National Institute for Health and Care Excellence

Draft for consultation

RRT and conservative management

Evidence review for co-ordinating care

NICE guideline

Intervention evidence review

April 2018

Draft for Consultation

This evidence review was developed by the National Guideline Centre

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

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ISBN

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1 Co-ordinating care

1.1 Review question: What are the most clinical and cost effective ways of co-ordinating care during RRT or conservative management?

1.2 Introduction

People with CKD who require RRT or conservative management may have a lot of contact with healthcare professionals for a variety of reasons. In particular, those who receive in–centre haemodialysis (around 20,000 people) may go to hospital or satellite unit 3 or 4 times a week for e.g. 4 hours just for their dialysis. In addition there may well be appointments for other reasons such as issues related directly to kidney care (for example, transplant work up or access review) and other co-morbid conditions (for example, diabetes or heart disease). Lack of co-ordination of care can result in a high burden on the patient due to frequent hospital visits. The purpose of this review is to identify the clinical and cost effectiveness of a variety of measures aimed at improving the coordination of care.

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 with CKD stage 3 to 5 either being prepared for or undergoing RRT or CM Stratified by: • Age (<2, 2 to <16, 16 to <25, 25 to <70, ≥70 • BAME vs non-BAME • Diabetes mellitus vs no diabetes mellitus
Interventions	• Multispeciality clinic vs separate clinics (e.g. combined diabetologist + nephrologist clinic vs two separate clinics) • Multispecialty care vs nephrologist only (e.g. care involving multiple specialties vs care for co-existing conditions only involving nephrologist/renal team) • Co-located services vs disparate services (e.g. services at a single location vs services at multiple locations) • Review at home/in community vs in hospital • Review in person vs remote review (e.g. via telephone/virtual consultation) • Information sharing strategies vs usual care • Dedicated key worker vs usual care
Comparisons	As above or combinations of comparisons
Outcomes	Critical • Patient, family/carer health-related QoL (continuous) • Symptom scores and functional measures (continuous) • Mortality (dichotomous and time to event) • Hospitalisation or other resource use (rates or continuous) • Time to failure of RRT form (time to event) Important • Pre-emptive transplantation (dichotomous) • Psychological distress and mental wellbeing (continuous)

	• Patient, family/carer experience of care (continuous) • Control of co-existing conditions (e.g. HbA1c for Diabetes mellitus, blood pressure for hypertension, continuous or dichotomous) • Adverse events
Study design	RCTs only, if insufficient RCT evidence, NRS that adjust for key confounders (age, ethnicity, comorbidities and baseline health) will be included

1.4 Clinical evidence

1.4.1 Included studies

Two studies were included in the review;[10, 29] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

Both studies were RCTs comparing post-discharge key worker with usual care in adults on PD and in fact used near identical methods. No RCTs or NRS were identified for any other population or intervention that met the protocol.

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
Chow 2010[10]	Case-management (n = 50) – enhanced post discharge planning with comprehensive assessment and 6 weeks of nurse led telephone follow-up Usual care (n = 50) – usual discharge service	Adults aged 25 to 70 (mean age 56.9 (SD 13.5)) Hong Kong PD (all participants on CAPD) Recently admitted to a hospital renal unit, not for elective procedure	Reported at 12 weeks (6 weeks after end of intervention): Symptom scores Functional measures Experience of care Mental wellbeing	
Li 2014[29]	Case-management (n = 80) – enhanced post discharge planning with comprehensive assessment and 6 weeks of nurse led telephone follow-up	Adults aged 25 to 70 (mean age 56.3 (SD 12.4)) China PD (all participants on CAPD)	Reported at 12 weeks (6 weeks after end of intervention): Symptom scores Functional measures	

Study	Intervention and comparison	Population	Outcomes	Comments
	Usual care (n = 80) – usual discharge service	Recently admitted to a hospital renal unit, not for elective procedure	Experience of care Mental wellbeing Resource use	

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2 See appendix D for full evidence tables.

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1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Key worker vs usual care

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 Key worker (95% CI)
Symptoms (KDQOL symptom/problem, 0-100, high is better)	220 (2 studies) 12 weeks	VERY LOW[1,2] due to risk of bias, imprecision		The mean symptoms in the control groups was 66.5	The mean symptoms in the intervention groups was 3.62 higher (0.27 to 6.97 higher)
Functional measures (KDQOL burden of kidney disease, 0-100, high is better)	220 (2 studies) 12 weeks	MODERATE[1] due to risk of bias		The mean functional measures in the control groups was 21.5	The mean functional measures in the intervention groups was 0.72 higher (2.97 lower to 4.42 higher)
Rate of readmission	135 (1 study) 12 weeks	VERY LOW[1,2] due to risk of bias, imprecision	Rate Ratio 0.57 (0.21 to 1.58)	Moderate	
				150 per 1000	65 fewer per 1000 (from 119 fewer to 87 more)
Rate of clinic visits	135 (1 study) 12 weeks	LOW[1,2] due to risk of bias, imprecision	Rate Ratio 0.53 (0.34 to 0.82)	Moderate	
				880 per 1000	414 fewer per 1000 (from 158 fewer to 581 fewer)
Mental wellbeing (KDQOL emotional wellbeing, 0-100, high is better)	220 (2 studies) 12 weeks	MODERATE[1] due to risk of bias		The mean mental wellbeing in the control groups was 63.4	The mean mental wellbeing in the intervention groups was 1.49 higher (3.59 lower to 6.57 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 Key worker (95% CI)
Experience of care (KDQOL patient satisfaction, 0-100, high is better)	220 (2 studies) 12 weeks	LOW[1,2] due to risk of bias, imprecision		The mean experience of care in the control groups was 63.0	The mean experience of care in the intervention groups was 6.17 higher (2.33 to 10.01 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 See appendix F for full GRADE tables.

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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. Cost calculations based on resource use from the clinical review have also been included.

The clinical evidence identified two studies both about the same enhanced post-discharge planning with comprehensive assessment and 6 weeks of nurse led telephone follow-up compared to routine discharge. This is described as involving:

- Discharge plan (nurse grade and time involved not reported – nurse costs in Table 4)
  - Discussion involving patient and family
  - A pre-discharge comprehensive assessment of the patient's physical, social, cognitive and emotional needs
  - An individualised education programme conducted by the nurse case manager
- Weekly follow-up calls by nurse case manager for 6 weeks (first call 20-30 mins, others as required – see non-consultant led, non-face-to-face attendance costs in Table 5; estimated total cost £321)
- Patients were also able to call the case manager (or a 24 hour hotline service available to all patients) as they wished (information not provided about time involved with this)
- The case manager could refer the patient where further interventions were required e.g. for a home visit from community nurse or clinic follow-up (clinic visits was an outcome of the study)

Routine discharge care included:

- Standard information
- Telephone hotline service
- Printed material
- Reminder to attend their outpatient appointment

The clinical review reported resource utilisation data about readmission and clinic visits showing a possible reduction with the intervention. The weighted average cost of a non-elective CKD admission is £2409; a reduction of 65 admissions per 1000 (CI: -119 to 87) as reported in the clinical review would result in a cost saving of £156,616 (CI: -£286,727 to £209,624).The weighted average cost of an outpatient nephrology attendance is £151 (see Table 5 for details); based on this a reduction of 414 admissions per 1000 (CI: -158 to -581) as reported in the clinical review would result in a cost saving of £62,423 (CI: -£23,823 to -£87,604). Based on a total cost saving of £219,039 per 1000 patients, the intervention would be cost saving if it cost less than £219 per patient. Given that the estimated cost of the weekly follow-up calls alone is greater than this it is judged likely that there would be an overall additional cost of providing the intervention over usual care, although it is not possible to exactly estimate what this would be due to missing information about the resource use involved in providing the intervention.

Table 4: UK hospital-based nurse costs per working hour

Nurse	Cost per working hour
Band 2	£22
Band 3	£24
Band 4	£29
Band 5	£36
Band 6	£44

Nurse	Cost per working hour
Band 7	£52
Band 8a	£61
Band 8b	£73

Source: PSSRU Unit costs of health and social care 2016[13]

Table 5: UK NHS reference costs 2015/16 for nephrology outpatient appointments

Currency code	Currency Description	No. of attendances	National average unit cost
Consultant led			
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	576,355	£153
WF01B	Non-Admitted Face to Face Attendance, First	88,492	£194
WF01C	Non-Admitted Non-Face to Face Attendance, Follow-Up	9,450	£86
WF01D	Non-Admitted Non-Face to Face Attendance, First	1,399	£72
WF02A	Multiprofessional Non-Admitted Face to Face Attendance, Follow-Up	29,964	£169
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	2,951	£206
WF02C	Multiprofessional Non-Admitted Non Face to Face Attendance, Follow-Up	11	£139
Non-consultant led			
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	92,331	£108
WF01B	Non-Admitted Face to Face Attendance, First	6,947	£130
WF01C	Non-Admitted Non-Face to Face Attendance, Follow-Up	8,587	£45
WF01D	Non-Admitted Non-Face to Face Attendance, First	328	£96
WF02A	Multiprofessional Non-Admitted Face to Face Attendance, Follow-Up	452	£135
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	24	£139
Weighted average			**£151**

Source: NHS reference costs 2015-16[15]

1.6 Resource costs

The recommendations made in 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 Key worker vs usual care

No evidence was identified for quality of life, mortality, hospitalisation, psychological distress, control of co-existing conditions, infections, vascular access issues, dialysis access issues, acute transplant rejection episodes.

A clinically important benefit was found for clinic visits with a key worker (1 study, low quality).

No clinically important difference was found for symptoms (2 studies, very low quality), functional measures (1 study, moderate quality), readmission (1 study, very low quality), mental wellbeing (2 studies, moderate quality), experience of care (2 studies, low quality).

1.7.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.8 Recommendations

M1. Provide the person with the contact details of the healthcare professional responsible for their overall renal care:

- before they start RRT or conservative management, and
- when they switch from one modality to another.

M2. Coordinate care to reduce its effect on day-to-day life and wellbeing (treatment burden). For example, take account of people's preferences and avoid scheduling appointments on non-dialysis days for people on hospital dialysis wherever possible.

M3. Follow the recommendations on:

- delivering an approach to care that takes account of multimorbidity in NICE's guideline on multimorbidity, and
- continuity of care and relationships, and enabling patients to actively participate in their care in NICE's guideline on patient experience in adult NHS services.

1.8.1 Research recommendations

RR12. What is the clinical and cost effectiveness of having keyworkers present in the context of renal replacement therapy (RRT)? See also the rationale in appendix J.

1.9 Rationale and impact

1.9.1 Why the committee made the recommendations

There was limited evidence on the coordination of care but the committee agreed that people should know who to contact with questions about their condition or treatment. This is particularly important when they start or change RRT modalities. The committee noted that people on RRT experience considerable treatment burden and that strategies should be adopted to reduce this. There was no evidence on care coordination by a keyworker so the committee recommended the healthcare professional responsible for renal care as a first point of contact. They made a research recommendation on care coordination by a keyworker to inform future guidance.

1.9.2 Impact of the recommendations on practice

Current practice is variable in terms of when a person is given the details of the person responsible for care. This recommendation will ensure that this is done before starting treatment or when switching modalities or to conservative management. Similarly the recommendation on reducing treatment burden standardises and reinforces good practice. Some healthcare professionals may need to change their practice but this would not result in a substantial resource impact.

1.10 The committee's discussion of the evidence

1.10.1 Interpreting the evidence

1.10.1.1 The outcomes that matter most

The committee considered quality of life, symptom scores, functional measures, mortality, hospitalisation and time to failure of renal replacement therapy as critical outcomes. Important outcomes were pre-emptive transplantation, psychological distress and mental welling, experience of care, control of co-existing conditions and adverse events.

There was evidence for symptom scores, functional measures, and experience of care, mental wellbeing and resource use.

1.10.1.2 The quality of the evidence

Outcomes were rated as moderate to very low quality. Evidence was downgraded due risk of bias (due to lack of blinding with subjective outcomes) and imprecision.

1.10.1.3 Benefits and harms

The were no clinical important differences between the group who received post-discharge case management and those who received usual care for symptom scores, functional measures, experience of care and mental wellbeing. The committee noted that the intervention was for six weeks only and this may not have been long enough to facilitate improvement in these outcomes. There was a clinically important reduction in clinic appointments in the intervention group but not for readmissions.

The committee noted that the studies were in China and Hong Kong and it was difficult to know how their healthcare services compare with that of the UK. The limited description of usual care described a service that may be superior to that offered in the UK. The study population was restricted to people on PD who had been admitted to the renal unit, but not for an elective admission.

A case manager or keyworker is available in some areas of the country. The role is performed by a range of different health professionals including GPs, community matrons and specialist nurses. Keyworkers provide a single point of contact, organise appointments and help people to navigate the system by signposting to other services. The committee were in agreement that a keyworker was likely to provide clinically important benefits but were unable to recommend their use due to the unknown resource impact.

1.10.2 Cost effectiveness and resource use

No published economic evaluations were included.

The clinical review found evidence relating to post-discharge case management for people on PD who had been hospitalised. Case management as described in these studies would have additional costs due to the additional nurse timing required. However, there was evidence for a reduction in clinic visits and this would offset these costs. Readmission rates were also lower but not judged to be clinically important. A cost calculation based on this evidence suggested that it was likely there would be a net cost of this type of case management. There was no evidence to suggest QALYs would be higher with this intervention – no mortality or quality of life benefit was seen – therefore the intervention may not be cost effective. As described above there was uncertainty relating to the generalisability of the resource use in the clinical studies based in China and Hong Kong. This uncertainty also effects these economic considerations which are based on this evidence.

The committee agreed that the use of a key worker to coordinate care for people receiving RRT or conservative management was an important issue; however, no clinical or economic evidence was identified relating to this. The committee concluded that this could have an important benefit to patients as better coordination of care may mean they spend less of their time in hospital (many patients are already in hospital 3 or more days a week for dialysis but also require additional appointments related to concomitant conditions such as diabetes) and that could improve quality of life. The committee discussed what the resource use implications would be of people having a key worker to coordinate care including whether this would require a separate role or if this could be accommodated within an existing team member's role, and who might be best placed to do it. The committee concluded there would be a resource use implication of having a key worker to coordinate care, whoever undertook the role. It was unclear if there would be any cost offsets to the NHS although it was conceivable that there could be if for example patients were seen in primary care for some appointments rather than secondary care, or if patient transport journeys were reduced. In addition, as described above there would be benefits to patients which may justify any additional cost.

The committee also discussed to what extent this role already existed and whether there would be a resource impact of recommending a key worker to coordinate care for people receiving RRT or conservative management. The committee concluded that it was not current practice in many areas and as such a recommendation may have a substantial resource impact.

Given the lack of clinical or cost effectiveness evidence and potential for a substantial resource impact the committee concluded they were not able to specifically recommend a key worker to coordinate care for people receiving RRT or conservative management. Although they noted that more general recommendations already exist about co-coordinating care in the NICE guidelines on Multimorbidity: clinical assessment and management NICE guideline [NG56] and Patient experience in adult NHS services: improving the experience of care for people using adult NHS services (CG138) and made a more general recommendation reflecting these given the importance of this issue for people undergoing RRT and conservative management.

Providing contact details of the lead healthcare professional responsible for care was not considered to have any resource use implications.

1.103 Other factors the committee took into account

A person may undergo a number of different transitions of care after starting renal replacement therapy. During these periods people often report not knowing who is responsible for their care or who to contact. This lead health professional is not responsible for coordinating care but should signpost to the most appropriate person to contact.

The committee emphasised the importance of the partnership between primary, secondary and social care. People undergoing renal replacement therapy or conservative management often have complex needs which are met by a number of different health professionals and services. The input of these professionals varies over time and depends on where the person is in the patient pathway. Good timely communication with the general practitioner is important so that the primary care team is fully aware of developments and ongoing management as this may have implications whilst managing other co-morbidities, poly-pharmacy as well as providing psycho-social support as necessary. It is important to involve the primary care team at all stages of the RRT pathway. Though the RRT pathway is secondary care/specialist led, primary care should remain in the loop to ensure optimal management of co-existing co-morbidities, effective medicines management, safe prescribing, help in promoting lifestyle changes, primary/secondary prevention of cardiovascular disease. Primary care health professionals can continue to provide holistic care, psychological support and sign post to specialists for problems relating to RRT and

associated problems. Seamless transfer of care between primary and secondary care with effective sharing of information is likely to improve quality of care and improve the patient experience.

People often have to attend a number of different appointments for their renal condition and other conditions. The treatment burden for people on in-centre haemodialysis is particularly high. It is therefore important that treatment burden is discussed with each person, their families and carers and that strategies are adopted to minimise it.

The committee confirmed that the recommendations were applicable to children and young people. They highlighted the importance of good communication and coordination of care when a young person is transitioning to adult services. They were aware of NICE's guidance on Transition from children's to adults' services for young people using health or social care services (NG43).

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43. Wei SY, Chang YY, Mau LW, Lin MY, Chiu HC, Tsai JC et al. Chronic kidney disease care program improves quality of pre-end-stage renal disease care and reduces medical costs. Nephrology. 2010; 15(1):108-15

44. Wingard R. Reducing early mortality in patients on dialysis: lessons from the RightStart program. Nephrology Nursing Journal. 2009; 36(2):215-20

1 Appendices

2 Appendix A: Review protocols

3 **Table 6: Review protocol: co-ordinating care**

Field	Content
Review question	What are the most clinical and cost effective ways of co-ordinating care during RRT or conservative management?
Type of review question	Intervention
Objective of the review	Determine the most clinical and cost effective ways of co-ordinating care during RRT or conservative management
Eligibility criteria – population / disease / condition / issue / domain	Children, young people and adults with CKD stage 3 to 5 either being prepared for or undergoing RRT or CM Stratified by: Age (<2, 2 to <16, 16 to <25, 25 to <70, ≥70 BAME vs non-BAME DM vs no DM
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Multispeciality clinic vs separate clinics (e.g. combined diabetologist + nephrologist clinic vs two separate clinics) Multispecialty care vs nephrologist only (e.g. care involving multiple specialties vs care for co-existing conditions only involving nephrologist/renal team) Co-located services vs disparate services (e.g. services at a single location vs services at multiple locations) Review at home/in community vs in hospital Review in person vs remote review (e.g. via telephone/virtual consultation) Information sharing strategies vs usual care Dedicated key worker vs usual care
Eligibility criteria – comparator(s) / control or reference (gold) standard	As above or combinations of comparisons
Outcomes and prioritisation	Critical Patient, family/carer health-related QoL (continuous) Symptom scores and functional measures (continuous) Mortality (dichotomous and time to event) Hospitalisation or other resource use (rates or continuous) Time to failure of RRT form (time to event) Important Pre-emptive transplantation (dichotomous) Psychological distress and mental wellbeing (continuous) Patient, family/carer experience of care (continuous) Control of co-existing conditions (e.g. HbA1c for DM, BP for hypertension, continuous or dichotomous) Adverse events Infections (dichotomous) Vascular access issues (dichotomous)

Field	Content
	Dialysis access issues (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 only, if insufficient RCT evidence, NRS that adjust for key confounders (age, ethnicity, comorbidities and baseline health) will be included
Other inclusion exclusion criteria	Not applicable
Proposed sensitivity / subgroup analysis, or meta-regression	Pre or during RRT/CM Different modalities of RRT
Selection process – duplicate screening / selection / analysis	A sample of at least 10% of the abstract lists were double-sifted by a senior research fellow and discrepancies rectified, with committee input where consensus could not be reached, 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, HMIC 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

Field	Content
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 7: 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.[32] 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.

1 Appendix B: Literature search strategies

B.1 2 Clinical search literature search strategy

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

7 *For more detailed information, please see the Methodology Review*.

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

13 **Table 8: 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 Observational studies
Embase (OVID)	1974 – 11 December 2017	Exclusions Randomised controlled trials

Database	Dates searched	Search filter used
		Systematic review studies Observational 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
HMIC, Health Management Information Consortium (OVID)	1979 – 11 December 2017	Exclusions

1. Line 81 (Medline) and line 75 (Embase) were added to the search strategy to reduce the number of items retrieved for observational studies as the overall results from the search were very large.

This was checked to ensure that relevant studies were not excluded.

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)
54.	exp Renal Replacement Therapy/
55.	((renal or kidney*) adj2 replace*).ti,ab.
56.	(hemodiafilt* or haemodiafilt* or haemofilt* or hemofilt*).ti,ab.
57.	(hemodialys* or haemodialys*).ti,ab.
58.	((kidney* or renal or pre-empt* or preempt*) adj3 (transplant* or graft*)).ti,ab.
59.	(capd or apd or ccpd or dialys*).ti,ab.
60.	or/54-59
61.	letter/
62.	editorial/
63.	news/
64.	exp historical article/
65.	Anecdotes as Topic/
66.	comment/
67.	case report/
68.	(letter or comment*).ti.
69.	or/61-68
70.	randomized controlled trial/ or random*.ti,ab.
71.	147 not 148
72.	animals/ not humans/
73.	Animals, Laboratory/

74.	exp Animal Experimentation/
75.	exp Models, Animal/
76.	exp Rodentia/
77.	(rat or rats or mouse or mice).ti.
78.	or/72-77
79.	60 not 78
80.	limit 79 to English language
81.	(mycophenolic acid or azathioprine or sirolimus or everolimus or tacrolimus or cyclosporin* or steroid or calcineurin inhibitor or anaemi* or anemi* or vitamin d or immunosuppres*).ti.[1]
82.	80 not 81
83.	Epidemiologic studies/
84.	Observational study/
85.	exp Cohort studies/
86.	(cohort adj (study or studies or analys* or data)).ti,ab.
87.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
88.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
89.	Controlled Before-After Studies/
90.	Historically Controlled Study/
91.	Interrupted Time Series Analysis/
92.	(before adj2 after adj2 (study or studies or data)).ti,ab.
93.	or/83-92
94.	Registries/
95.	Management Audit/ or Clinical Audit/ or Nursing Audit/ or Medical Audit/
96.	(registry or registries).ti,ab.
97.	(audit or audits or auditor or auditors or auditing or auditable).ti,ab.
98.	or/94-97
99.	93 or 98
100.	82 and 99
101.	100 not 53
102.	53 or 101

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)
50.	*renal replacement therapy/
51.	((renal or kidney*) adj2 replace*).ti,ab.
52.	(hemodiafilt* or haemodiafilt* or haemofilt* or hemofilt*).ti,ab.
53.	(hemodialys* or haemodialys*).ti,ab.
54.	((kidney* or renal or pre-empt* or preempt*) adj3 (transplant* or graft*)).ti,ab.
55.	(capd or apd or ccpd or dialys*).ti,ab.

56.	or/50-55
57.	letter.pt. or letter/
58.	note.pt.
59.	editorial.pt.
60.	case report/ or case study/
61.	(letter or comment*).ti.
62.	or/57-61
63.	randomized controlled trial/ or random*.ti,ab.
64.	62 not 63
65.	animal/ not human/
66.	nonhuman/
67.	exp Animal Experiment/
68.	exp Experimental Animal/
69.	animal model/
70.	exp Rodent/
71.	(rat or rats or mouse or mice).ti.
72.	or/64-71
73.	56 not 72
74.	limit 73 to English language
75.	(mycophenolic acid or azathioprine or sirolimus or everolimus or tacrolimus or cyclosporin* or steroid or calcineurin inhibitor or anaemi* or anemi* or vitamin d or immunosuppres*).ti.[1]
76.	74 not 75
77.	Clinical study/
78.	Observational study/
79.	family study/
80.	longitudinal study/
81.	retrospective study/
82.	prospective study/
83.	cohort analysis/
84.	follow-up/
85.	cohort*.ti,ab.
86.	84 and 85
87.	(cohort adj (study or studies or analys* or data)).ti,ab.
88.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
89.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
90.	(before adj2 after adj2 (study or studies or data)).ti,ab.
91.	or/77-83,86-90
92.	register/
93.	medical audit/
94.	(registry or registries).ti,ab.
95.	(audit or audits or auditor or auditors or auditing or auditable).ti,ab.
96.	or/92-95
97.	91 or 96

98.	76 and 97
99.	98 not 49
100.	49 or 99

1 **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)

2 **HMIC (Ovid) search terms**

1.	exp Kidney diseases/ or exp Haemodialysis/ or exp Renal services/ or exp Kidney transplants/ or Kidney Transplantation units/
2.	exp Kidneys/ or exp Artificial kidneys/
3.	exp Peritoneal dialysis/ or exp Continuous ambulatory peritoneal dialysis/ or Haemodialysis/ or Haemodialysis Units/
4.	exp Renal nursing/ or exp Renal treatment/ or exp Renal units/
5.	((renal or kidney*) adj2 replace*).ti,ab.
6.	(hemodiafilt* or haemodiafilt* or haemofilt* or hemofilt*).ti,ab.
7.	(hemodialys* or haemodialys*).ti,ab.
8.	((kidney* or renal or pre-empt* or preempt*) adj3 (transplant* or graft*)).ti,ab.
9.	(capd or apd or ccpd or dialys*).ti,ab.
10.	or/1-9
11.	(mycophenolic acid or azathioprine or sirolimus or everolimus or tacrolimus or cyclosporin* or steroid or calcineurin inhibitor or anaemi* or anemi* or vitamin d or immunosuppres*).ti.
12.	10 not 11
13.	limit 12 to English
14.	animals/ not humans/
15.	(rat or rats or mouse or mice).ti.
16.	14 or 15
17.	13 not 16
18.	limit 17 to (audiovis or book or chapter dh helmis or circular or microfiche dh helmis or multimedias or website)
19.	limit 17 to (audiocass or books or cdrom or chapter or dept pubs or diskettes or folio pamp or "map" or marc or microfiche or multimedia or pamphlet or parly or press or press rel or thesis or trustdoc or video or website)
20.	18 or 19
21.	17 not 20

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 9: 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.

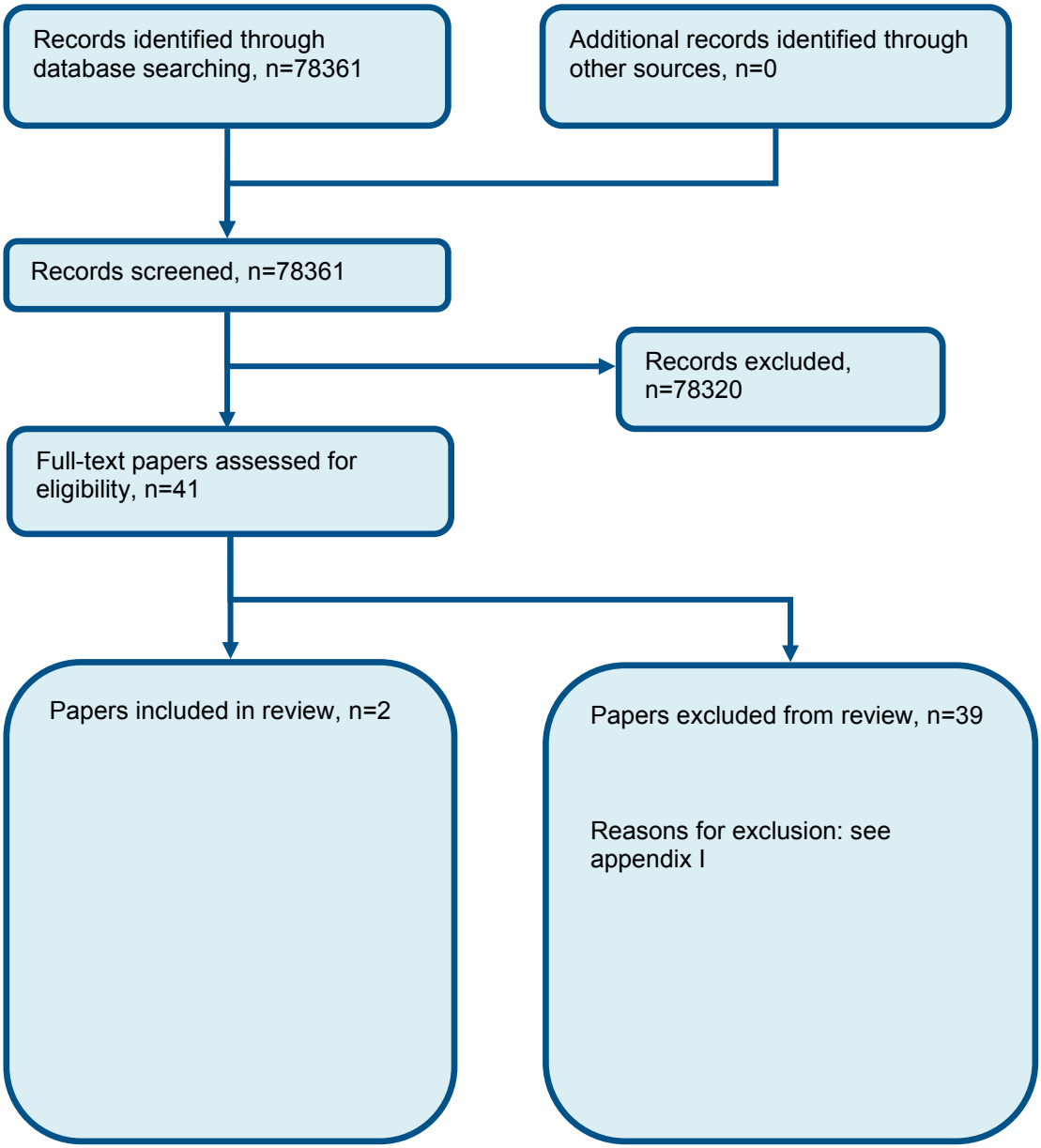
26.	or/18-25
27.	10 not 26
28.	*health economics/
29.	exp *economic evaluation/
30.	exp *health care cost/
31.	exp *fee/
32.	budget/
33.	funding/
34.	budget*.ti,ab.
35.	cost*.ti.
36.	(economic* or pharmaco?economic*).ti.
37.	(price* or pricing*).ti,ab.
38.	(cost* adj2 (effective* or utilit* or benefit* 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

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 co-ordinating care



Appendix D: Clinical evidence tables

Study	Chow 2010[10]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=85)
Countries and setting	Conducted in Hong Kong (China); Setting: Renal units of hospitals in Hong Kong
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	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients admitted to and then discharged from renal units of study hospitals, able to access a telephone after discharge
Exclusion criteria	Intermittent PD, HD, planned admissions for special treatment procedures, Tenckhoff catheter in situ for less than 3 months
Recruitment/selection of patients	Consecutive admissions screened
Age, gender and ethnicity	Age - Mean (SD): 56.9 (13.5). Gender (M:F): 61:39. Ethnicity: Not stated
Further population details	1. Modality of RRT: PD 2. Pre-RRT or during RRT/CM: During RRT/CM
Extra comments	40% comorbid DM, 32% comorbid heart disease, mean 3.2 years on CAPD
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Dedicated key worker. Comprehensive discharge planning protocol (involved family and patient, comprehensive assessment of physical, social and cognitive needs, individualised education programme (aimed at strengthening previous education)), standardised 6 week nurse-initiated telephone follow-up regimen with weekly telephone calls for 6 weeks, calls focused on checking and reinforcing behaviours, any problems that had occurred and organising referrals. Duration 6 weeks. Concurrent medication/care: Nil else specified (n=50) Intervention 2: Usual care. Routine discharge care with standard information, telephone hotline service, self-help printed materials and a reminder to attend their outpatient appointment. Duration 6 weeks.

	Concurrent medication/care: Nil else specified
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEDICATED KEY WORKER versus USUAL CARE

Protocol outcome 1: Symptom scores/functional measures
- Actual outcome for General population: KDQOL, symptom/problem subscale at 12 weeks; Group 1: mean 66.1 (SD 17.4); n=43, Group 2: mean 64.3 (SD 14.7); n=42
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: 7, Reason: lost to follow-up, died, TPx, change of Tx; Group 2 Number missing: 8, Reason: lost to follow-up, discontinued Tx
- Actual outcome for General population: KDQOL, burden of kidney disease subscale at 12 weeks; Group 1: mean 24.6 (SD 24.4); n=43, Group 2: mean 22.2 (SD 18.6); n=42
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: 7, Reason: lost to follow-up, died, TPx, change of Tx; Group 2 Number missing: 8, Reason: lost to follow-up, discontinued Tx

Protocol outcome 2: Psychological distress and mental wellbeing
- Actual outcome for General population: KDQOL, emotional wellbeing subscale at 12 weeks; Group 1: mean 63.8 (SD 22.7); n=43, Group 2: mean 63.3 (SD 21.3); n=42
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: 7, Reason: lost to follow-up, died, TPx, change of Tx; Group 2 Number missing: 8, Reason: lost to follow-up, discontinued Tx

Protocol outcome 3: Patient/family/carer experience of care
- Actual outcome for General population: KDQOL, emotional wellbeing subscale at 12 weeks; Group 1: mean 65.1 (SD 19.5); n=43, Group 2: mean 54 (SD 17.2); n=42
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: 7, Reason: lost to follow-up, died, TPx, change of Tx; Group 2 Number missing: 8, Reason: lost to follow-up, discontinued Tx

Protocol outcomes not reported by the study	Quality of life ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Pre-emptive transplantation (dichotomous) ; Cognitive impairment ; Control of co-existing conditions (e.g. HbA1c for DM, BP for HTN) ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Li 2014[29]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=160)
Countries and setting	Conducted in China; Setting: Local regional hospitals in China
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	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	PD patients, admitted to renal units of two local regional hospitals in Guangdong, Mandarin speaking, able to communicate via telephone at home,
Exclusion criteria	Intermittent PD, HD, planned admission for elective procedure, Tenckhoff catheter in situ for <3 months, psychosis/dementia, dying
Recruitment/selection of patients	Consecutive admissions screened
Age, gender and ethnicity	Age - Mean (SD): 56.3 (12.4). Gender (M:F): 59:41. Ethnicity: Not stated
Further population details	1. Modality of RRT: PD 2. Pre-RRT or during RRT/CM: During RRT/CM
Indirectness of population	No indirectness
Interventions	(n=80) Intervention 1: Dedicated key worker. Comprehensive discharge planning protocol (involved family and patient, comprehensive assessment of physical, social and cognitive needs, individualised education programme (aimed at strengthening of previous education)), standardised 6 week nurse initiated follow-up regimen with weekly telephone calls for 6 weeks, calls focused on checking and reinforcing behaviours, any problems that had occurred and organising referrals. Duration 6 weeks. Concurrent medication/care: Nil else specified. Indirectness: No indirectness (n=80) Intervention 2: Usual care. Routine discharge care with standard information, telephone hotline service, self-help printed materials and a reminder to attend their outpatient appointment. Duration 6 weeks. Concurrent medication/care: Nil else specified. Indirectness: No indirectness
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEDICATED KEY WORKER versus USUAL CARE	

Protocol outcome 1: Symptom scores/functional measures - Actual outcome for General population: Symptoms (KDQOL symptom/problem) at 12 weeks; Group 1: mean 72.8 (SD 15); n=69, Group 2: mean 68.6 (SD 6.2); n=66 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 ; Group 1 Number missing: 11, Reason: 5 lost to follow-up, 6 discontinued intervention; Group 2 Number missing: 14, Reason: 6 lost to follow-up, 8 discontinued intervention - Actual outcome for General population: Functional measures (KDQOL burden of disease) at 12 weeks; Group 1: mean 21.5 (SD 11.7); n=69, Group 2: mean 21.1 (SD 12.2); n=66 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: 11, Reason: 5 lost to follow-up, 6 discontinued intervention; Group 2 Number missing: 14, Reason: 6 lost to follow-up, 8 discontinued intervention Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months - Actual outcome for General population: Rate of readmission at 12 weeks; rate ratio, SE 0.52; 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: 11, Reason: 5 lost to follow-up, 6 discontinued intervention; Group 2 Number missing: 14, Reason: 6 lost to follow-up, 8 discontinued intervention - Actual outcome for General population: Rate of clinic visits at 12 weeks; rate ratio, SE 0.22; 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: 11, Reason: 5 lost to follow-up, 6 discontinued intervention; Group 2 Number missing: 14, Reason: 6 lost to follow-up, 8 discontinued intervention Protocol outcome 3: Psychological distress and mental wellbeing - Actual outcome for General population: Mental wellbeing (KDQOL emotional well-being) at 12 weeks; Group 1: mean 65.4 (SD 17.2); n=69, Group 2: mean 63.5 (SD 18.6); n=66 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: 11, Reason: 5 lost to follow-up, 6 discontinued intervention; Group 2 Number missing: 14, Reason: 6 lost to follow-up, 8 discontinued intervention Protocol outcome 4: Patient/family/carer experience of care - Actual outcome for General population: Experience of care (KDQOL satisfaction) at 12 weeks; Group 1: mean 75.9 (SD 13.8); n=69, Group 2: mean 71.3 (SD 12.3); n=66 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: 11, Reason: 5 lost to follow-up, 6 discontinued intervention; Group 2 Number missing: 14, Reason: 6 lost to follow-up, 8 discontinued intervention	
Protocol outcomes not reported by the study	Quality of life ; Mortality at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Pre-emptive transplantation (dichotomous) ; Cognitive impairment ; Control of co-existing

conditions (e.g. HbA1c for DM, BP for HTN) ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes	

1 2 3 4

Appendix E: Forest plots

E.1 Key worker vs usual care

Figure 2: Symptoms (KDQOL, symptom/problem, 0-100, higher is better, 12 weeks)

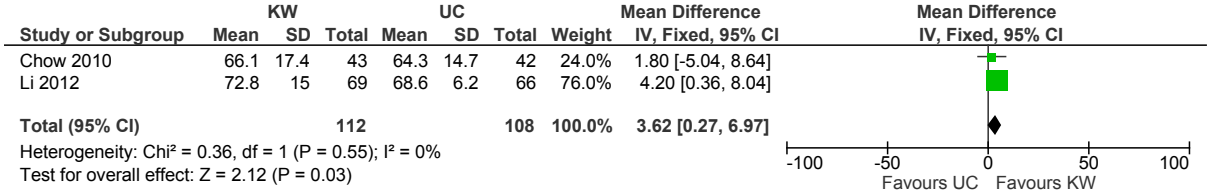


Figure 3: Functional measures (KDQOL, burden of kidney disease, 0-100, higher is better, 12 weeks)

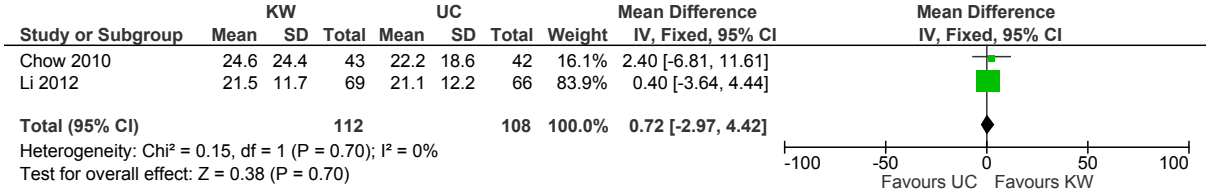


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Figure 4: Rate of readmission (by 12 weeks)

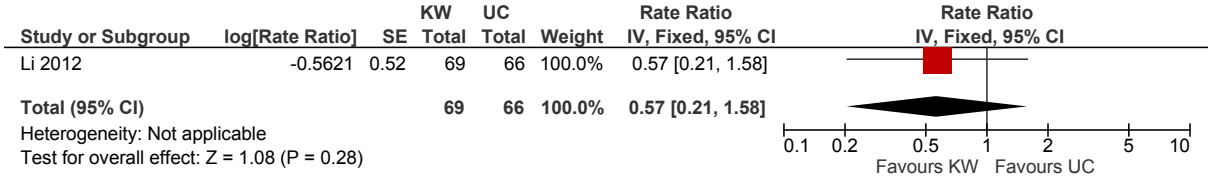

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Figure 5: Rate of clinic visits (by 12 weeks)

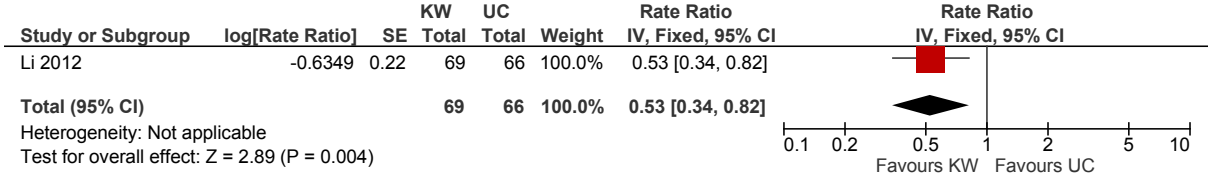

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Figure 6: Mental wellbeing (KDQOL, emotional wellbeing, 0-100, higher is better, 12 weeks)

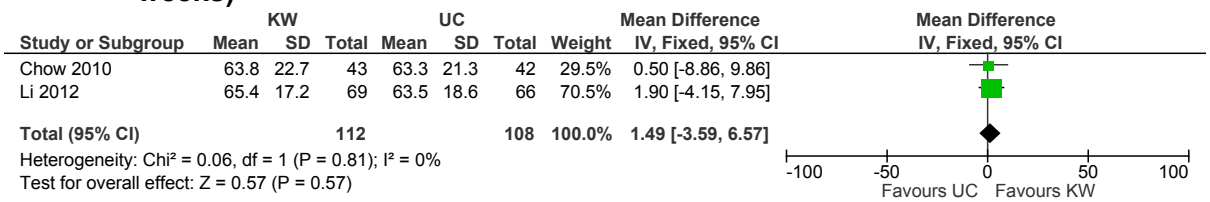

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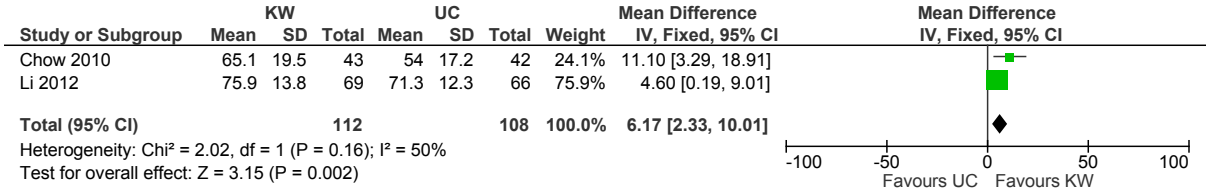
Figure 7: Experience of care (KDQOL patient satisfaction, 0-100, higher is better, 12 weeks)



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Appendix F: GRADE tables

Table 10: Clinical evidence profile: Key worker vs usual care

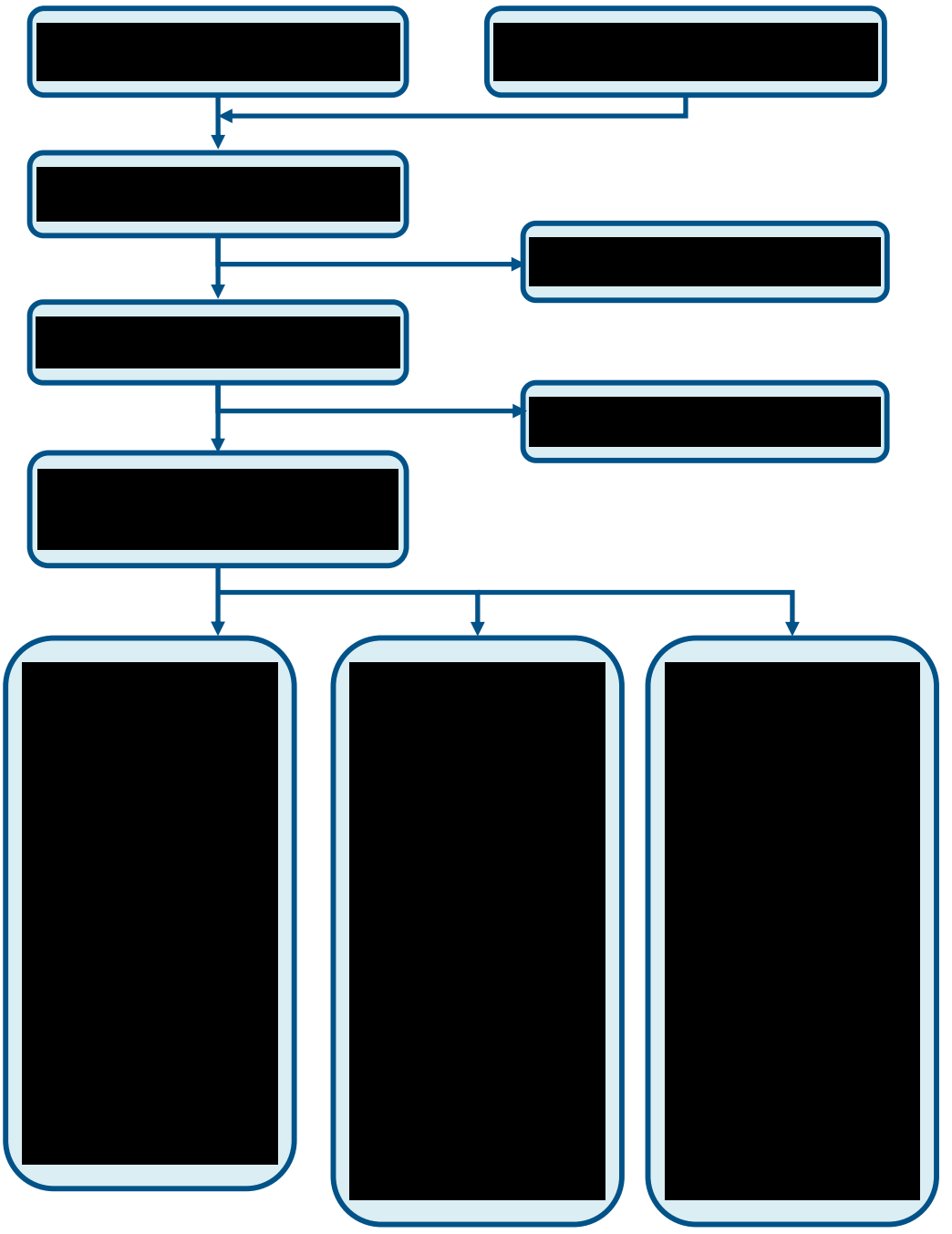
Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Key worker	Usual care	Relative (95% CI)	Absolute		
Symptoms (KDQOL symptom/problem, 0-100, high is better) (follow-up 12 weeks; Better indicated by higher values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	112	108	-	MD 3.62 higher (0.27 to 6.97 higher)	⊕OOO VERY LOW	CRITICAL
Functional measures (KDQOL burden of kidney disease, 0-100, high is better) (follow-up 12 weeks; Better indicated by higher values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	112	108	-	MD 0.72 higher (2.97 lower to 4.42 higher)	⊕⊕⊕O MODERATE	CRITICAL
Rate of readmission (follow-up 12 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/69 (0%)	15%	Rate Ratio 0.57 (0.21 to 1.58)	65 fewer per 1000 (from 119 fewer to 87 more)	⊕OOO VERY LOW	CRITICAL
Rate of clinic visits (follow-up 12 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/69 (0%)	88%	Rate Ratio 0.53 (0.34 to 0.82)	414 fewer per 1000 (from 158 fewer to 581 fewer)	⊕⊕OO LOW	CRITICAL
Mental wellbeing (KDQOL emotional wellbeing, 0-100, high is better) (follow-up 12 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	112	108	-	MD 1.49 higher (3.59 lower to 6.57 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Experience of care (KDQOL patient satisfaction, 0-100, high is better) (follow-up 12 weeks; Better indicated by lower values)												

2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	112	108	-	MD 6.17 higher (2.33 to 10.01 higher)	⊕⊕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

Appendix G: Health economic evidence selection

Figure 8: 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.

1 Appendix I: Excluded studies

I.1 2 Excluded clinical studies

3 **Table 11: Studies excluded from the clinical review**

Study	Exclusion reason
Bessa 2016[1]	Incorrect interventions
Boulware 2013[2]	Incorrect interventions
Breu-Dejean 2016[3]	Incorrect interventions
Chen 2011[5]	Not guideline condition
Chen 2013[6]	NRS without adequate adjustment
Chen 2014[7]	NRS without adequate adjustment
Chen 2015[4]	Not guideline condition
Chisholm 2001[8]	Incorrect interventions
Chisholm 2002[9]	Incorrect interventions
Chow 2006[11]	PhD thesis, results reported elsewhere
Connor 2011[12]	Wrong study design
Dashti-Khavidaki 2013[14]	Incorrect interventions
Devins 2003[16]	Incorrect interventions
Dixon 2011[17]	NRS without adequate adjustment
El Borolossy 2014[18]	Incorrect interventions
Fishbane 2017[20]	Incorrect population
Fenton 2010[19]	NRS without adequate adjustment
Gallar 2007[21]	NRS without adequate adjustment
Goldstein 2004[22]	NRS without adequate adjustment
Huang 2017[23]	Incorrect interventions
Ismail 2014[24]	Incorrect interventions
Jahromi 2016[25]	Incorrect interventions
Jenq 2017[26]	NRS without adequate adjustment
Joost 2014[27]	Incorrect interventions
Kargar Jahromi 2016[28]	Inappropriate comparison
Manley 2003[30]	Wrong study design
Martino 2014[31]	NRS without adequate adjustment
Navaneethan 2017[33]	Incorrect interventions
Pai 2009[34]	Incorrect interventions
Pai 2009[35]	Incorrect interventions
Poorgholami 2016[36]	Incorrect interventions
Russell 2002[37]	Incorrect interventions
Schoch 2014[39]	Systematic review is not relevant to review question or unclear PICO
Schmid 2017[38]	Incorrect interventions
Sicotte 2011[40]	NRS without adequate adjustment
Sullivan 2012[41]	No usable outcomes
Thilly 2017[42]	Protocol only
Wei 2010[43]	NRS without adequate adjustment

Study	Exclusion reason
Wingard 2009[44]	Commentary

I.21 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 12: Studies excluded from the health economic review

Reference	Reason for exclusion
None	

Appendix J: Research recommendations

J.1 Clinical and cost effectiveness of keyworkers

Research question: What is the clinical and cost effectiveness of having keyworkers present in the context of renal replacement therapy (RRT)?

Why this is important: The committee were unable to make a recommendation due to limited evidence and no evidence on the resource impact of a keyworker in this review. Recommendations regarding keyworkers are important to ensure people requiring RRT or conservative management are efficiently provided with the most clinical and cost effective treatment in regards to their care.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Children, young people and adults with CKD stage 3 to 5 either being prepared for or undergoing RRT or CM Intervention: Keyworkers present as part of people's care during RRT/CM Comparison: No keyworkers present Outcomes: Patient, family/carer health-related QoL, symptom scores and functional measures, mortality, hospitalisation, time to failure of RRT form, pre-emptive transplantation rates, psychological distress and mental wellbeing, patient, family/carer experience of care, control of co-existing conditions, adverse events
Importance to patients or the population	If effective and cost-effective, such an intervention could potentially provide significant benefits in terms of health-related quality of life and by demonstrating the effectiveness of keyworkers to patients during RRT.
Relevance to NICE guidance	There is current uncertainty about the effectiveness of keyworkers.
Relevance to the NHS	Research in this area will inform NICE recommendations for service delivery and provide information about clinical and cost-effectiveness.
Current evidence base	There is no evidence on the clinical and cost effectiveness of keyworkers during RRT or conservative management. It is important to have sufficient information on keyworkers so more evidence based information can be given in regards to the different RRT options and conservative management.
Equality	Not applicable
Study design	RCT ideally, if not then a non-randomised cohort study with adequate adjustment for key confounders including age, ethnicity, co-morbidities and some measure of baseline health (e.g. quality of life). Cluster randomised design may be required given nature of intervention
Feasibility	No obvious feasibility issues
Other comments	Not applicable
Importance	• High: the research is essential to inform future updates of key recommendations in the guideline.