National Institute for Health and Care Excellence

Final

RRT and conservative management

Evidence review for indicators for transferring/discontinuing RRT

NICE guideline NG107

Intervention evidence review

October 2018

Final

This evidence review was developed by the National Guideline Centre

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1.1 Review questions: What are the indicators for transferring between the different modalities of RRT? What are the indicators for discontinuing RRT?

1.2 Introduction

People may need to transfer between forms of renal replacement therapy (e.g. from haemodialysis to peritoneal dialysis or from home dialysis to in centre dialysis) or to discontinue for example, conservative management. The decisions about when to transfer between forms of renal replacement therapy are difficult and there is some variability in terms of the strategies employed across the UK. Discontinuation of renal replacement therapy and transferring to conservative management is often poorly managed and not infrequently people are kept on dialysis longer than may be appropriate, particularly during a terminal phase of their illness. The purpose of this review is to determine if there are any established strategies for determining the timing of transfers, that are shown to be more clinically and cost effective than others.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Adults and children currently receiving RRT
Interventions	Transferring/discontinuing based on any suitable indicator
Comparisons	Not transferring/discontinuing Transferring/discontinuing at a later stage (e.g. transferring from PD to HD after 1 year on PD vs after 2 years on PD)

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)
	• Preferred place of death (dichotomous)
	• Symptom scores and functional measures (continuous)
	• Psychological distress and mental wellbeing (continuous)
	• Patient, family and carer experience of care (continuous)
	• Growth (continuous)
	• Malignancy (dichotomous)
	• Adverse events
	  ○ Infections (dichotomous)
	  ○ New onset diabetes mellitus/worsening control (dichotomous)

	○ Vascular access issues (dichotomous) ○ Dialysis access issues (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)

1.4 Clinical evidence

1.4.1 Included studies

No relevant clinical studies comparing various strategies for transferring or discontinuing RRT were identified.

See also the study selection flow chart in appendix C.

1.4.2 Excluded studies

See the excluded studies list in appendix E.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified.

1.5.2 Excluded studies

One economic study relating to this review question was identified but was excluded due to methodological limitations.[19] This is listed in appendix E, with reasons for exclusion given.

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

1.5.3 Summary of studies included in the economic evidence review

None.

1.5.4 Unit costs

Relevant current UK unit costs were provided to the committee aid consideration of cost effectiveness.

Different strategies in terms of indications for switching (e.g. switch after 1 infection vs 3 infections) may result in different numbers of people switching RRT modality and thus differences in resource use. The cost of switching to a different RRT modality will relate to preparation for the new modality (e.g. new access creation and any additional health care contacts required) and provision of the modality itself. If there are differences in monitoring requirements in order to assess the indicator for switching this could also be an additional cost.

Costs of dialysis access-related admissions and outpatient procedures are summarised in Table 2.

Costs of nephrology outpatient appointments are summarised in Table 3. Some tests and procedures would be additional to this.

Table 2: UK NHS reference costs 2015/16 for dialysis access-related inpatient and outpatient procedures

Currency description	Currency code	Admission	Number of FCEs	National average unit cost	Weighted average
HD access: tunnelled line					
Adults					
Insertion of Tunnelled Central Venous Catheter, 19 years and over	YR41A	Elective inpatient	544	£1,558	£1,149
		Non-elective long stay	280	£2,157	
		Non-elective short stay	1,042	£2,043	
		Day case	3573	£750	
		Regular Day or Night Admissions	73	£1,038	
		Out-patient	2	£368	
Attention to Central Venous Catheter, 19 years and over	YR43A	Elective inpatient	752	£1,062	£383
		Non-elective long stay	9	£3,738	
		Non-elective short stay	946	£917	
		Day case	44697	£354	
		Regular Day or Night Admissions	10651	£407	
		Out-patient	90	£98	
Removal of Central Venous Catheter, 19 years and over	YR44A	Elective inpatient	314	£1,043	£570
		Non-elective long stay	25	£4,336	
		Non-elective short stay	797	£1,109	
		Day case	6880	£459	
		Regular Day or Night Admissions	793	£727	
		Out-patient	95	£198	
Children					
Insertion of Tunnelled Central Venous Catheter, 18 years and under	YR41B	Elective inpatient	114	£2,886	£2,367
		Non-elective long stay	11	£5,926	
		Non-elective short stay	77	£2,536	
		Day case	145	£1,640	
		Regular Day or Night Admissions	3	£343	
Attention to Central Venous	YR43B	Elective inpatient	95	£1,209	£650

Currency description	Currency code	Admission	Number of FCEs	National average unit cost	Weighted average
Catheter, 18 years and under		Non-elective long stay	8	£4,672	
		Non-elective short stay	232	£712	
		Day case	2392	£654	
		Regular Day or Night Admissions	353	£342	
Removal of Central Venous Catheter, 18 years and under	YR44B	Elective inpatient	172	£1,533	£1,323
		Non-elective long stay	11	£16,682	
		Non-elective short stay	164	£1,243	
		Day case	894	£1,163	
		Regular Day or Night Admissions	80	£708	
HD access: AV fistula or graft					
Open Arteriovenous Fistula, Graft or Shunt Procedures	YQ42Z	Elective inpatient	2735	£2,451	£2,012
		Non-elective long stay	144	£3,661	
		Non-elective short stay	306	£1,826	
		Day case	5291	£1,763	
		Regular Day or Night Admissions	9	£665	
		Out-patient	28	£199	
Attention to Arteriovenous Fistula, Graft or Shunt	YR48Z	Elective inpatient	647	£1,715	£1,433
		Non-elective long stay	140	£2,824	
		Non-elective short stay	359	£2,079	
		Day case	2978	£1,235	
		Regular Day or Night Admissions	17	£523	
		Out-patient	3	£228	
PD access: PD catheter					
Renal Replacement Peritoneal Dialysis Associated Procedures	LA05Z	Elective inpatient	892	£1,819	£1,148
		Non-elective long stay	32	£5,701	
		Non-elective short stay	297	£1,288	
		Day case	1,588	£996	
		Regular Day or Night Admissions	46	£339	

Currency description	Currency code	Admission	Number of FCEs	National average unit cost	Weighted average
		Out-patient	470	£71	

Source: NHS reference costs 2015/16[6]

Abbreviations: FCE = finished consultant episodes

(a) HRG YR43A/B Attention to Central Venous Catheter, includes OPCS L921 Fibrin sheath stripping of access catheter, L922 Wire brushing of access catheter, L923 Thrombolysis of access catheter, L928 Other specified unblocking of access catheter, L929 Unspecified unblocking of access catheter, L913 Attention to central venous catheter NEC
(b) HRG YQ42 includes OPCS L746 Creation of graft fistula for dialysis, L741 Insertion of arteriovenous prosthesis, L742 Creation of arteriovenous fistula NEC, L743 Attention to arteriovenous shunt, L744 Banding of arteriovenous fistula, L745 Thrombectomy of arteriovenous fistula, L748 Other specified arteriovenous shunt, L749 Unspecified arteriovenous shunt, L752 Repair of acquired arteriovenous fistula
(c) HRG YR48 includes OPCS L746 Injection of radiocontrast substance into arteriovenous fistula
(d) HRG LA05 includes OPCS X411 Insertion of ambulatory peritoneal dialysis catheter, X412 Removal of ambulatory peritoneal dialysis catheter, X418 Other specified placement of ambulatory apparatus for compensation for renal failure, X419 Unspecified placement of ambulatory apparatus for compensation for renal failure, X421 Insertion of temporary peritoneal dialysis catheter, X428 Other specified placement of other apparatus for compensation for renal failure, X429 Unspecified placement of other apparatus for compensation for renal failure.

Table 3: 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

Currency code	Currency description	No. of attendances	National average unit cost
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	24	£139

Source: NHS reference costs 2015/16[6]

1.6 Resource impact

The recommendations made based on this review (see section **Error! Reference source not found.**) are not expected to have a substantial impact on resources.

1.7 Evidence statements

1.7.1 Clinical evidence statements

- No relevant published evidence was identified.

1.7.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.7.3 Interpreting the evidence

1.7.3.1 The outcomes that matter most

Critical outcomes included patient/family/carer quality of life, mortality and time to failure of RRT form. Important outcomes included hospitalisation, preferred place of death, symptom scores and functional measures, psychological distress and mental wellbeing, patient/family/carer experience of care, growth, malignancy and adverse events. There was no evidence available for this review.

1.7.3.2 The quality of the evidence

There was no evidence available for this review.

1.7.3.3 Benefits and harms

No evidence was identified to inform what are the benefits and harms of any particular strategy for transferring between RRT modalities or for discontinuing RRT. The committee agreed that any decision to transfer between RRT modalities or discontinue RRT will have to be one made collaboratively with the person on RRT, taking into account the possible risks and benefits of a transfer (or discontinuation) for that person.

1.7.4 Cost effectiveness and resource use

No published economic evidence was identified for this review.

Given the lack of clinical or cost effectiveness evidence, specific recommendation about indicators for switching or discontinuing were not made, however it was felt that it was appropriate to make some recommendations based on current good practice. These were not expected to have a substantial resource impact to the NHS in England.

1.7.5 Other factors the committee took into account

The committee noted that duration of peritoneal dialysis may be used as a reason to switch treatment in anticipation of rare but significant adverse events, such as encapsulating peritoneal sclerosis. There is no accepted optimal duration of peritoneal dialysis. In the absence of any evidence the committee considered that people should remain on the dialysis modality that is most effective and not switch unless there are clinical reasons to do so, or the patient or carers express a wish to switch. The committee highlighted the importance of

monitoring for complications that could potentially lead to a decision to switch. It is important that if complications are detected, and the possible implications of these, are discussed with the person, family members and carers (as appropriate). The guideline committee noted that switching dialysis modality is complex and has multiple components to it including the impact of co-morbidity and suitability for access.

The committee wished to reinforce current clinical practice for obtaining specialist advice when a woman is pregnant or wishes to become pregnant. The committee agreed that the need for a switch would depend on the adequacy of dialysis, the health of the foetus and the control of urea. Options may include switching modalities or increasing the frequency of dialysis sessions.

The committee noted people with failing transplants may not be offered regular opportunities to discuss the option to switch modality, which may results in a delay in planning for other forms of RRT. It is important that people who switch treatment modalities or to conservative management are provided with the same information, and given the same amount of time, as when starting treatment. The decision to switch should be discussed in the context of shared decision making. The guideline committee were aware of the recommendations on continuity of care and relationships in the NICE guideline CG138 on Patient experience in adult NHS services: improving the experience of care for people using adult NHS services

The committee confirmed that the recommendations were applicable to children and young people.

Those people who choose conservative management should have the opportunity to switch to RRT if their circumstances change or they change their mind. If people who have chosen conservative management continue to receive care on this pathway it is not discontinued, but instead merges with end of life care which usually means an increase in the level of support they are receiving as part of their conservative management

The committee noted that if the person lacks the capacity to make a decision, the provisions

of the Mental Capacity Act (2005) must be followed.

The committee made research recommendations on switching treatment modality after a first fungal, *Pseudomonasor Staphylococcus aureus* infection, after 5 years, in pregnancy and at early signs of fluid overload.

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Appendices

Appendix A: Review protocols

Table 4: Review protocol: transferring and discontinuing

Field	Content
Review question	What are the indicators for transferring between forms of RRT? What are the indicators for discontinuing RRT?
Type of review question	Intervention
Objective of the review	Determine appropriate indications that a person should transfer between forms of RRT or discontinue RRT
Eligibility criteria – population / disease / condition / issue / domain	Adults and children currently receiving RRT Stratified by age: • <2, 2 to <18, 18 to <70, ≥70) Stratified by sequence: • HD to PD • PD to HD • TPx to re-transplant/re-listing • TPx to other form of RRT • Any RRT being discontinued
Eligibility criteria – interventions	Transferring/discontinuing based on any suitable indicator Suitable indicators will vary between sequences, studies will not be chosen based on these criteria but examples include: • Time on modality (longer vs shorter, PD to HD) • Infection (first fungal/*Pseudomonas* infection vs continuing, PD to HD) • Imaging (early signs of encapsulating peritoneal sclerosis (EPS) vs later signs of EPS, PD to HD) • Ultrafiltration failure/adequacy targets (early signs of UFF vs later signs of UFF, PD to HD) • Heart failure (mild symptom vs moderate/severe, HD to PD) • Frailty/functional status (low frailty score vs high frailty score, RRT discontinuation) • eGFR (higher vs lower, re-transplantation) • Choice
Eligibility criteria – comparator(s) / control or reference (gold) standard	Any indication for transfer/discontinuation compared with any other
Outcomes and prioritisation	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) • Preferred place of death (dichotomous)

	• Symptom scores and functional measures (continuous)
	• Psychological distress and mental wellbeing (continuous)
	• Patient, family and carer experience of care (continuous)
	• Growth (continuous)
	• Malignancy (dichotomous)
	• Adverse events
	  ○ Infections (dichotomous)
	  ○ New onset DM/worsening control (dichotomous)
	  ○ Vascular access issues (dichotomous)
	  ○ Dialysis access issues (dichotomous)
	  ○ Acute transplant rejection episodes (dichotomous)
	
	Strategy:
	• When outcomes are reported at multiple timepoints, the later timepoints will be prioritised. Minimum duration of studies will be 3 months.
	• For the outcomes of quality of life, symptom scores/functional measures, psychological distress/mental wellbeing and experience of care – any validated measure 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 delivered in a level 2 or 3 care setting will be excluded.
Proposed sensitivity / subgroup analysis, or meta-regression	None
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 selection in Appendix C (clinical evidence selection) or D (health economic evidence selection).
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	Not registered

number	

Table 5: 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.[14] 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 E). **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 6: 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

Database	Dates searched	Search filter used
		Randomised controlled trials 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

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

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

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 7: 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

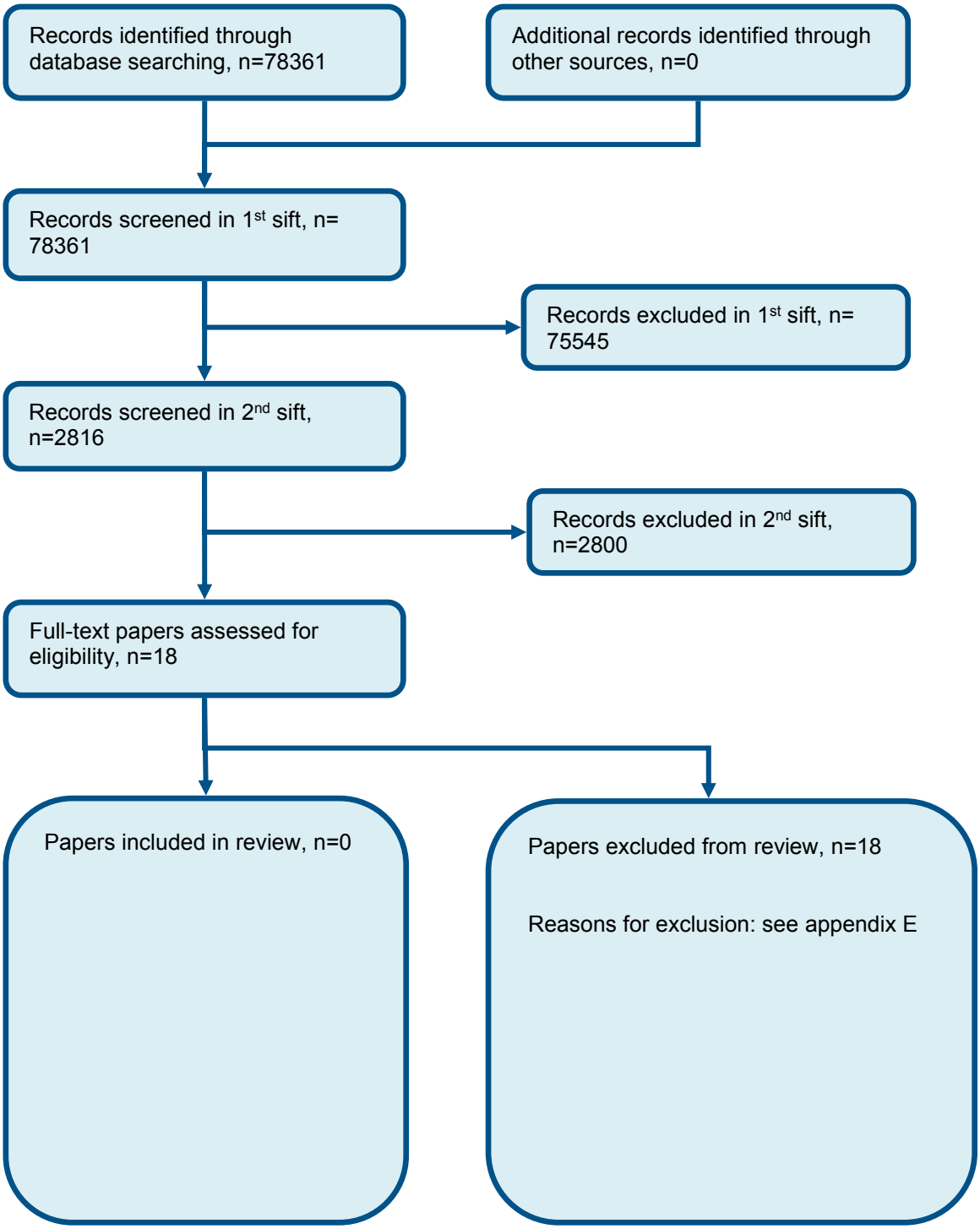
NHS EED and HTA (CRD) search terms

#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

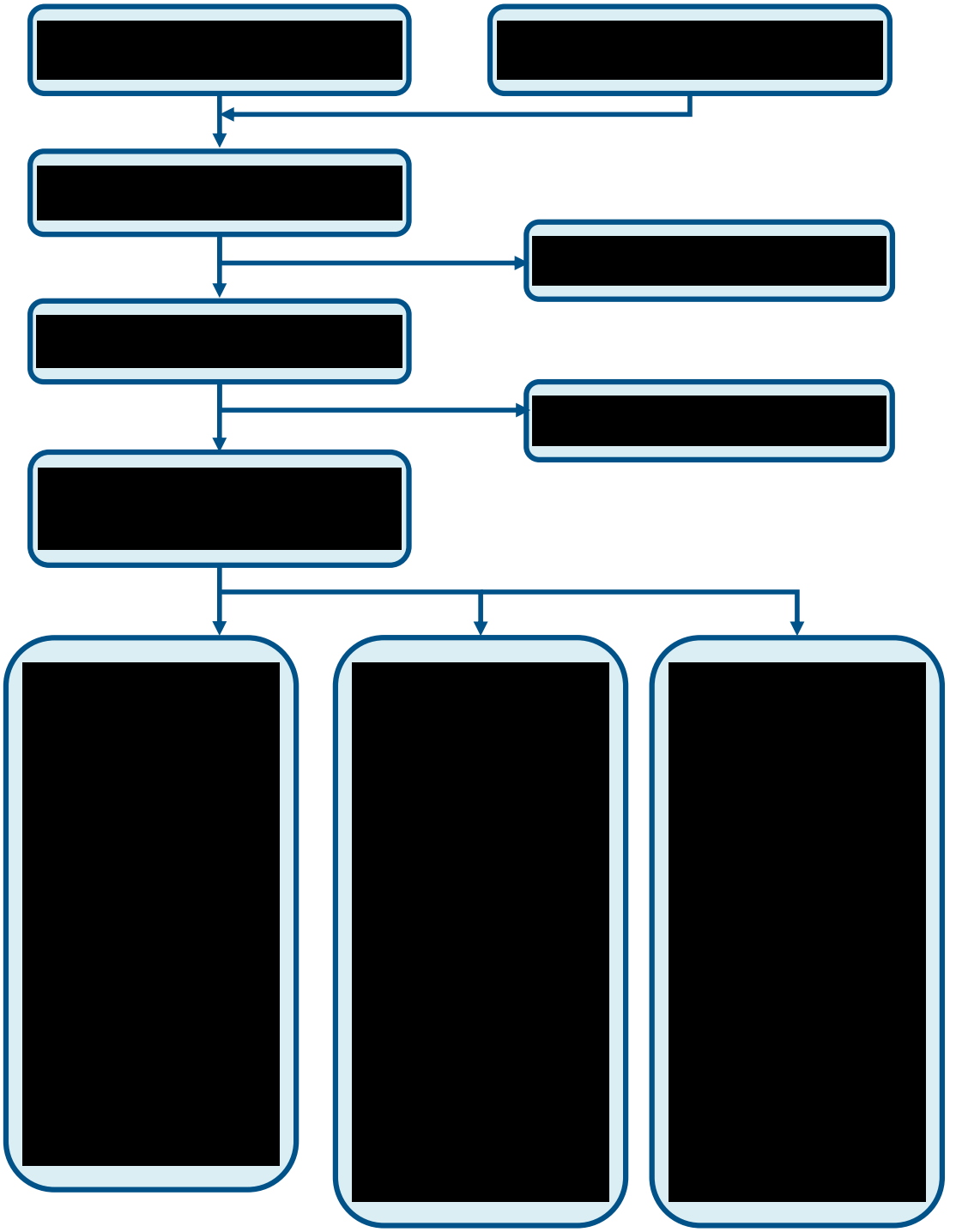
Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of transferring/discontinuing



Appendix D: Health economic evidence selection

Figure 2: Flow chart of economic study selection for the review of transferring/discontinuing



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
Note: Reviews H and K do not have an economic component

Appendix E: Excluded studies

E.1 Excluded clinical studies

Table 8: Studies excluded from the clinical review

Study	Exclusion reason
Aggarwal 2014[1]	Non-randomised study without adequate adjustment
Bajwa 1996[2]	Wrong comparison
Birmele 2004[3]	Wrong comparison
Chan 2012[4]	Wrong comparison
Cho 2014[5]	Wrong comparison
Findlay 2016[7]	Wrong comparison
Garonzik Wang 2011[8]	Abstract only
Gessert 2013[9]	Wrong comparison
Heldal 2015[10]	Abstract only
Jaar 2009[11]	No usable outcomes
Lan 2015[12]	Wrong comparison
Leggat 1997[13]	Wrong comparison
Nessim 2015[15]	Wrong comparison
Panagoutsos 2006[16]	Wrong comparison
Rao 2006[17]	Wrong comparison
See 2017[18]	Wrong comparison
Ye 2017[20]	Wrong comparison
Zhang 2013[21]	Wrong comparison

E.2 Excluded health economic studies

Table 9: Studies excluded from the health economic review

Reference	Reason for exclusion
Villa 2012[19]	This study was assessed as partially applicable with very serious limitations due to the relative differences between comparators not being based on a comparative study included in the clinical review.

Appendix F: Research recommendations

F.1 Effectiveness of switching RRT

Research question: What is the clinical and cost effectiveness of strategies for switching RRT treatment modality?

Why this is important: In the absence of evidence for the review the committee were unable to form recommendations on the clinical and cost effectiveness of switching RRT treatment modalities. Recommendations in this area are important as the process of switching between modalities incurs risk and requires a considerable treatment burden, advice to people to switch modalities on clinical ground needs to be evidence based.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults and children currently receiving RRT Intervention/comparison: 1. RRT treatment modality switched after a first fungal, *Pseudomonas* or *Staphylococcus aureus* infection vs continuing on current modality 2. RRT treatment modality switched after 5 years vs continuing on current modality 3. RRT treatment modality switched at early signs of fluid overload vs continuing on current modality Outcomes: Patient, family/carer health-related quality of life, mortality, time to failure of RRT form, hospitalisation, symptom scores and functional measures, psychological distress and mental wellbeing, patient, family and carer experience of care, adverse events (infections, vascular access issues, dialysis access issues)
Importance to patients or the population	If effective and cost-effective, such interventions could potentially provide significant benefits in terms of health-related quality of life through offering insight to the effectiveness of RRT modality switching.
Relevance to NICE guidance	There is current uncertainty about the clinical and cost effectiveness of switching RRT modality after the event of a fungal infection or at the early signs of fluid overload.
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 directly comparing different strategies for switching between modalities.
Equality	Not applicable
Study design	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)
Feasibility	No obvious feasibility issues
Other comments	Not applicable
Importance	• Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.