a specialist renal dietitian for this group given it would be a change in practice in many areas that could result in a substantial resource impact. The committee agreed that following initial assessment further dietary assessment would be determined by specific circumstances or indicators.

The committee noted there may however be downstream savings if dietary management reduces problematic accumulations of minerals or fluid as clinical events may be avoided. For example, reduced incidence of malnutrition may decrease inpatient length of stay and frequency of admission and the need for nutritional supplements. In transplant patients, improving blood pressure control could ultimately improve transplant longevity thus also resulting in downstream saving.

Dietary management may also lead to improved patient outcomes in terms of quality of life (as symptoms are improved) which may result in an increase in QALYs.

The included clinical studies provided some limited support for the potential resource use benefits of dietary management such as reduced blood pressure and for improved patient outcomes that would improve QALYs such as improved quality of life. However, there were limitations in the evidence as described in the previous section. The intervention arms were very variable in terms of the level of resource use involved and while the usual care arms were generally not well described it seemed likely that they also included some level of dietary advice.

The committee concluded that dietary management and a fluid allowance are important components of the long term management of people who have progressed through to later stages of CKD and RRT and they are likely to be cost effective. However, the evidence was limited and not sufficient to specify the level of input and so recommendations were based on current practice and existing recommendations in the area. The committee noted that dietitian availability varied however the recommendations broadly reflect current practice and so are not expected to result in a substantial resource impact to the NHS in England.

1.10.35 Other factors the committee took into account

The committee noted that the format of dietary management may be face to face or may involve telephone consultation. The committee did not make recommendations for a specific format of dietary management as there was no evidence supporting a difference between the two and the consensus view was that both could be useful, depending on the context.

The committee noted that involving family members or carers in any discussions about dietary or fluid advice was critical in increasing the likelihood of adherence.

The committee agreed that it was important that a specialist renal dietitian was involved in the process of dietary management and fluid assessment. This was based on their own experience and supported by previous recommendations in the NICE guideline on hyperphosphatemia (CG157). The committee noted that this broadly reflects current practice for people receiving dialysis and conservative management, however people with a (functioning) transplant may not see a specialist renal dietitian. The committee agreed that dietary advice is still important in this group, particularly immediately post-transplant as dietary requirements will have changed substantially. Dietary advice in this group was also supported by the review. However the committee agreed that while it was important that advice was given by someone with specialist experience of dietary advice in renal disease the evidence was not strong enough to specifically recommend that this should be routinely done by a specialist renal dietitian given that it would be a change in practice in many areas.

Current practice is that different health professionals provide dietary advice to this group including for example specialist nurses. The committee highlighted that input from a specialist renal dietician may be sought based on individual patients factors.

The committee discussed the duration of involvement of the specialist renal dietitian, noting that the longer they were involved (for example in ongoing monitoring) the greater the resource impact but also likely the greater the clinical benefit. It is noted that a dietitian would be expected to follow the cycle of assessment, intervention and evaluation that would be repeated until an identified problem achieves a satisfactory outcome (usually involving collaboration with the multidisciplinary team). The duration of the intervention in the evidence varied between studies but was generally no more than 3 months.

The committee agreed that it was important that dietary management and fluid assessment was not considered to be a one step process and that people's needs should be reviewed when circumstances dictated (for example if switching RRT modalities, developing co-existing conditions influencing dietary or fluid requirements or when biochemical measures indicate (for example level of protein or salt). Children would be more frequently assessed and monitored for example to monitor growth but the same principles of dietary assessment apply.

The committee noted that the NICE guideline on chronic kidney disease (CG182) contains recommendations on dietary interventions relevant to people attending low clearance clinics.

The committee noted that while all people should have a dietary assessment, only in some people will this require a specific dietary intervention. The details of specific dietary interventions, their indication and use are beyond the scope of this guideline although the committee included the example of the use of phosphate binders from the related NICE guideline on Chronic kidney disease (stage 4 or 5): management of hyperphosphataemia (CG157).

References

1. Akpele L, Bailey JL. Nutrition counseling impacts serum albumin levels. Journal of Renal Nutrition. 2004; 14(3):143-8

2. Allman MA, Stewart PM, Tiller DJ, Horvath JS, Duggin GG, Truswell AS. Energy supplementation and the nutritional status of hemodialysis patients. American Journal of Clinical Nutrition. 1990; 51(4):558-62

3. Ash S, Campbell KL, Bogard J, Millichamp A. Nutrition prescription to achieve positive outcomes in chronic kidney disease: a systematic review. Nutrients. 2014; 6(1):416-51

4. Baraz S, Parvardeh S, Mohammadi E, Broumand B. Dietary and fluid compliance: an educational intervention for patients having haemodialysis. Journal of Advanced Nursing. 2010; 66(1):60-8

5. Beddhu S, Filipowicz R, Chen X, Neilson JL, Wei G, Huang Y et al. Supervised oral protein supplementation during dialysis in patients with elevated C-reactive protein levels: A two phase, longitudinal, single center, open labeled study Clinical Research. BMC Nephrology. 2015; 16:87

6. Bellizzi V, Chiodini P, Cupisti A, Viola BF, Pezzotta M, De Nicola L et al. Very low-protein diet plus ketoacids in chronic kidney disease and risk of death during end-stage renal disease: a historical cohort controlled study. Nephrology Dialysis Transplantation. 2015; 30(1):71-7

7. Bellomo G, Coccetta P, Pasticci F, Rossi D, Selvi A. The effect of psychological intervention on thirst and interdialytic weight gain in patients on chronic hemodialysis: A randomized controlled trial. Journal of Renal Nutrition. 2015; 25(5):426-32

8. Borges W, Gonzalez Caraballo Z, Delpin EA, Morales Otero L. Chronic effect of a high-protein low-fat diet in transplant patients. Transplantation Proceedings. 1996; 28(6):3400-1

9. Boudville N. Oral nutritional supplementation in peritoneal dialysis patients--does it work? Peritoneal Dialysis International. 2005; 25(2):157-60

10. Brunori G, Viola BF, Parrinello G, De Biase V, Como G, Franco V et al. Efficacy and safety of a very-low-protein diet when postponing dialysis in the elderly: a prospective randomized multicenter controlled study. American Journal of Kidney Diseases. 2007; 49(5):569-80

11. Campbell J, Porter J. Dietary mobile apps and their effect on nutritional indicators in chronic renal disease: A systematic review. Nephrology. 2015; 20(10):744-751

12. Campbell KL, Ash S, Bauer JD. The impact of nutrition intervention on quality of life in pre-dialysis chronic kidney disease patients. Clinical Nutrition. 2008; 27(4):537-44

13. Caria S, Cupisti A, Sau G, Bolasco P. The incremental treatment of ESRD: a low-protein diet combined with weekly hemodialysis may be beneficial for selected patients. BMC Nephrology. 2014; 15:172

14. Chertow GM, Ling J, Lew NL, Lazarus JM, Lowrie EG. The association of intradialytic parenteral nutrition administration with survival in hemodialysis patients. American Journal of Kidney Diseases. 1994; 24(6):912-20

15. Cianciaruso B, Pota A, Bellizzi V, Di Giuseppe D, Di Micco L, Minutolo R et al. Effect of a low- versus moderate-protein diet on progression of CKD: follow-up of a

randomized controlled trial. American Journal of Kidney Diseases. 2009; 54(6):1052-61

16. Cotten-Sheldon K, Martinelli S, Cagan K, Begin B, Salsbery K, Wong C. You can do it: Educational incentive project for children on hemodialysis. Hemodialysis International. 2011; 15 (1):162

17. Cupisti A, D'Alessandro C, Di Iorio B, Bottai A, Zullo C, Giannese D et al. Nutritional support in the tertiary care of patients affected by chronic renal insufficiency: Report of a step-wise, personalized, pragmatic approach. BMC Nephrology. 2016; 17 124

18. Curtis L. Unit costs of health and social care 2010. Canterbury. Personal Social Services Research Unit University of Kent, 2010. Available from: http://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2010/

19. Curtis L, Burns A. Unit costs of health and social care 2016. Canterbury. Personal Social Services Research Unit University of Kent, 2016. Available from: http://www.pssru.ac.uk/project-pages/unit-costs/2016/

20. Dagdeviren A, Savaser S. Education to reduce potassium levels in adolescent, heamodialysis patients. Edtna-Erca Journal. 2003; 29(4):195-197

21. de Vries LV, Dobrowolski LC, van den Bosch JJ, Riphagen IJ, Krediet CT, Bemelman FJ et al. Effects of dietary sodium restriction in kidney transplant recipients treated with renin-angiotensin-aldosterone system blockade: A randomized clinical trial. American Journal of Kidney Diseases. 2016; 67(6):936-44

22. Ebrahimi H, Sadeghi M, Amanpour F, Dadgari A. Influence of nutritional education on hemodialysis patients' knowledge and quality of life. Saudi Journal of Kidney Diseases and Transplantation. 2016; 27(2):250-5

23. Fine A, Fontaine B, Ma M. Commonly prescribed salt intake in continuous ambulatory peritoneal dialysis patients is too restrictive: results of a double-blind crossover study. Journal of the American Society of Nephrology. 1997; 8(8):1311-4

24. Ford JC, Pope JF, Hunt AE, Gerald B. The effect of diet education on the laboratory values and knowledge of hemodialysis patients with hyperphosphatemia. Journal of Renal Nutrition. 2004; 14(1):36-44

25. Fouque D, Laville M. Low protein diets for chronic kidney disease in non diabetic adults. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD001892. DOI: 10.1002/14651858.CD001892.pub3.

26. Fouque D, McKenzie J, de Mutsert R, Azar R, Teta D, Plauth M et al. Use of a renal-specific oral supplement by haemodialysis patients with low protein intake does not increase the need for phosphate binders and may prevent a decline in nutritional status and quality of life. Nephrology Dialysis Transplantation. 2008; 23(9):2902-10

27. Fouque D, Wang P, Laville M, Boissel JP. Low protein diets delay end-stage renal disease in non-diabetic adults with chronic renal failure. Nephrology Dialysis Transplantation. 2000; 15(12):1986-92

28. Fry KM, Chan M. Long-term nutritional interventions for adult kidney transplant recipients. Cochrane Database of Systematic Reviews 2007, Issue 4. Art. No.: CD006862. DOI: dx.doi.org/10.1002/14651858.CD006862.

29. Hansen HP, Tauber-Lassen E, Jensen BR, Parving HH. Effect of dietary protein restriction on prognosis in patients with diabetic nephropathy. Kidney International. 2002; 62(1):220-8

30. Hare J, Clark-Carter D, Forshaw M. A randomized controlled trial to evaluate the effectiveness of a cognitive behavioural group approach to improve patient adherence to peritoneal dialysis fluid restrictions: a pilot study. Nephrology Dialysis Transplantation. 2014; 29(3):555-64

31. Harty J, Boulton H, Faragher B, Venning M, Gokal R. The influence of small solute clearance on dietary protein intake in continuous ambulatory peritoneal dialysis patients: a methodologic analysis based on cross-sectional and prospective studies. American Journal of Kidney Diseases. 1996; 28(4):553-60

32. Hatch DA, Barry JM, Norman DJ. A randomized study of intravenous fluid replacement following living-donor renal transplantation. Transplantation. 1985; 40(6):648-51

33. Hernandez Morante JJ, Sanchez-Villazala A, Cutillas RC, Fuentes MC. Effectiveness of a nutrition education program for the prevention and treatment of malnutrition in end-stage renal disease. Journal of Renal Nutrition. 2014; 24(1):42-9

34. Howren MB, Kellerman QD, Hillis SL, Cvengros J, Lawton W, Christensen AJ. Effect of a behavioral self-regulation intervention on patient adherence to fluid-intake restrictions in hemodialysis: A randomized controlled trial. Annals of Behavioral Medicine. 2016; 50(2):167-76

35. Jeloka TK, Dharmatti G, Jamdade T, Pandit M. Are oral protein supplements helpful in the management of malnutrition in dialysis patients? Indian Journal of Nephrology. 2013; 23(1):1-4

36. Jiang N, Qian J, Lin A, Fang W, Cao L, Wang Q et al. Improved plasma amino acids pattern following 12 months of supplemented low-protein diet in peritoneal dialysis patients. Renal Failure. 2010; 32(6):709-15

37. Jiang N, Qian J, Lin A, Fang W, Zhang W, Cao L et al. Low-protein diet supplemented with keto acids is associated with suppression of small-solute peritoneal transport rate in peritoneal dialysis patients. International Journal of Nephrology. 2011; 2011:542704

38. Jiang N, Qian J, Sun W, Lin A, Cao L, Wang Q et al. Better preservation of residual renal function in peritoneal dialysis patients treated with a low-protein diet supplemented with keto acids: a prospective, randomized trial. Nephrology Dialysis Transplantation. 2009; 24(8):2551-8

39. Jungers P, Chauveau P, Ployard F, Lebkiri B, Ciancioni C, Man NK. Comparison of ketoacids and low protein diet on advanced chronic renal failure progression. Kidney International. 1987; 32(Suppl. 22):S-67-S-71

40. Karavetian M, Ghaddar S. Nutritional education for the management of osteodystrophy (nemo) in patients on haemodialysis: a randomised controlled trial. Journal of Renal Care. 2013; 39(1):19-30

41. Kauric-Klein Z. Blood pressure knowledge in hypertensive hemodialysis patients. CANNT Journal. 2012; 22(4):18-25

42. Kauric-Klein Z. Improving blood pressure control in end stage renal disease through a supportive educative nursing intervention. Nephrology Nursing Journal. 2012; 39(3):217-28

43. Keven K, Yalcin S, Canbakan B, Kutlay S, Sengul S, Erturk S et al. The impact of daily sodium intake on posttransplant hypertension in kidney allograft recipients. Transplantation Proceedings. 2006; 38(5):1323-6

44. Kloppenburg WD, Stegeman CA, Hovinga TK, Vastenburg G, Vos P, de Jong PE et al. Effect of prescribing a high protein diet and increasing the dose of dialysis on nutrition in stable chronic haemodialysis patients: a randomized, controlled trial. Nephrology Dialysis Transplantation. 2004; 19(5):1212-23

45. Kullgren KA, Scholl P, Kidwell KM, Hmiel SP. Using an interactive water bottle to target fluid adherence in pediatric kidney transplant recipients: a pilot study. Pediatric Transplantation. 2015; 19(1):35-41

46. Kuo MC, Hwang SJ, Hung CC, Tsai YY, Lee SC, Lin T et al. Fluid overload - An easily ignored and difficultly controlled problem in peritoneal dialysis patients. Nephrology. 2010; 15(S3):128

47. Lacson E, Wang W, Zebrowski B, Wingard R, Hakim RM. Outcomes associated with intradialytic oral nutritional supplements in patients undergoing maintenance hemodialysis: A quality improvement report. American Journal of Kidney Diseases. 2012; 60(4):591-600

48. Lawrence I, Thomson A, Hartley GH, Wilkinson R, Day J, Goodship TJ. The effect of dietary intervention on the management of hyperlipidemia in British renal transplant patients. Journal of Renal Nutrition. 1995; 5(2):73-7

49. Lee IH, Kang SW, Noh HJ, Shin SK, Choi KH, Ha SK. The effect of oral nutritional supplement in malnourished CAPD patients. Korean Journal of Nephrology. 1998; 17(2):299-310

50. Leon JB, Albert JM, Gilchrist G, Kushner I, Lerner E, Mach S et al. Improving albumin levels among hemodialysis patients: a community-based randomized controlled trial. American Journal of Kidney Diseases. 2006; 48(1):28-36

51. Leon JB, Majerle AD, Soinski JA, Kushner I, Ohri-Vachaspati P, Sehgal AR. Can a nutrition intervention improve albumin levels among hemodialysis patients? A pilot study. Journal of Renal Nutrition. 2001; 11(1):9-15

52. Li H, Long Q, Shao C, Fan H, Yuan L, Huang B et al. Effect of short-term low-protein diet supplemented with keto acids on hyperphosphatemia in maintenance hemodialysis patients. Blood Purification. 2011; 31(1-3):33-40

53. Li XQ, Fan YR. Clinical application of nutritional support therapy for maintenance hemodialysis patients. Modern Journal of Integrated Traditional Chinese and Western Medicine. 2008; 17(1):52-3

54. Locatelli F, Alberti D, Graziani G, Buccianti G, Redaelli B, Giangrande A. Prospective, randomised, multicentre trial of effect of protein restriction on progression of chronic renal insufficiency. Northern Italian Cooperative Study Group. Lancet. 1991; 337(8753):1299-304

55. Magden K, Hur E, Yildiz G, Kose SB, Bicak S, Yildirim I et al. The effects of strict salt control on blood pressure and cardiac condition in end-stage renal disease: Prospective-study. Renal Failure. 2013; 35(10):1344-1347

56. Magpantay L, Ziai F, Oberbauer R, Haas M. The effect of fluid intake on chronic kidney transplant failure: a pilot study. Journal of Renal Nutrition. 2011; 21(6):499-505

57. Martin-Del-Campo F, Gonzalez-Espinoza L, Rojas-Campos E, Ruiz N, Gonzalez J, Pazarin L et al. Conventional nutritional counselling maintains nutritional status of patients on continuous ambulatory peritoneal dialysis in spite of systemic inflammation and decrease of residual renal function. Nephrology. 2009; 14(5):493-8

58. McMahon EJ, Campbell KL, Bauer JD, Mudge DW. Altered dietary salt intake for people with chronic kidney disease. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD010070. DOI: 10.1002/14651858.CD010070.pub2.

59. Menon V, Kopple JD, Wang X, Beck GJ, Collins AJ, Kusek JW et al. Effect of a very low-protein diet on outcomes: Long-term follow-up of the Modification of Diet in Renal Disease (MDRD) study. American Journal of Kidney Diseases. 2009; 53(2):208-217

60. Mircescu G, Garneata L, Stancu SH, Capusa C. Effects of a supplemented hypoproteic diet in chronic kidney disease. Journal of Renal Nutrition. 2007; 17(3):179-88

61. Misra M, Ashworth J, Reaveley DA, Muller B, Brown EA. Nutritional effects of amino acid dialysate (Nutrineal) in CAPD patients. Advances in Peritoneal Dialysis. 1996; 12:311-4

62. Molaison EF, Yadrick MK. Stages of change and fluid intake in dialysis patients. Patient Education and Counseling. 2003; 49(1):5-12

63. Moretti HD, Johnson AM, Keeling-Hathaway TJ. Effects of protein supplementation in chronic hemodialysis and peritoneal dialysis patients. Journal of Renal Nutrition. 2009; 19(4):298-303

64. National Institute for Health and Clinical Excellence. The guidelines manual. London. National Institute for Health and Clinical Excellence, 2012. Available from: http://www.nice.org.uk/article/pmg6/

65. Orazio LK, Isbel NM, Armstrong KA, Tarnarskyj J, Johnson DW, Hale RE et al. Evaluation of dietetic advice for modification of cardiovascular disease risk factors in renal transplant recipients. Journal of Renal Nutrition. 2011; 21(6):462-71

66. Rangarajan D, Ramakrishnan S, Patro KC, Vakrani G, Badrinath S. A study of impact of cost-effective nutritional supplement in patients on maintenance hemodialysis. Indian Journal of Nephrology. 2014; 24(4):222-5

67. Renal Replacement Therapy Study Investigators, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M et al. An observational study fluid balance and patient outcomes in the Randomized Evaluation of Normal vs. Augmented Level of Replacement Therapy trial. Critical Care Medicine. 2012; 40(6):1753-60

68. Rhee CM, You AS, Koontz Parsons T, Tortorici AR, Bross R, St-Jules DE et al. Effect of high-protein meals during hemodialysis combined with lanthanum carbonate in hypoalbuminemic dialysis patients: findings from the FrEDI randomized controlled trial. Nephrology Dialysis Transplantation. 2016; 32(7):1233-1243

69. Rizk R, Hiligsmann M, Karavetian M, Evers S. Cost-effectiveness of dedicated dietitians for hyperphosphatemia management among hemodialysis patients in Lebanon: results from the Nutrition Education for Management of Osteodystrophy trial. Journal of Medical Economics. 2017; 20(10):1024-1038

70. Rizk R, Karavetian M, Hiligsmann M, Evers SM. Effect of stage-based education provided by dedicated dietitians on hyperphosphataemic haemodialysis patients: results from the Nutrition Education for Management of Osteodystrophy randomised controlled trial. Journal of Human Nutrition & Dietetics. 2017; 30:554-562

71. Rodrigues Telini LS, de Carvalho Beduschi G, Caramori JC, Castro JH, Martin LC, Barretti P. Effect of dietary sodium restriction on body water, blood pressure, and inflammation in hemodialysis patients: a prospective randomized controlled study. International Urology and Nephrology. 2014; 46(1):91-7

72. Rupp JW, Stone RA, Gunning BE. Sodium versus sodium fluid restriction in hemodialysis: Control of weight gains and blood pressures. American Journal of Clinical Nutrition. 1978; 31(10):1952-1955

73. Sagawa M, Oka M, Chaboyer W. The utility of cognitive behavioural therapy on chronic haemodialysis patients' fluid intake: a preliminary examination. International Journal of Nursing Studies. 2003; 40(4):367-73

74. Scholl P, Kullgren K, Hmiel P. Intervention to increase fluid intake following pediatric renal transplant. Pediatric Transplantation. 2011; 15(S1):81

75. Sharp J, Wild MR, Gumley AI, Deighan CJ. A cognitive behavioral group approach to enhance adherence to hemodialysis fluid restrictions: a randomized controlled trial. American Journal of Kidney Diseases. 2005; 45(6):1046-57

76. Stachowska E, Wesolowska T, Safranow K, Domanski L, Rac M, Dziedziejko V et al. Simple dietary interventions reduce the risk factors of atherosclerosis in renal graft recipients. Journal of Renal Nutrition. 2005; 15(3):291-7

77. Steiber AL, Handu DJ, Cataline DR, Deighton TR, Weatherspoon LJ. The impact of nutrition intervention on a reliable morbidity and mortality indicator: the hemodialysis-prognostic nutrition index. Journal of Renal Nutrition. 2003; 13(3):186-90

78. Teixido-Planas J, Ortiz A, Coronel F, Montenegro J, Lopez-Menchero R, Ortiz R et al. Oral protein-energy supplements in peritoneal dialysis: a multicenter study. Peritoneal Dialysis International. 2005; 25(2):163-72

79. Tsay SL. Self-efficacy training for patients with end-stage renal disease. Journal of Advanced Nursing. 2003; 43(4):370-5

80. Waugh NR, Robertson AM. Protein restriction for diabetic renal disease. Cochrane Database of Systematic Reviews 2000, Issue 2. Art. No.: CD002181. DOI: 10.1002/14651858.CD002181.

81. Welch JL, Thomas-Hawkins C. Psycho-educational strategies to promote fluid adherence in adult hemodialysis patients: a review of intervention studies. International Journal of Nursing Studies. 2005; 42(5):597-608

82. Williams PS, Stevens ME, Fass G, Irons L, Bone JM. Failure of dietary protein and phosphate restriction to retard the rate of progression of chronic renal failure: A prospective, randomized, controlled trial. Quarterly Journal of Medicine. 1991; 81(294):837-855

Appendices

Appendix A: Review protocols

Table 8: Review protocol: Dietary management and fluid restriction

Field	Content
Review question	What is the clinical and cost effectiveness of dietary management and/or fluid restriction for people undergoing RRT or conservative management?
Type of review question	Intervention
Objective of the review	Determining the clinical and cost effectiveness of diet management and fluid restriction for people undergoing RRT or conservative management.
Eligibility criteria – population / disease / condition / issue / domain	Children, young people and adults undergoing RRT or conservative management Children and young people (0 to 18) being prepared for RRT or conservative management Stratified by: Age (<2, 2 to <18, 18 to <70, ≥70) Dialysis, transplant, conservative management DM vs no DM
Eligibility criteria – interventions	Diet management (as a minimum including assessment and general dietary advice aimed at ≥1 of sodium, potassium or protein) Fluid restriction (including advice) Usual care/sham
Eligibility criteria – comparator(s) / control or reference (gold) standard	Diet management vs usual care/sham Fluid restriction vs usual care/sham Combined* diet and fluid management vs usual care/sham *Studies in which for example sodium intake and fluid intake are part of the intervention
Outcomes and prioritisation	Critical Patient, family/carer health-related quality of life (continuous) Mortality (dichotomous and time to event) Important Hospitalisation (rates or continuous) Subjective global assessment or malnutrition universal screen tool (continuous) Interdialytic weight gain (continuous) Symptom scores and functional measures (including grip strength, continuous) Psychological distress and mental wellbeing (continuous) Blood pressure (continuous) Patient, family and carer experience of care (continuous) Growth (continuous) Adverse events

	Infections (dichotomous) Acute transplant rejection episodes (dichotomous) When outcomes are reported at multiple timepoints, the later timepoints will be prioritised. All outcomes must be reported after at least 4 weeks of the intervention under investigation. The outcomes of mortality and hospitalisation must be reported after at least 6 months. For quality of life, symptom scores/functional measures, psychological distress/mental wellbeing and experience of care, any validated measures will be accepted. Absolute MIDs of 30 per 1000 will be used for mortality and modality failure. Absolute MIDs of 100 per 1000 will be used for all other outcomes dichotomous outcomes. Where relative MIDs are required (if absolute effects are unavailable), 0.90 to 1.11 will be used for mortality and modality failure. The default relative MIDs of 0.8 to 1.25 will be used for all other dichotomous outcomes. Default continuous MIDs of 0.5x SD will be used for all continuous outcomes, except where published, validated MIDs exist.
Eligibility criteria – study design	RCTs will be prioritised. If insufficient evidence is found for any specified comparisons non-randomised studies will be considered but only if outcomes are adjusted for the following key confounders: Age Health at baseline Co-morbidities Ethnicity
Other inclusion exclusion criteria	Any studies where the RRT is being delivered for acute kidney injury, not in the context of chronic kidney disease, will be excluded. Any studies where the RRT is being predominantly (i.e. >50%) delivered in a level 2 or 3 care setting, will be excluded. Studies exclusively investigating supplementation interventions (for example IDPN) will be excluded
Proposed sensitivity / subgroup analysis, or meta-regression	General vs sodium vs potassium vs protein Adherence to program >/=50% vs <50% Advice only vs advice plus structured follow-up and monitoring
Selection process – duplicate screening / selection / analysis	No duplicate screening was deemed necessary for this question, for more information please see the separate Methods report for this guideline.
Data management (software)	• Pairwise meta-analyses were performed using Cochrane Review Manager (RevMan5). • GRADEpro was used to assess the quality of evidence for each outcome. • Endnote was used for bibliography, citations, sifting and reference management.
Information sources – databases and dates	Clinical search databases to be used: Medline, Embase, Cochrane Library Date: All years Health economics search databases to be used: Medline, Embase, NHSEED, HTA

	Date: Medline, Embase from 2014 NHSEED, HTA – all years Language: Restrict to English only Supplementary search techniques: backward citation searching Key papers: Not known
Identify if an update	Not an update
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10019
Highlight if amendment to previous protocol	Not an amendment
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendices of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Jan Dudley in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

1

2 **Table 9: Health economic review protocol**

Review question	All questions – health economic evidence
Objectives	To identify economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the individual review protocol above. • Studies must be of a relevant economic study design (cost-utility analysis, cost-effectiveness analysis, cost-benefit analysis, cost-consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of economic evaluations. (Recent reviews will be ordered although not reviewed; the bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix B.2 Health economics literature search strategy.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2001, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the 2012 NICE guidelines manual.[64] Each included study is summarised in an economic evidence profile and an evidence table. Any excluded studies are detailed in the excluded studies table with the reason for exclusion in Appendix I. **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the Committee if required. The ultimate aim is to include economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the Committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. For example, if a high quality study from a UK perspective is available a similar study from another country's perspective may be excluded. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example,

	Switzerland). • Studies set in non-OECD countries or in the USA will have been excluded before being assessed for applicability and methodological limitations. *Economic study type:* • Cost-utility analysis (most applicable). • Other type of full economic evaluation (cost-benefit analysis, cost-effectiveness analysis, cost-consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will have been excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2001 or later but that depend on unit costs and resource data entirely or predominantly from before 2001 will be rated as 'Not applicable'. • Studies published before 2001 will have been excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the economic analysis:* • The more closely the clinical effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. • The following will be rated as 'Very serious limitations' and excluded: economic analyses undertaken as part of clinical studies that are excluded from the clinical review; economic models where relative treatment effects are based entirely on studies that are excluded from the clinical review; comparative costing analyses that only look at the cost of delivering dialysis (as current UK NHS reference costs are considered a more relevant estimate of this for the guideline); within-trial economic analyses based on non-randomised studies that do not meet the minimum adjustment criteria outlined in the main review protocol.

Appendix B: Literature search strategies

B.1 Clinical search literature search strategy

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017 https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869

For more detailed information, please see the Methodology Review.

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 10: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 11 December 2017	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 – 11 December 2017	Exclusions Randomised controlled trials

Database	Dates searched	Search filter used
		Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2017 Issue 12 of12 CENTRAL to 2017 Issue 11 of12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 4 of 4	None

1 **Medline (Ovid) search terms**

1.	exp Renal Replacement Therapy/
2.	((renal or kidney) adj2 replace*).ti,ab.
3.	(hemodiafilt* or haemodiafilt* or (biofilt* adj1 acetate-free)).ti,ab.
4.	(hemodialys* or haemodialys*).ti,ab.
5.	((kidney* or renal) adj3 (transplant* or graft*)).ti,ab.
6.	capd.ti,ab.
7.	dialys*.ti,ab.
8.	(artificial adj1 kidney*).ti,ab.
9.	or/1-8
10.	limit 9 to English language
11.	letter/
12.	editorial/
13.	news/
14.	exp historical article/
15.	Anecdotes as Topic/
16.	comment/
17.	case report/
18.	(letter or comment*).ti.
19.	or/11-18
20.	randomized controlled trial/ or random*.ti,ab.
21.	19 not 20
22.	animals/ not humans/
23.	Animals, Laboratory/
24.	exp animal experiment/
25.	exp animal model/
26.	exp Rodentia/
27.	(rat or rats or mouse or mice).ti.
28.	or/21-27
29.	10 not 28
30.	randomized controlled trial.pt.
31.	controlled clinical trial.pt.
32.	randomi#ed.ti,ab.
33.	placebo.ab.
34.	drug therapy.fs.
35.	randomly.ti,ab.
36.	trial.ab.

37.	groups.ab.
38.	or/30-37
39.	Clinical Trials as topic.sh.
40.	trial.ti.
41.	or/30-33,35,39-40
42.	Meta-Analysis/
43.	Meta-Analysis as Topic/
44.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
45.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
46.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
47.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
48.	(search* adj4 literature).ab.
49.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
50.	cochrane.jw.
51.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
52.	or/42-51
53.	29 and (41 or 52)

1 **Embase (Ovid) search terms**

1.	exp *renal replacement therapy/
2.	((renal or kidney) adj2 replace*).ti,ab.
3.	(hemodiafilt* or haemodiafilt* or (biofilt* adj1 acetate-free)).ti,ab.
4.	(hemodialys* or haemodialys*).ti,ab.
5.	((kidney* or renal) adj3 (transplant* or graft*)).ti,ab.
6.	capd.ti,ab.
7.	dialys*.ti,ab.
8.	(artificial adj1 kidney*).ti,ab.
9.	or/1-8
10.	limit 9 to English language
11.	letter.pt. or letter/
12.	note.pt.
13.	editorial.pt.
14.	case report/ or case study/
15.	(letter or comment*).ti.
16.	or/11-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animal/ not human/
20.	nonhuman/
21.	exp Animal Experiment/
22.	exp Experimental Animal/
23.	animal model/
24.	exp Rodent/

25.	(rat or rats or mouse or mice).ti.
26.	or/18-25
27.	10 not 26
28.	random*.ti,ab.
29.	factorial*.ti,ab.
30.	(crossover* or cross over*).ti,ab.
31.	((doubl* or singl*) adj blind*).ti,ab.
32.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
33.	crossover procedure/
34.	single blind procedure/
35.	randomized controlled trial/
36.	double blind procedure/
37.	or/28-36
38.	systematic review/
39.	meta-analysis/
40.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
41.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
42.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
43.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
44.	(search* adj4 literature).ab.
45.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
46.	cochrane.jw.
47.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
48.	or/38-47
49.	27 and (37 or 48)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Renal Replacement Therapy] explode all trees
#2.	((renal or kidney*) near/2 replace*):ti,ab
#3.	(hemodiafilt* or haemodiafilt* or haemofilt* or hemofilt*):ti,ab
#4.	(hemodialys* or haemodialys*):ti,ab
#5.	((kidney* or renal or pre-empt* or preempt*) near/3 (transplant* or graft*)):ti,ab
#6.	(capd or apd or ccpd or dialys*):ti,ab
#7.	(biofilt* near/1 acetate-free):ti,ab
#8.	(artificial near/1 kidney*):ti,ab
#9.	(or #1-#8)

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to renal replacement therapy population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 11: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline & Embase	2014 – 11 December 2017	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA & NHS EED- Inception – 11 December 2017	None

Medline (Ovid) search terms

1.	exp Renal Replacement Therapy/
2.	((renal or kidney) adj2 replace*).ti,ab.
3.	(hemodiafilt* or haemodiafilt* or (biofilt* adj1 acetate-free)).ti,ab.
4.	(hemodialys* or haemodialys*).ti,ab.
5.	((kidney* or renal) adj3 (transplant* or graft*)).ti,ab.
6.	capd.ti,ab.
7.	dialys*.ti,ab.
8.	(artificial adj1 kidney*).ti,ab.
9.	or/1-8
10.	limit 9 to English language
11.	letter/
12.	editorial/
13.	news/
14.	exp historical article/
15.	Anecdotes as Topic/
16.	comment/
17.	case report/
18.	(letter or comment*).ti.
19.	or/11-18
20.	randomized controlled trial/ or random*.ti,ab.
21.	19 not 20
22.	animals/ not humans/
23.	Animals, Laboratory/
24.	exp animal experiment/
25.	exp animal model/
26.	exp Rodentia/
27.	(rat or rats or mouse or mice).ti.
28.	or/21-27
29.	10 not 28
30.	Economics/
31.	Value of life/
32.	exp "Costs and Cost Analysis"/
33.	exp Economics, Hospital/
34.	exp Economics, Medical/
35.	Economics, Nursing/
36.	Economics, Pharmaceutical/

37.	exp "Fees and Charges"/
38.	exp Budgets/
39.	budget*.ti,ab.
40.	cost*.ti.
41.	(economic* or pharmaco?economic*).ti.
42.	(price* or pricing*).ti,ab.
43.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
44.	(financ* or fee or fees).ti,ab.
45.	(value adj2 (money or monetary)).ti,ab.
46.	or/30-45
47.	29 and 46

1 **Embase (Ovid) search terms**

1.	exp renal replacement therapy/
2.	((renal or kidney) adj2 replace*).ti,ab.
3.	(hemodiafilt* or haemodiafilt* or (biofilt* adj1 acetate-free)).ti,ab.
4.	(hemodialys* or haemodialys*).ti,ab.
5.	((kidney* or renal) adj3 (transplant* or graft*)).ti,ab.
6.	capd.ti,ab.
7.	dialys*.ti,ab.
8.	(artificial adj1 kidney*).ti,ab.
9.	or/1-8
10.	limit 9 to English language
11.	letter.pt. or letter/
12.	note.pt.
13.	editorial.pt.
14.	case report/ or case study/
15.	(letter or comment*).ti.
16.	or/11-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animal/ not human/
20.	nonhuman/
21.	exp Animal Experiment/
22.	exp Experimental Animal/
23.	animal model/
24.	exp Rodent/
25.	(rat or rats or mouse or mice).ti.
26.	or/18-25
27.	10 not 26
28.	*health economics/

29.	exp *economic evaluation/
30.	exp *health care cost/
31.	exp *fee/
32.	budget/
33.	funding/
34.	budget*.ti,ab.
35.	cost*.ti.
36.	(economic* or pharmaco?economic*).ti.
37.	(price* or pricing*).ti,ab.
38.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
39.	(financ* or fee or fees).ti,ab.
40.	(value adj2 (money or monetary)).ti,ab.
41.	or/28-40
42.	27 and 41

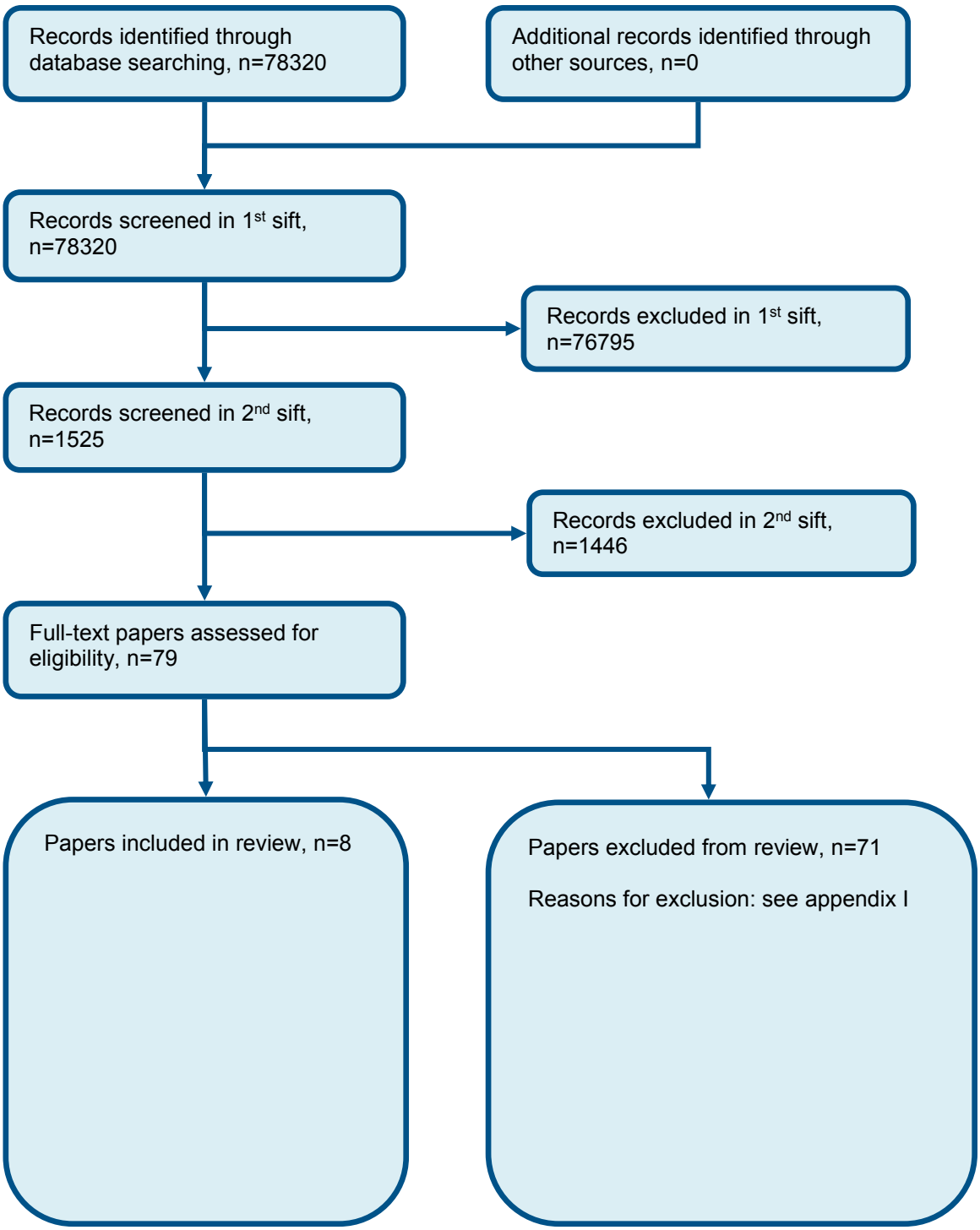
1 **NHS EED and HTA (CRD) search terms**

#1.	MeSH DESCRIPTOR Renal Replacement Therapy EXPLODE ALL TREES
#2.	(((renal or kidney) adj2 replace*))
#3.	((hemodiafilt* or haemodiafilt* or (biofilt* adj1 acetate-free)))
#4.	((hemodialys* or haemodialys*))
#5.	(((kidney* or renal) adj3 (transplant* or graft*)))
#6.	(capd)
#7.	(dialys*)
#8.	((artificial adj1 kidney*))
#9.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

2

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of dietary management and fluid restriction



Appendix D: Clinical evidence tables

Study	De Vries 2016[21]
Study type	RCT (Patient randomised; Crossover: None)
Number of studies (number of participants)	1 (n=23)
Countries and setting	Conducted in Netherlands; Setting:
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis:
Stratum	Transplant
Subgroup analysis within study	Not applicable
Inclusion criteria	Kidney transplant recipients, transplant at least 1 year previous, over 18, stable transplant function, BP >/= 120/80 mmHg
Exclusion criteria	SBP >180, DBP >100, use of IS withdrawal regimen
Recruitment/selection of patients	Screened all kidney transplant recipients who came to nephrology outpatient clinic
Age, gender and ethnicity	Age - Mean (SD): 58 (8). Gender (M:F): 50:50. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=23) Intervention 1: Diet management. Low sodium diet - targeted at 50mmol/d. 24hr urine samples at midpoint and oral feedback given after. Duration 6 weeks. Concurrent medication/care: Usual care + BP medication was kept stable unless orthostatic hypotension occurred. Indirectness: No indirectness (n=23) Intervention 2: Usual care. Normal sodium diet - aimed at 150mmol/d. Duration 6 weeks . Concurrent medication/care: Usual care + stable BP medication unless orthostatic hypotension. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIET MANAGEMENT - SODIUM RESTRICTION versus USUAL CARE Protocol outcome 1: Blood pressure - Actual outcome for Transplant: SBP at 6 weeks; Group 1: mean 129 (SD 12); n=22, Group 2: mean 140 (SD 14); n=22 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Transplant: DBP at 6 weeks; Group 1: mean 79 (SD 8); n=22, Group 2: mean 86 (SD 8); n=22 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Hospitalisation ; SGA/MUST ; Interdialytic weight gain ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Experience of care ; Growth ; Infections ; Transplant rejection episodes

Study	Ebrahimi 2016[22]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=99)
Countries and setting	Conducted in Iran
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Dialysis
Subgroup analysis within study	Not applicable
Inclusion criteria	Older than 18, on HD for last 12 months, compliant with HD treatment
Exclusion criteria	Psychoemotional problems, psychotropic medication
Age, gender and ethnicity	Age - Mean (SD): 51 (11). Gender (M:F): 62:38. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=48) Intervention 1: Combined diet and fluid - Combined diet and fluids. Face to face educational sessions, 30-40 minute with 10-15 minutes of Q&A, twice a week for 12 weeks (total of 24 sessions), accompanied by pamphlet focused on importance of adherence to healthy diet, avoiding harmful consequences of poison accumulation in blood and tissues, a list of food restriction and limits in fluid intake. Duration 12 weeks. Concurrent medication/care: Usual care . Indirectness: No indirectness (n=51) Intervention 2: Usual care. Nil specified. Duration 12 weeks . Concurrent medication/care: Usual care. Indirectness: No indirectness
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED DIET AND FLUIDS versus USUAL CARE

Protocol outcome 1: Quality of life
- Actual outcome for Dialysis: KDQOL - overall (0-100, higher is better) at 12 weeks; Group 1: mean 67.4 (SD 5.99); n=48, Group 2: mean 58.8 (SD 6.21); n=51
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

	Mortality ; Hospitalisation ; SGA/MUST ; Interdialytic weight gain ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Blood pressure ; Experience of care ; Growth ; Infections ; Transplant rejection episodes
Protocol outcomes not reported by the study	

Study	Kauric-Klein 2012[42]
Study type	RCT (Centre randomised; Parallel)
Number of studies (number of participants)	(n=118)
Countries and setting	Conducted in USA; Setting: HD units in Detroit
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 4 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Dialysis
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Age, gender and ethnicity	Age - Range of means: 56-63. Gender (M:F): Define. Ethnicity: 80% African American, 15% Caucasian, 5% Middle Eastern
Further population details	
Indirectness of population	No indirectness
Interventions	(n=59) Intervention 1: Combined diet and fluid - Combined diet and fluids. 2 BP education sessions, 12 week monitoring, aiming for pre-HD BP <140/90 and post-HD BP <130/80, sodium intake <2g/d, fluid intake <1500ml/d or less than 2.5kg WG between HD sessions, 100% adherence to HD and medication regimens. Duration 4 months . Concurrent medication/care: Usual care. Indirectness: No indirectness (n=59) Intervention 2: Usual care. BP monitoring and medication adjustment by HCPs in HD unit as needed. Duration 4 months . Concurrent medication/care: Usual care. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED DIET AND FLUIDS versus USUAL CARE

Protocol outcome 1: Interdialytic weight gain
- Actual outcome for Dialysis: Average fluid gain, kg at 16 weeks; Group 1: mean 2.4 (SD 1.2); n=59, Group 2: mean 2.5 (SD 1); n=59
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: RoB mostly introduced via cluster randomisation of only 6 HD units; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Blood pressure - Actual outcome for Dialysis: SBP at 16 weeks; Group 1: mean 153.5 (SD 12.2); n=59, Group 2: mean 160 (SD 14.8); n=59 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: RoB mostly introduced via cluster randomisation of only 6 HD units; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Dialysis: DBP at 16 weeks; Group 1: mean -3.9 (SD 9.3); n=59, Group 2: mean -3.1 (SD 10.3); n=59; Comments: Calculated with assumed CC of 0.5 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: RoB mostly introduced via cluster randomisation of only 6 HD units; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Hospitalisation ; SGA/MUST ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Experience of care ; Growth ; Infections ; Transplant rejection episodes

Study	Keven 2006[43]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=32)
Countries and setting	Conducted in Turkey
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Transplant
Subgroup analysis within study	Not applicable
Inclusion criteria	Kidney transplant, stable graft function, no renal artery stenosis, receiving hypertensive medication
Exclusion criteria	Nil else
Age, gender and ethnicity	Age - Range of means: 40-43. Gender (M:F): 25:7. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=18) Intervention 1: Diet management. 80-100mmol/d salt intake, seen at 4, 8 and 12 weeks by dietician . Duration 12 weeks. Concurrent medication/care: Blood pressure medication could be titrated by HCP (n=14) Intervention 2: Usual care. Usual care. Duration 12 weeks. Concurrent medication/care: BP medication could be titrated
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIET MANAGEMENT versus USUAL CARE

Protocol outcome 1: Blood pressure
- Actual outcome for Transplant: SBP at 12 weeks; Group 1: mean 116 (SD 11); n=18, Group 2: mean 132 (SD 13); n=14
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Transplant: DBP at 12 weeks; Group 1: mean 72 (SD 10); n=18, Group 2: mean 80 (SD 9); n=14
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Quality of life ; Mortality ; Hospitalisation ; SGA/MUST ; Interdialytic weight gain ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Experience of care ; Growth ; Infections ; Transplant rejection episodes	
Protocol outcomes not reported by the study	

Study	Molaison 2003[62]
Study type	RCT (Centre randomised; Parallel)
Number of studies (number of participants)	1 (n=314)
Countries and setting	Conducted in USA
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Dialysis
Subgroup analysis within study	Not applicable
Inclusion criteria	Receiving dialysis in centre
Exclusion criteria	Nil specified
Age, gender and ethnicity	Age - Mean (SD): 53 (15). Gender (M:F): 52:48. Ethnicity: 82% African American
Further population details	
Indirectness of population	No indirectness
Interventions	(n=216) Intervention 1: Fluid restriction. Group education sessions with dieticians supported by handouts and specific feedback for those exceeding the average 2.5kg weight limit for each month, intervention aimed at increasing adherence to fluid restrictions, increasing knowledge of sources of fluid, understanding meaning and consequences of IDWG, how to aim for 1000ml/d of fluid and avoid excessive fluid intake. Duration 12 weeks . Concurrent medication/care: Usual care. Indirectness: No indirectness (n=100) Intervention 2: Usual care. Nil specified beyond "follow usual protocol". Duration 12 weeks. Concurrent medication/care: Usual care. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: FLUID RESTRICTION versus USUAL CARE

Protocol outcome 1: Interdialytic weight gain
- Actual outcome for Dialysis: IDWG at 12 weeks; Group 1: mean 3.41 (SD 1.14); n=215, Group 2: mean 3.57 (SD 1.21); n=99
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Mortality ; Hospitalisation ; SGA/MUST ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Blood pressure ; Experience of care ; Growth ; Infections ; Transplant rejection episodes

Study	Rodrigues Telini 2014[71]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=39)
Countries and setting	Conducted in Brazil
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 16 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Dialysis
Subgroup analysis within study	Not applicable
Inclusion criteria	At least 18, on haemodialysis, CRP at least 0.7mg/dL
Exclusion criteria	Acute inflammatory process, chronic inflammatory disease, antibiotic use in last 2 months, malignancies, CVC use
Age, gender and ethnicity	Age - Range of means: 56-60. Gender (M:F): 69:31. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=21) Intervention 1: Diet management. Sodium restriction, aim for 2g reduction in sodium intake, equating to 5g reduction in salt intake. Dietary instructions provided to all participants. Duration 16 weeks. Concurrent medication/care: Usual care . Indirectness: No indirectness (n=18) Intervention 2: Usual care. Nil else specified. Duration 16 weeks. Concurrent medication/care: Usual care. Indirectness: No indirectness
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIET MANAGEMENT versus USUAL CARE

Protocol outcome 1: Blood pressure
- Actual outcome for Dialysis: SBP at 16 weeks; Group 1: mean 147.5 (SD 18.25); n=21, Group 2: mean 149.22 (SD 20.44); n=18
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Dialysis: DBP at 16 weeks; Group 1: mean 87.38 (SD 11.91); n=21, Group 2: mean 83.6 (SD 22.9); n=18
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Hospitalisation ; SGA/MUST ; Interdialytic weight gain ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Experience of care ; Growth ; Infections ; Transplant rejection episodes

Study	Sharp 2005[75]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=56)
Countries and setting	Conducted in United Kingdom; Setting: NHS OP HD units in Scotland
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Dialysis
Subgroup analysis within study	Not applicable
Inclusion criteria	Hx of problematic fluid restriction adherence (avg. IDWG >2.5kg), HD 3x a week for at least 3 months, at least 18, living at home, no cognitive disorders, no visual or hearing impairments
Exclusion criteria	Nil else
Age, gender and ethnicity	Age - Mean (SD): 54 (13). Gender (M:F): 65:35. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=29) Intervention 1: Fluid restriction. GULP (Glasgow University Liquid intake Program), group format (3-8 people), hour long sessions, once weekly for 4 weeks, supervised by trainee clinical psychologist, information focused on importance of fluid restrictions, elements of CBT. Duration 4 weeks. Concurrent medication/care: Usual care. Indirectness: No indirectness (n=27) Intervention 2: Usual care. Nil else specified. Duration 4 weeks . Concurrent medication/care: Usual care. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: FLUID RESTRICTION versus USUAL CARE

Protocol outcome 1: Quality of life
- Actual outcome: SF-36 physical function at 4 weeks; MD; 7.28 (95%CI -5.2 to 19.76);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Outcome based on change scores and adjusted but 0.3kg difference at baseline; Group 1 Number missing: 6, Reason: 3 ill health, 1 transferred, 1 transplant, 1 deceased; Group 2 Number missing: 4, Reason: 2 ill health, 1

deceased, 1 transferred - Actual outcome: SF-36 mental function at 4 weeks; MD; 12.64 (95%CI 5.59 to 19.69); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Outcome based on change scores and adjusted but 0.3kg difference at baseline; Group 1 Number missing: 6, Reason: 3 ill health, 1 transferred, 1 transplant, 1 deceased; Group 2 Number missing: 4, Reason: 2 ill health, 1 deceased, 1 transferred Protocol outcome 2: Interdialytic weight gain - Actual outcome: IDWG kg at 4 weeks; MD; -0.25 (95%CI -0.66 to 0.16); Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Outcome based on change scores and adjusted but 0.3kg difference at baseline; Group 1 Number missing: 6, Reason: 3 ill health, 1 transferred, 1 transplant, 1 deceased; Group 2 Number missing: 4, Reason: 2 ill health, 1 deceased, 1 transferred	
Protocol outcomes not reported by the study	Mortality ; Hospitalisation ; SGA/MUST ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Blood pressure ; Experience of care ; Growth ; Infections ; Transplant rejection episodes

Study	Tsay 2003[79]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=64)
Countries and setting	Conducted in Taiwan
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 24 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Dialysis
Subgroup analysis within study	Not applicable
Inclusion criteria	Receiving HD 3x a week, over 18, lived at home
Exclusion criteria	Acute illness, psychological or cognitive disorders
Age, gender and ethnicity	Age - Mean (SD): 58 (12). Gender (M:F): Not specified. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: Combined diet and fluid - Combined diet and fluids. 12 sessions, each 1 hour, 3x a week by two trained nurse nephrology specialists, focused on pathophysiology of renal failure, HD, medications, complications, nutrition, fluid restriction, control of thirst/urge to drink, stress management, interviewed about dietary habits and fluid intake. Duration 4 weeks. Concurrent medication/care: Usual care . Indirectness: No indirectness (n=32) Intervention 2: Usual care. Nil else specified. Duration 4 weeks. Concurrent medication/care: Usual care. Indirectness: No indirectness
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED DIET AND FLUIDS versus USUAL CARE

Protocol outcome 1: Interdialytic weight gain
- Actual outcome for Dialysis: IDWG at 6 months; Group 1: mean -0.72 kg (SD 0.71); n=32, Group 2: mean -0.06 kg (SD 0.86); n=32; Comments: Calculated with assumed 0.5 correlation coefficient from baseline and final scores
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Baseline IDWG for intervention 3.3, 2.6 for control; Group 1 Number

missing: 1, Reason: Hospitalisation or relocation; Group 2 Number missing: 1, Reason: Hospitalisation or relocation	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Hospitalisation ; SGA/MUST ; Symptom scores/functional measures ; Psychological distress/mental wellbeing ; Blood pressure ; Experience of care ; Growth ; Infections ; Transplant rejection episodes

1

2

3

Appendix E: Forest plots

E.1 Dietary management vs usual care, transplant

Figure 2: Systolic blood pressure

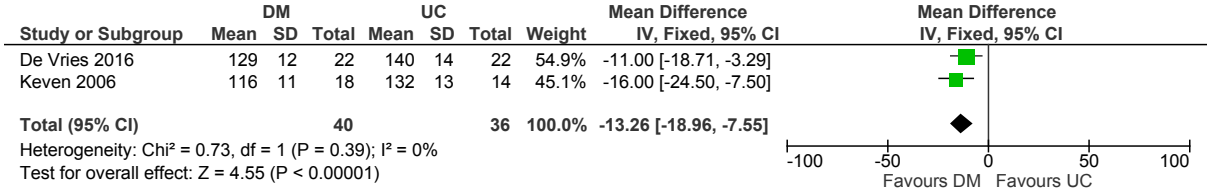
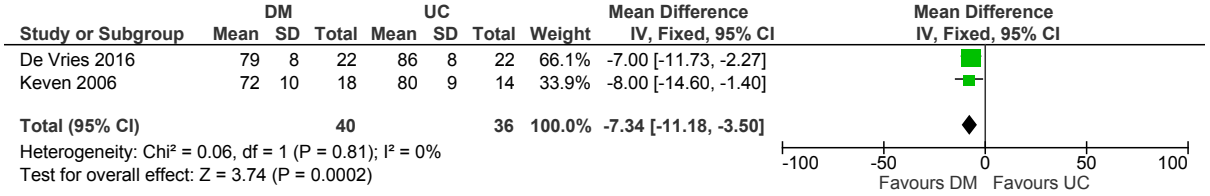


Figure 3: Diastolic blood pressure



E.2 Dietary management vs usual care, dialysis

Figure 4: Systolic blood pressure

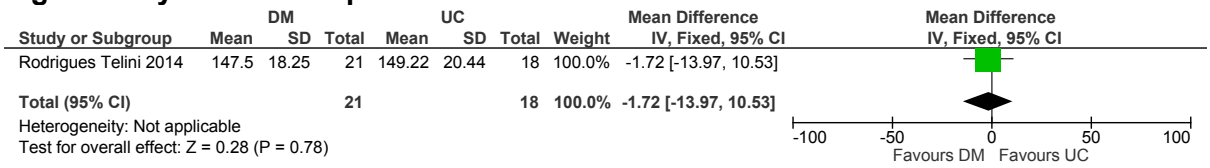
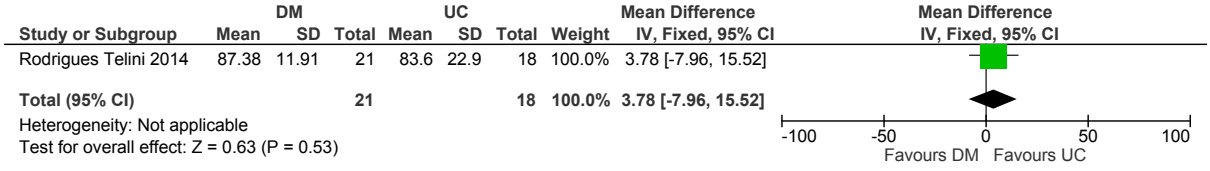


Figure 5: Diastolic blood pressure



E.3 Fluid restriction vs usual care, dialysis

Figure 6: QoL (SF36, physical, 0-100, higher is better)

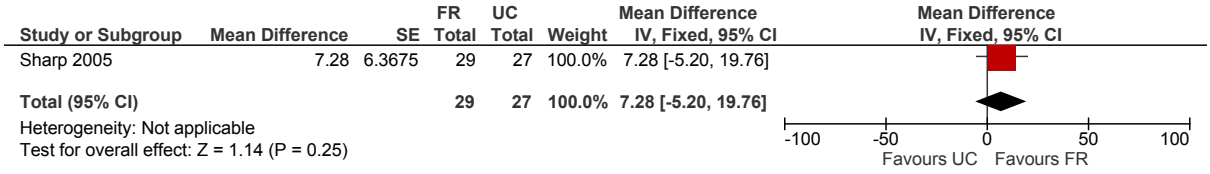


Figure 7: QoL (SF36, mental, 0-100, higher is better)

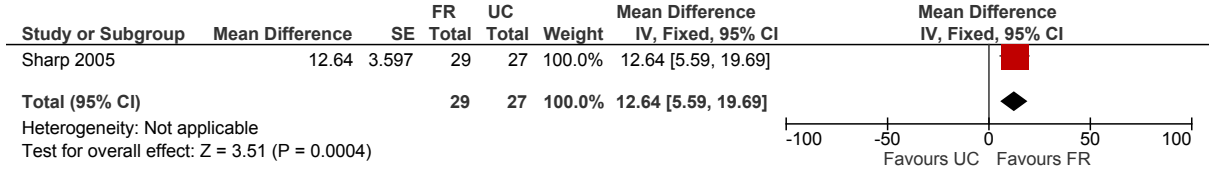
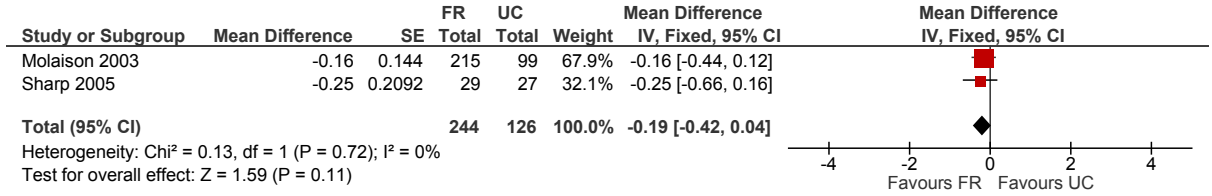


Figure 8: Interdialytic weight gain (kg)



E.4 Combined dietary and fluid management vs usual care, dialysis

Figure 9: QoL (KDQOL, 0-100, higher is better)

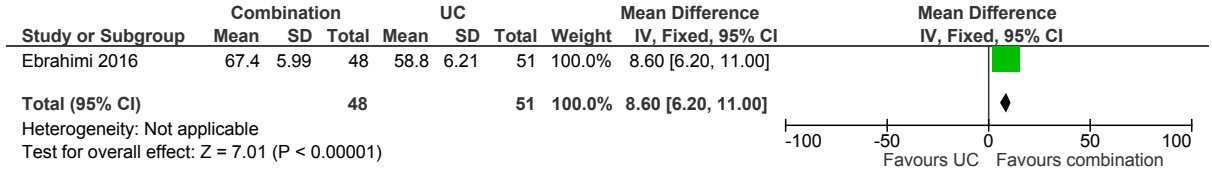


Figure 10: Interdialytic weight gain (kg)

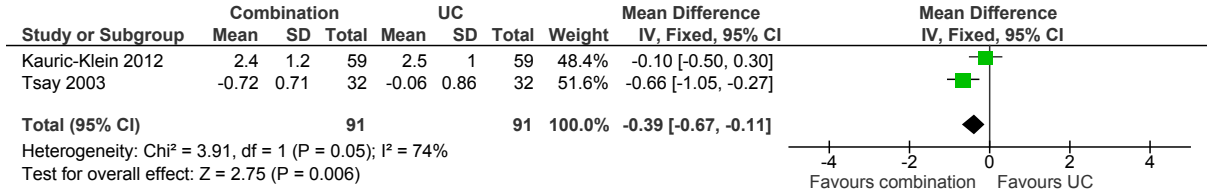


Figure 11: Systolic blood pressure

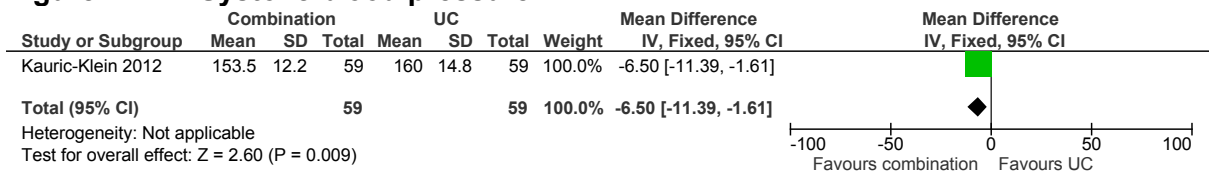
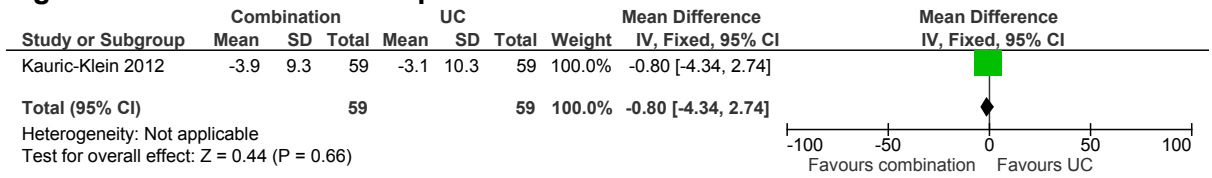


Figure 12: Diastolic blood pressure



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Appendix F: GRADE tables

Table 12: Clinical evidence profile: dietary management vs usual care, transplant, >18 to 70

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dietary management	Usual care	Relative (95% CI)	Absolute		
Systolic blood pressure (6-12w) (follow-up 6-12 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	36	-	MD 13.26 lower (18.96 to 7.55 lower)	⊕⊕OO LOW	IMPORTANT
Diastolic blood pressure (6-12w) (follow-up 6-12 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	36	-	MD 7.34 lower (11.18 to 3.5 lower)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 13: Clinical evidence profile: dietary management vs usual care, dialysis, >18 to 70

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dietary management	Usual care	Relative (95% CI)	Absolute		
Systolic blood pressure (16 weeks) (follow-up 16 weeks; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	21	18	-	MD 1.72 lower (13.97 lower to 10.53 higher)	⊕OOO VERY LOW	IMPORTANT
Diastolic blood pressure (16 weeks) (follow-up 16 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	21	18	-	MD 3.78 higher (7.96 lower to 15.52 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 14: Clinical evidence profile: fluid restriction vs usual care, dialysis, >18 to 70

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fluid restriction**	**Usual care**	**Relative (95% CI)**	**Absolute**		
QoL (SF-36, physical, 0-100, higher is better, 4 weeks) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	29	27	-	MD 7.28 higher (5.2 lower to 19.76 higher)	⊕OOO VERY LOW	CRITICAL
QoL (SF-36, mental, 0-100, higher is better, 4 weeks) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	29	27	-	MD 12.64 higher (5.59 to 19.69 higher)	⊕⊕OO LOW	CRITICAL
Interdialytic weight gain (kg, 4-12 weeks) (follow-up 4-12 weeks; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	244	126	-	MD 0.19 lower (0.42 lower to 0.04 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

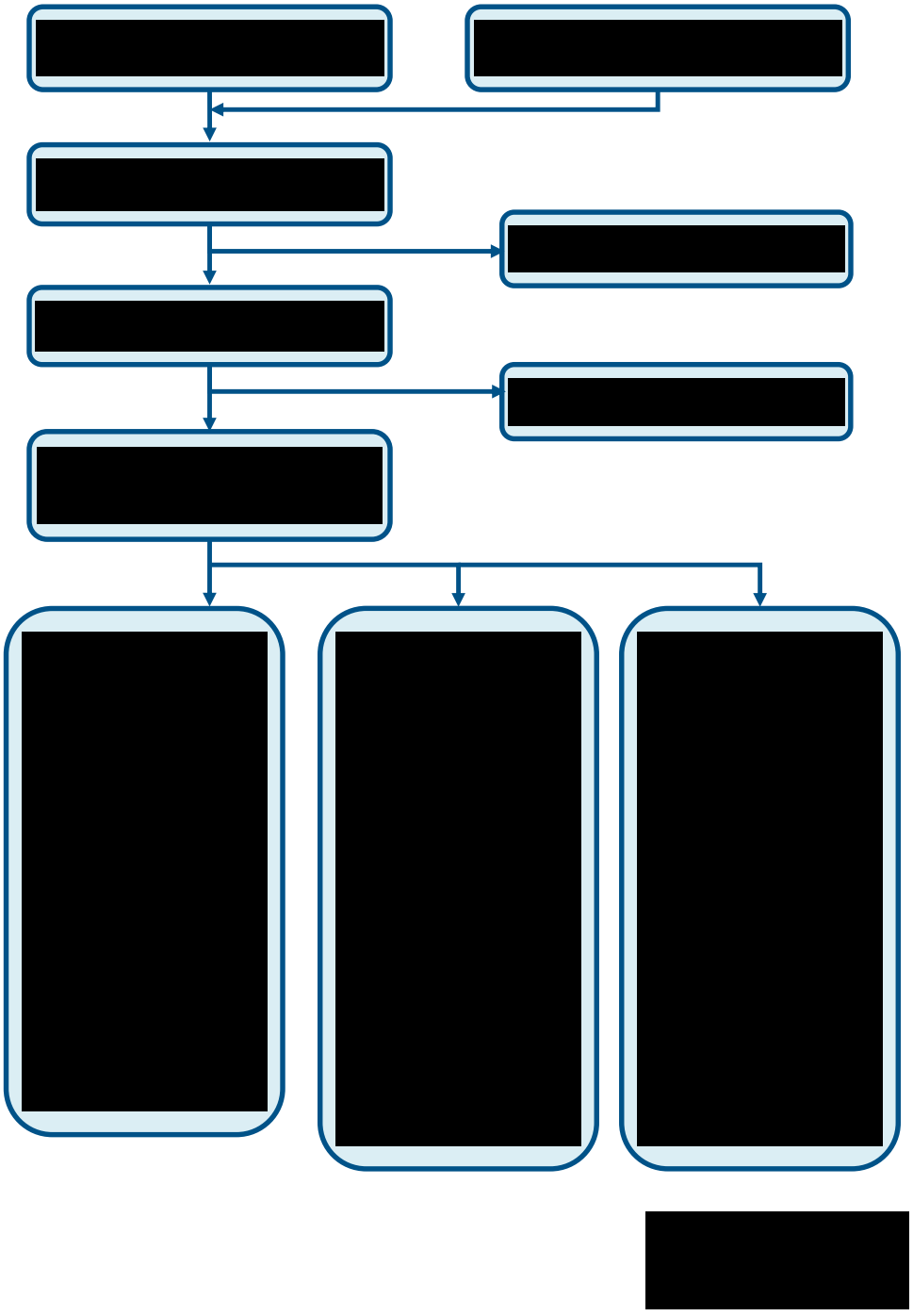
Table 15: Clinical evidence profile: dietary management and fluid restriction vs usual care, dialysis, >18 to 70

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Combined diet and fluid management	Usual care	Relative (95% CI)	Absolute		
QoL (KDQOL, 0-100, higher is better, 12w) (follow-up 12 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	48	51	-	MD 8.6 higher (6.2 to 11 higher)	⊕⊕⊕O MODERATE	CRITICAL
Interdialytic weight gain (kg, 16w) (follow-up 16 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	91	91	-	MD 0.39 lower (0.67 to 0.11 lower)	⊕⊕OO LOW	IMPORTANT
Systolic blood pressure (16w) (follow-up 16 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	59	59	-	MD 6.5 lower (11.39 to 1.61 lower)	⊕⊕OO LOW	IMPORTANT
Diastolic blood pressure (16w) (follow-up 16 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	59	59	-	MD 0.8 lower (4.34 lower to 2.74 higher)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Appendix G: Health economic evidence selection

Figure 13: Flow chart of economic study selection for the guideline



A = starting RRT
B = modality of RRT, subgroups and CM
C = sequencing
D = planning for RRT
E = When to assess
F = what to assess
G = Indicators for switching or stopping RRT
I = diet and fluids
J = frequency of review
L = decision support interventions
M = coordinating care

Appendix H: Health economic evidence tables

None.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 16: Studies excluded from the clinical review

Study	Exclusion reason
Akpele 2004[1]	Incorrect interventions
Allman 1990[2]	Incorrect interventions
Ash 2014[3]	SR, references checked
Baraz 2010[4]	Incorrect interventions
Beddhu 2015[5]	Incorrect interventions
Bellizzi 2015[6]	NRS (RCTs available)
Bellomo 2015[7]	Incorrect interventions
Borges 1996[8]	NRS (RCTs available)
Boudville 2005[9]	Review, not systematic
Brunori 2007[10]	Inappropriate comparison
Campbell 2008[12]	Not guideline condition
Campbell 2015[11]	Review, not systematic
Caria 2014[13]	Inappropriate comparison
Chertow 1994[14]	NRS (RCTs available)
Cianciaruso 2009[15]	Not guideline condition
Cotten-Sheldon 2011[16]	Abstract only
Cupisti 2016[17]	NRS (RCTs available)
Dagdeviren 2003[20]	NRS (RCTs available)
Fine 1997[23]	Incorrect interventions
Ford 2004[24]	Incorrect interventions
Fouque 2000[27]	SR, references checked
Fouque 2008[26]	Incorrect interventions
Fouque 2009[25]	SR, references checked
Fry 2007[28]	Protocol only
Hansen 2002[29]	Not guideline condition
Hare 2014[30]	No usable outcomes
Harty 1996[31]	Incorrect interventions
Hatch 1985[32]	Incorrect interventions
Hernandez Morante 2014[33]	Inappropriate comparison
Howren 2016[34]	Inappropriate comparison
Jeloka 2013[35]	Inappropriate comparison
Jiang 2009[38]	Inappropriate comparison
Jiang 2010[36]	Inappropriate comparison
Jiang 2011[37]	Inappropriate comparison
Jungers 1987[39]	Inappropriate comparison
Karavetian 2013[40]	Inappropriate comparison
Kauric-Klein 2012[41]	No usable outcomes
Kloppenburg 2004[44]	Incorrect interventions
Kullgren 2015[45]	Incorrect interventions

Study	Exclusion reason
Kuo 2010[46]	Abstract only
Lacson 2012[47]	NRS (RCTs available)
Lawrence 1995[48]	No usable outcomes
Lee 1998[49]	Not in English
Leon 2001[51]	No usable outcomes
Leon 2006[50]	Incorrect interventions
Li 2008[53]	Not in English
Li 2011[52]	No usable outcomes
Locatelli 1991[54]	Not review population
Magden 2013[55]	Wrong study design
Magpantay 2011[56]	No usable outcomes
Martin-del-Campo 2009[57]	Wrong study design
McMahon 2015[58]	SR, references checked
Menon 2009[59]	Not review population
Mircescu 2007[60]	Not guideline condition
Misra 1996[61]	Incorrect interventions
Moretti 2009[63]	Incorrect interventions
Orazio 2011[65]	Incorrect interventions
Rangarajan 2014[66]	Incorrect interventions
Renal Replacement Therapy Study Investigators 2012[67]	NRS (RCTs available)
Rhee 2016[68]	Inappropriate comparison
Rizk 2017[69]	Inappropriate comparison
Rizk 2017[70]	Incorrect interventions
Rupp 1978[72]	NRS (RCTs available)
Sagawa 2003[73]	Wrong study design
Scholl 2011[74]	Abstract only
Stachowska 2005[76]	Incorrect interventions
Steiber 2003[77]	Wrong study design
Teixido-Planas 2005[78]	Incorrect interventions
Waugh 2000[80]	SR, references checked
Welch 2005[81]	SR, references checked
Williams 1991[82]	Not guideline condition

I.21 Excluded health economic studies

2 Studies that meet the review protocol population and interventions and economic study
3 design criteria but have not been included in the review based on applicability and/or
4 methodological quality are summarised below with reasons for exclusion.

5 **Table 17: Studies excluded from the health economic review**

Reference	Reason for exclusion
None.	

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