National Institute for Health and Care Excellence

Final

RRT and conservative management

Evidence review for frequency of review

NICE guideline NG107

Intervention evidence review

October 2018

Final

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.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN: 978-1-4731-3107-1

Contents

1 Frequency of review

1.1 Review questions: How frequently should people on the different forms of RRT and conservative management be reviewed?

1.2 Introduction

The frequency of review may relate to whether a person is on conservative management or RRT and its modality. For example, people on in-centre haemodialysis may have their biochemistry reviewed more frequently than those on home haemodialysis or peritoneal dialysis as they are in hospital more frequently. People who have had a transplant will be seen more frequently in the months immediately following the transplant surgery than once they have stabilised. Children are often reviewed more frequently than adults. The purpose of this review is to determine the clinical and cost effectiveness of different frequencies of review for the different renal replacement modalities and for conservative management.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People requiring RRT for CKD or opting for conservative management, once they are established on their option of choice (no cut-off for conservative management, >1 year for transplant >3 months for HD/PD) Stratified by: • HD vs PD vs transplant vs conservative management • Suspended on transplant list vs active on transplant list • Age (<2, 2 to <16, 16 to <25, 25 to <70, ≥70) • Diabetes mellitus vs no diabetes mellitus
Interventions	• Yearly review • 6 monthly review • 2-3 monthly review • Monthly review • Weekly review
Comparisons	Any review frequency strategy compared with any other
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 • Transplantation/transplant listing (rates/dichotomous) • 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)
	  ○ 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

No relevant clinical studies comparing how frequently people on different forms of RRT should be reviewed were identified.

1.4.1 Excluded studies

See the excluded studies list in appendix F.

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 D.

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. More frequent review will be associated with more healthcare appointments. Costs of nephrology outpatient appointments are summarised in Table 2. Some tests and procedures would be additional to this.

Table 2: 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

Source: NHS reference costs 2015/16[2]

1.6 Resource impact

No recommendations were made based on this review (section 1.8).

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.

1.8 The committee's discussion of the evidence

1.8.1 Interpreting the evidence

The outcomes that matter most

Critical outcomes for this review were quality of life, mortality and time to failure of RRT modality. Important outcomes for this review were transplant and transplant listing rates, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/mental wellbeing, experience of care, growth, malignancy and adverse events.

The quality of the evidence

There was no evidence identified for this review.

Benefits and harms

The committee noted that the aim of the review was not to provide recommendations on who should be reviewing people, this would depend on the context with some circumstances in which a specialist renal physician would be absolutely required and others in which review by a GP, specialist or non-specialist nurse would be appropriate. The committee discussed that what is reviewed may vary according to clinical circumstances, but may include serum biochemistry, blood pressure and weight. The committee noted that some reviews need to be carried out face to face whilst others can be done remotely.

Increasing the frequency of review may allow for quicker recognition of deterioration in the health state of people on RRT and conservative management and may improve communication, adherence with treatment and the prevention of complications. However, these benefits must be weighed against the potential harms in terms of treatment burden both on the person undergoing RRT or conservative management and on the healthcare services. This burden is particularly relevant in RRT where people may have many different healthcare contacts and multiple weekly hospital visits due to the severity of their condition and comorbidities.

Transplant

Current practice varies between centres in terms of assessing transplant function but commonly involves eGFR being measured 3 monthly and eGFRs being reviewed by a member of the renal team on a 3 to 6 monthly basis. Children would be assessed at least every three months. The general health of people with a stable renal transplant is typically assessed at least once a year and includes an assessment of cardiovascular risk factors.

Dialysis

The committee noted that people receiving in-centre dialysis may be reviewed too frequently because it is logistically easier to do, however it is difficult to make more specific recommendations about the ideal frequency in the absence of any evidence.

Conservative management

Frequency of review in conservative management is highly dependent on the prognosis of the person and the stage of their treatment. The guideline committee were aware of the NICE guideline on End of life care for adults in the last year of life: service delivery (in development). For example someone who has made an informed decision not to have RRT but has some residual renal function and is currently relatively well within themselves may not need to be reviewed as frequently as someone who has recently discontinued RRT and has very limited life expectancy. The frequency of review will increase if a person's condition deteriorates and will be based on individual circumstances and preferences. Although in general the committee did not specify the format of review in these recommendations, they noted that face to face review in this population is likely to be particularly important for example to assess current functional status.

1.8.2 Cost effectiveness and resource use

No published economic evaluations were identified for this review.

More frequent review will be more costly than less frequent review as there will be more healthcare contacts for example appointments. As described above, there may be health benefits to the patients of more frequent review; however the additional burden of more appointments could also impact patients. There was no evidence available to assess these trade-offs from a clinical or health economic perspective. It is also likely there would be a substantial resource impact of any recommendations that changed review frequency from current practice due to the large population it would affect. The committee considered making recommendations based on current practice but could not reach consensus and so no recommendations were made.

1.8.3 Other factors the committee took into account

The committee emphasised that the aim of this review was to determine the optimum frequency of review in a number of situations during RRT or conservative management. No evidence was identified to support any particular strategy of timing of review. The committee discussed the prospect of consensus based recommendations; however, there was considerable variation in practice for the frequency of review for all modalities of renal replacement therapy and for conservative management. For example the frequency of review may vary according to whether the person is receiving a hospital or home based therapy. The committee did not consider the consensus to be strong enough to define the different types of review and then subsequently the frequency each of those reviews should be occurring. The committee prioritised this as a key area for further research given the resource implications and lack of current evidence based practice.

References

1. Casey ET, Murad MH, Rizvi AZ, Sidawy AN, McGrath MM, Elamin MB et al. Surveillance of arteriovenous hemodialysis access: a systematic review and meta-analysis. Journal of Vascular Surgery. 2008; 48(5 Suppl):48S-54S

2. Department of Health. NHS reference costs 2015-16. Available from: https://www.gov.uk/government/publications/nhs-reference-costs-2015-to-2016 Last accessed: 17/01/2018.

3. Devereaux PJ, Schunemann HJ, Ravindran N, Bhandari M, Garg AX, Choi PT et al. Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis. JAMA. 2002; 288(19):2449-57

4. Jiang S, Stewart G, Barnes E, Jardine M, Razavian M, Gallagher M. Effect of a vascular access surveillance program on service provision and access thrombosis. Seminars in Dialysis. 2013; 26(3):361-5

5. Josephson MA. Monitoring and managing graft health in the kidney transplant recipient. Clinical Journal of the American Society of Nephrology. 2011; 6(7):1774-1780

6. Lok CE, Bhola C, Croxford R, Richardson RMA. Reducing vascular access morbidity: A comparative trial of two vascular access monitoring strategies. Nephrology Dialysis Transplantation. 2003; 18(6):1174-1180

7. McCarley P, Wingard RL, Shyr Y, Pettus W, Hakim RM, Ikizler TA. Vascular access blood flow monitoring reduces access morbidity and costs. Kidney International. 2001; 60(3):1164-72

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

9. Paulson WD. Access monitoring does not really improve outcomes. Blood Purification. 2005; 23(1):50-6

10. Pisoni RL, Zepel L, Port FK, Robinson BM. Trends in us vascular access use, patient preferences, and related practices: An update from the US DOPPS practice monitor with international comparisons. American Journal of Kidney Diseases. 2015; 65(6):905-915

11. Plantinga LC, Jaar BG, Astor B, Fink NE, Eustace JA, Klag MJ et al. Association of clinic vascular access monitoring practices with clinical outcomes in hemodialysis patients. Nephron. 2006; 104(4):c151-9

12. Polkinghorne KR, Lau KK, Saunder A, Atkins RC, Kerr PG. Does monthly native arteriovenous fistula blood-flow surveillance detect significant stenosis--a randomized controlled trial. Nephrology Dialysis Transplantation. 2006; 21(9):2498-506

13. Robbin ML, Oser RF, Lee JY, Heudebert GR, Mennemeyer ST, Allon M. Randomized comparison of ultrasound surveillance and clinical monitoring on arteriovenous graft outcomes. Kidney International. 2006; 69(4):730-5

14. Sands JJ. Vascular access monitoring improves outcomes. Blood Purification. 2005; 23(1):45-9

15. Sands JJ, Jabyac PA, Miranda CL, Kapsick BJ. Intervention based on monthly monitoring decreases hemodialysis access thrombosis. ASAIO Journal. 1999; 45(3):147-50

16. Tessitore N, Bedogna V, Poli A. The role of surveillance in mature arteriovenous fistula management. Journal of Vascular Access. 2004; 5(2):57-61

17. Valliant A, McComb K. Vascular access monitoring and surveillance: An update. Advances in Chronic Kidney Disease. 2015; 22(6):446-452

18. Young EW, Goodkin DA, Mapes DL, Port FK, Keen ML, Chen K et al. The Dialysis Outcomes and Practice Patterns Study (DOPPS): An international hemodialysis study. Kidney International, Supplement. 2000; 57(74):S74-S81

Appendices

Appendix A: Review protocols

Table 3: Review protocol: Frequency of review

Field	Content
Review question	How frequently should people on the different forms of RRT and conservative management be reviewed?
Type of review question	Intervention
Objective of the review	Determine optimum frequency of review for each of the forms of RRT and conservative management
Eligibility criteria – population / disease / condition / issue / domain	People requiring RRT for CKD or opting for conservative management, once they are established on their option of choice (no cut-off for CM, >1 year for TPx, >3 months for HD/PD) Stratified by: HD vs PD vs TPx vs CM Suspended on TPx list vs active on TPx list Age (<2, 2 to <16, 16 to <25, 25 to <70, ≥70) DM vs no DM
Eligibility criteria – interventions	Yearly review 6 monthly review 2-3 monthly review Monthly review Weekly review Review defined as monitoring beyond basic observations (e.g. weight, blood pressure) as would be provided at a dialysis session. Exact components of review to vary depending on modality and population, transplant likely to include a review of the health of the patient and of their transplant function, PD may involve a peritoneal equilibration test (PET), HD may involve an assessment of Kt/V, both PD and HD likely to involve an assessment of adequacy, access, technique and the appropriateness of home therapy
Eligibility criteria – comparator(s) / control or reference (gold) standard	Any review strategy 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 Transplantation/transplant listing (rates/dichotomous) 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

Field	Content
	Infections (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 1 year. 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	Person conducting review - MDT vs individual Method of review – in person vs other BAME vs non-BAME
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

Field	Content
	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) or D (health economic evidence).
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 4: 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.[8] 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 F). **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 5: 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 Systematic review studies

Database	Dates searched	Search filter used
		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 6: 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

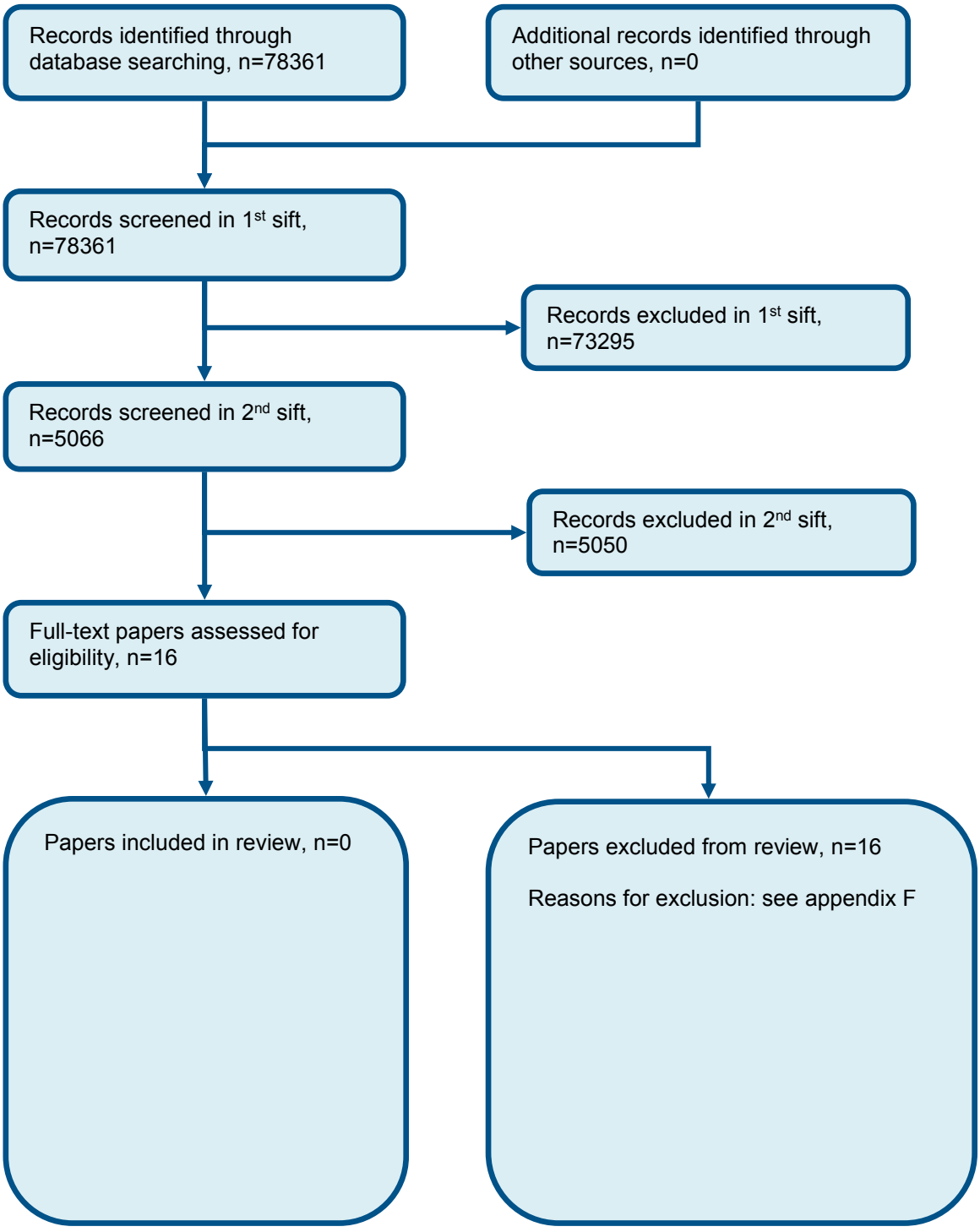
NHS EED and HTA (CRD) search terms

#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*))

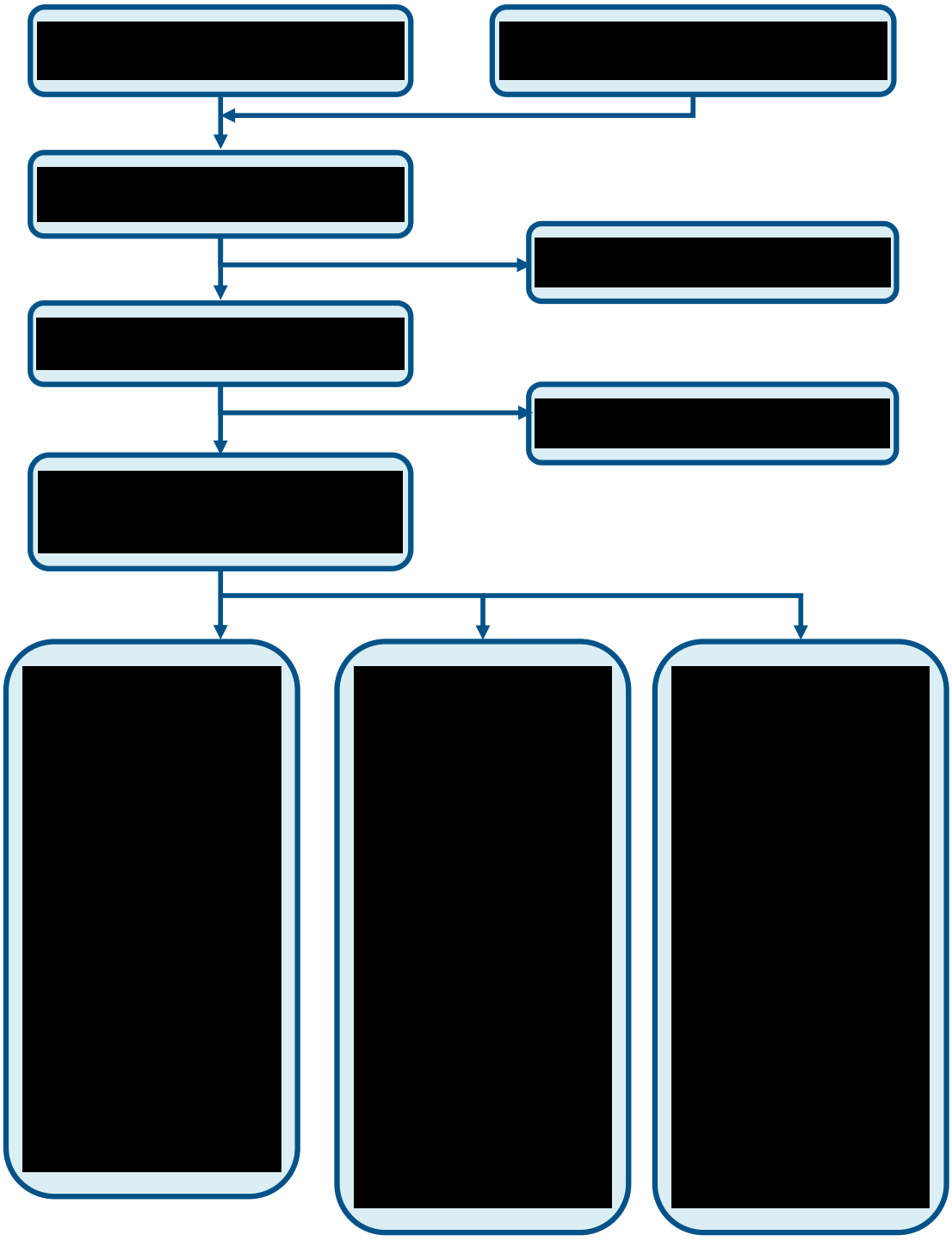
#9.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of frequency of review



Appendix D: Health economic evidence selection



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: Health economic evidence tables

None.

Appendix F:Excluded studies

F.1 Excluded clinical studies

Table 7: Studies excluded from the clinical review

Study	Exclusion reason
Casey 2008[1]	SR, references checked
Devereaux 2002[3]	SR, not matching PICO
Jiang 2013[4]	No usable outcomes
Josephson 2011[5]	Review, not systematic
Lok 2003[6]	NRS without adequate adjustment
McCarley 2001[7]	Wrong comparison
Paulson 2005[9]	Review, not systematic
Pisoni 2015[10]	Wrong study design
Plantinga 2006[11]	Wrong comparison
Polkinghorne 2006[12]	Wrong comparison
Robbin 2006[13]	Wrong comparison
Sands 1999[15]	Wrong comparison
Sands 2005[14]	Review, not systematic
Tessitore 2004[16]	Review, not systematic
Valliant 2015[17]	Review, not systematic
Young 2000[18]	Wrong study design

F.2 Excluded health economic studies

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

Table 8: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	

Appendix G: Research recommendations

G.1 Ideal frequency of review for PD and HD

Research question: What is the most clinical and cost-effective frequency of review of people on PD, haemodiafiltration, haemodialysis or conservative management?

Why this is important: The committee were unable to make recommendations on which frequency of review offers the best clinical and cost effectiveness for those on PD, HD, HDF or conservative management due to a lack of evidence identified in this review and insufficient consensus. Recommendations in this area are important to optimise the frequency of review for people requiring RRT and to enable services to efficiently provide clinically effective treatment.

Criteria for selecting high-priority research recommendations:

PICO question	Population: People requiring PD, HD, HDF or conservative management for CKD, once they are established on their option of choice (>3 months) Intervention/comparison: Yearly review (review to include face to face assessment and review of biochemical measures) 6 monthly review 2-3 monthly review Monthly review Outcomes: Patient, family/carer health-related QoL, mortality, time to failure of RRT form, transplantation/transplant listing, resource use, symptom scores and functional measures, psychological distress and mental wellbeing, patient, family/carer experience of care, adverse events (infections, vascular access issues, dialysis access issues, acute transplant rejection episodes)
Importance to patients or the population	If effective and cost-effective, such an intervention could potentially identify the optimal frequency of reviewing those on PD, HD, HDF and conservative management and provide benefits in terms of health-related quality of life, time to failure of RRT form and potentially reducing unnecessary healthcare resource use and patient treatment burden.
Relevance to NICE guidance	There is current uncertainty about the clinical and cost effectiveness for the frequency of reviewing those on PD, HD, HDF or conservative management.
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 optimal frequency of review for PD and HD patients. It is important to have sufficient information on this topic so further evidence based information can be given in regards to the best frequency of reviewing those on PD, HD, HDF or 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)
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.