National Institute for Health and Care Excellence

Final

RRT and conservative management

Evidence review for dietary management and fluid restriction

NICE guideline NG107

Intervention evidence review

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This evidence review was developed by the National Guideline Centre

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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 professionals (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

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 Interpreting the evidence

1.8.1 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.

1.8.2 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.

1.8.3 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.

1.8.4 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.

1.8.5 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 noted that diabetes management, weight history, lifestyle, medications, the impact of other medical conditions and advice regarding fibre may also form part of the assessment.

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 recommended that individualised information should be offered ay key points in the patient pathway, for example when starting on RRT or conservative management or when they switch to a different form of RRT or to conservative management. The committee noted that other therapeutic diets that a person may require as well as their nutritional status and biochemistry need to be taken into account when giving information.

The committee noted that for those people who show a consistent trend in unintentional loss of flesh weight, weight gain, indication from body composition monitoring, abnormal electrolyte levels or problems with fluid balance; an opportunity to discuss these problems with a renal dietitian should be offered.

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).

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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

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

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)

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

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/

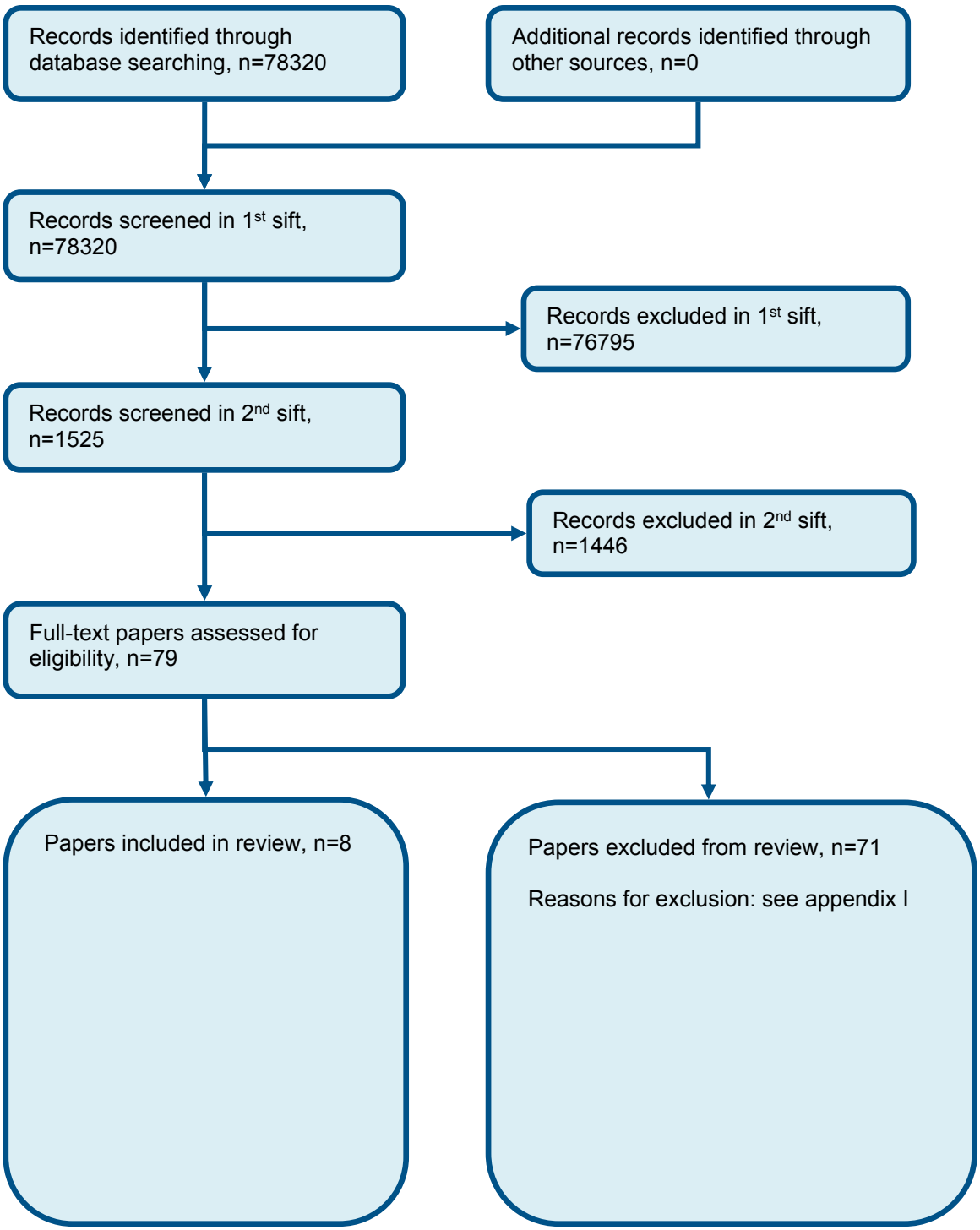
29.	exp *economic evaluation/
30.	exp *health care cost/
31.	exp *fee/
32.	budget/
33.	funding/
34.	budget*.ti,ab.
35.	cost*.ti.
36.	(economic* or pharmaco?economic*).ti.
37.	(price* or pricing*).ti,ab.
38.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.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

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

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:

Protocol outcomes not reported by the study	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

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:

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	
	Protocol outcomes not reported by the study

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

Appendix E: Forest plots

E.1 Dietary management vs usual care, transplant

Figure 2: Systolic blood pressure

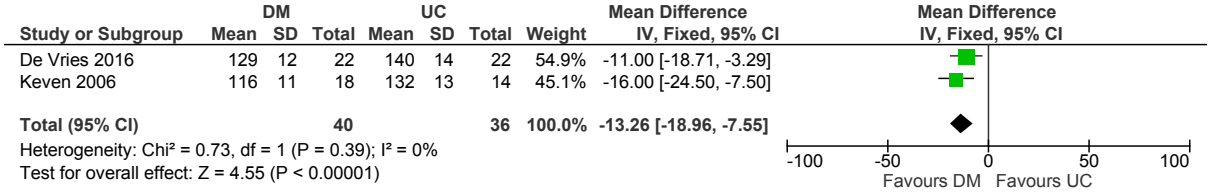
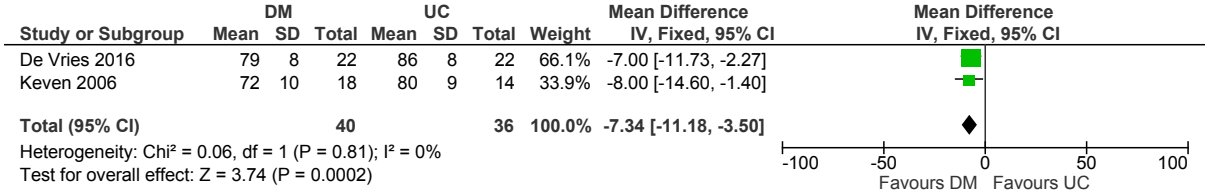


Figure 3: Diastolic blood pressure



E.2 Dietary management vs usual care, dialysis

Figure 4: Systolic blood pressure

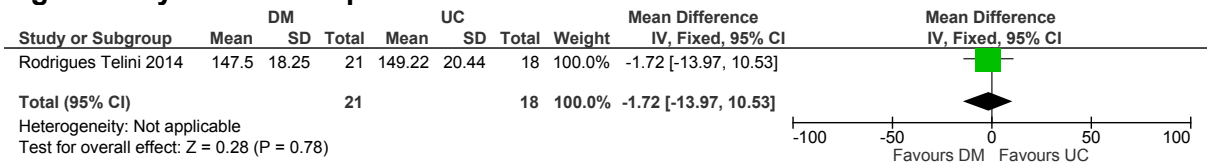
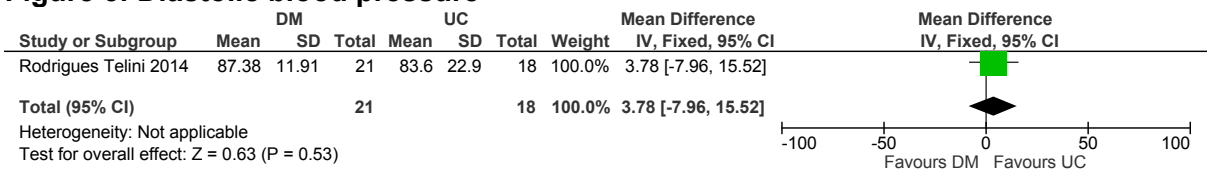


Figure 5: Diastolic blood pressure



E.3 Fluid restriction vs usual care, dialysis

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

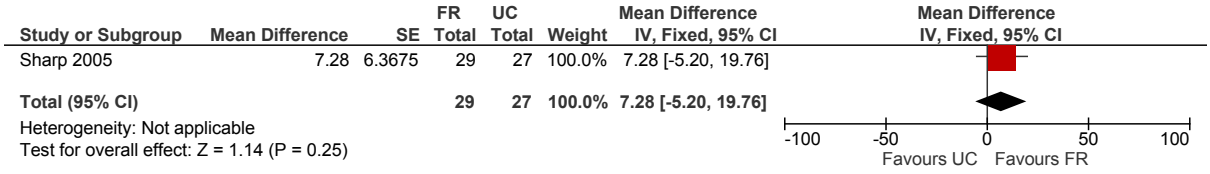


Figure 7: QoL (SF36, mental, 0-100, higher is better)

Study or Subgroup	Mean Difference	SE	FR Total	UC Total	Weight	Mean Difference IV, Fixed, 95% CI
Sharp 2005	12.64	3.597	29	27	100.0%	12.64 [5.59, 19.69]
Total (95% CI)			**29**	**27**	**100.0%**	**12.64 [5.59, 19.69]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.51 (P = 0.0004)

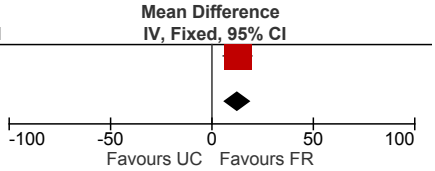
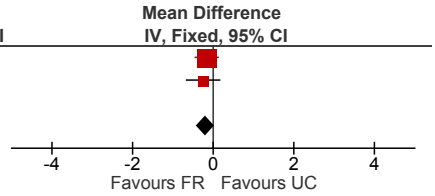


Figure 8: Interdialytic weight gain (kg)

Study or Subgroup	Mean Difference	SE	FR Total	UC Total	Weight	Mean Difference IV, Fixed, 95% CI
Molaison 2003	-0.16	0.144	215	99	67.9%	-0.16 [-0.44, 0.12]
Sharp 2005	-0.25	0.2092	29	27	32.1%	-0.25 [-0.66, 0.16]
Total (95% CI)			**244**	**126**	**100.0%**	**-0.19 [-0.42, 0.04]**

Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 1.59 (P = 0.11)



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

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

Study or Subgroup	Combination Mean	SD	Total	UC Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Ebrahimi 2016	67.4	5.99	48	58.8	6.21	51	100.0%	8.60 [6.20, 11.00]
Total (95% CI)			**48**			**51**	**100.0%**	**8.60 [6.20, 11.00]**

Heterogeneity: Not applicable
Test for overall effect: Z = 7.01 (P < 0.00001)

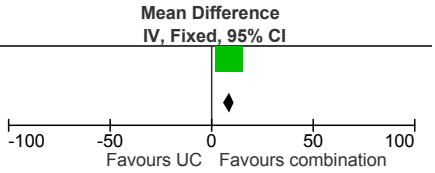


Figure 10: Interdialytic weight gain (kg)

Study or Subgroup	Combination Mean	SD	Total	UC Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kauric-Klein 2012	2.4	1.2	59	2.5	1	59	48.4%	-0.10 [-0.50, 0.30]
Tsay 2003	-0.72	0.71	32	-0.06	0.86	32	51.6%	-0.66 [-1.05, -0.27]
Total (95% CI)			**91**			**91**	**100.0%**	**-0.39 [-0.67, -0.11]**

Heterogeneity: Chi² = 3.91, df = 1 (P = 0.05); I² = 74%
Test for overall effect: Z = 2.75 (P = 0.006)

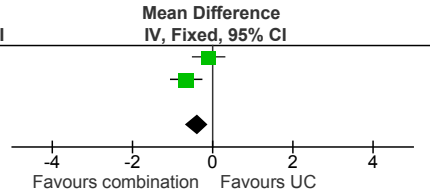


Figure 11: Systolic blood pressure

Study or Subgroup	Combination Mean	SD	Total	UC Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kauric-Klein 2012	153.5	12.2	59	160	14.8	59	100.0%	-6.50 [-11.39, -1.61]
Total (95% CI)			**59**			**59**	**100.0%**	**-6.50 [-11.39, -1.61]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.60 (P = 0.009)

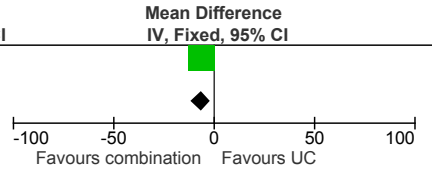
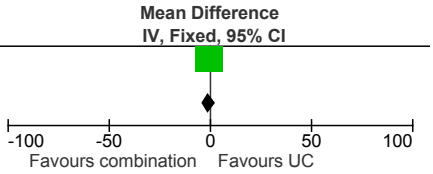


Figure 12: Diastolic blood pressure

Study or Subgroup	Combination Mean	SD	Total	UC Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Kauric-Klein 2012	-3.9	9.3	59	-3.1	10.3	59	100.0%	-0.80 [-4.34, 2.74]
Total (95% CI)			**59**			**59**	**100.0%**	**-0.80 [-4.34, 2.74]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.44 (P = 0.66)



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

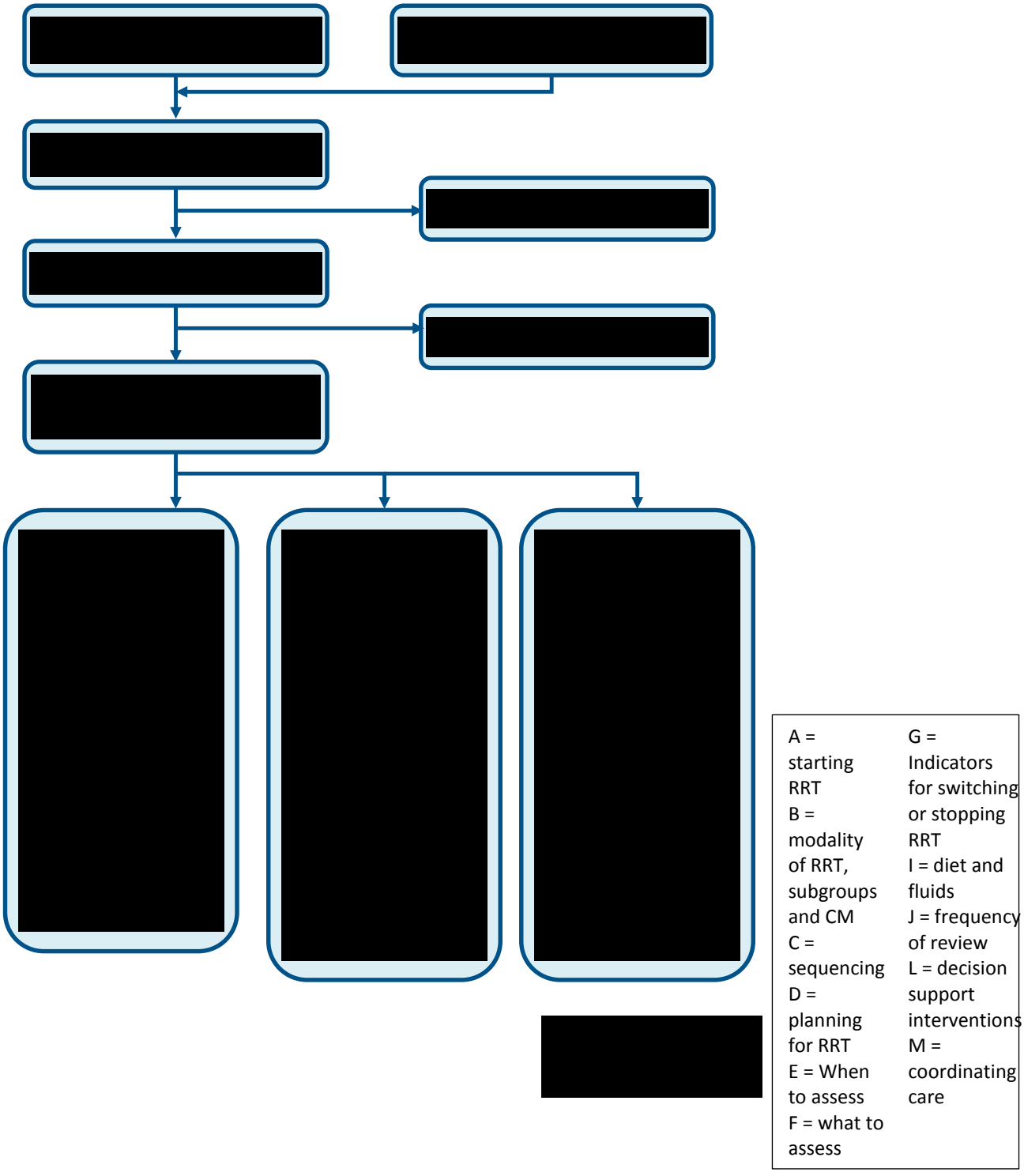
Table 15: Clinical evidence profile: dietary management and fluid restriction vs usual care, dialysis, >18 to 70

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



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.2 Excluded health economic studies

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

Table 17: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	