National Institute for Health and Care Excellence

Final

RRT and conservative management

How to assess people for RRT

NICE guideline

Guideline number NG107

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/or their carer or guardian.

Local commissioners and/or 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 All NICE guidance is subject to regular review and may be updated or withdrawn.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 How to assess people for RRT

1.1 Review question: What assessment is needed for people progressing through later stages of CKD for whom RRT or conservative management may be appropriate?

1.2 Introduction

This review explores which assessments need to be carried out in people who may start renal replacement therapy. The focus is on those tests where there are variations in practice. Specifically we look at cardiac assessment, ultrasound of iliac vessels, ultrasound mapping of vascular access sites and pre-transplant psychological assessment for living donor - recipient pair or recipient only.

While there is widespread agreement that a cardiovascular assessment is required for many patients prior to transplantation, there is no consensus regarding the optimal method of assessment. Similarly there is uncertainty regarding the value of ultrasound of iliac vessels to evaluate the calibre of these blood vessels prior to transplantation. In preparation for the creation of arteriovenous fistulae (AVF), ultrasound mapping of the vascular access sites may improve outcomes. However, the utility of this compared to physical examination alone is uncertain. The purpose of the psychological assessment of transplant recipients is to assess suitability and identify concerns that may affect transplant outcome. Issues such as informed consent and motivation for donating need to be explored with the living donor. This review identifies the evidence on the clinical and cost effectiveness of the above assessments.

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 considering RRT or conservative management of established renal failure
Interventions	Cardiac assessment (including at least a cardiac stress test or echocardiogram) Ultrasound of iliac vessels Ultrasound mapping of vascular access sites Psychological assessment for live donor – recipient pair or recipient
Comparisons	Any of the above strategies (alone or in combination) compared with any other or usual care/sham
Outcomes	Critical • Patient, family/carer health-related QoL (continuous) • Symptom scores and functional measures (continuous) • Mortality (dichotomous and time to event) • Hospitalisation (rates or continuous) • Time to failure of RRT form (time to event) Important • Psychological distress and mental wellbeing (continuous) • Cognitive impairment (dichotomous) • Patient, family/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, non-randomised studies will be considered but only if outcomes are adjusted for the following key confounders • Age • Health at baseline • Co-morbidities • Ethnicity

The guideline committee prioritised the interventions listed above for consideration as components of the assessment. The committee felt they represented interventions that are currently offered variably across the country and with uncertain clinical and cost effectiveness underlying their provision.

1.4 Clinical evidence

1.4.1 Included studies

Three studies were included in the review;[2, 5, 6] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3). Psychological assessment included psychosocial assessment, evaluation and support.

All three studies were RCTs that assessed the clinical effectiveness of ultrasound mapping of vascular access sites compared to clinical examination alone. No studies, RCT or NRS, were identified that assessed the clinical effectiveness of the other interventions identified by the committee.

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
Ferring 2010[2]	Ultrasound mapping + physical examination (n = 112) Physical examination only (n = 106)	UK Median age 68 People with end stage kidney disease referred for permanent access formation	Primary AVF failure (at 1 month)	Both groups received ultrasound but control group did not have their surgeon informed of ultrasound results

Study	Intervention and comparison	Population	Outcomes	Comments
Nursal 2006[5]	Ultrasound mapping + physical examination (n = 35) Physical examination only (n = 35)	Turkey Mean age 57 (SD 14) People with end stage kidney disease referred for permanent access formation	Lack of AVF patency (at end of follow-up)	Excluded people in whom a suitable site could not be found by physical examination alone
Smith 2014[6]	Ultrasound mapping + physical examination (n = 47) Physical examination + selective ultrasound mapping (n = 47)	UK Mean age 65 (range 23 to 85) People referred to vascular department to assess for AVF formation	Primary AVF failure (thrombosis within 30 days of formation)	Control arm received ultrasound mapping if physical examination deemed unsatisfactory

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Ultrasound vs physical examination

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Physical examination	Risk difference with Ultrasound (95% CI)
AVF failure	333 (3 studies) 1 to 6 months	MODERATE[1] due to imprecision	RR 0.73 (0.53 to 1.01)	Moderate	
				358 per 1000	97 fewer per 1000 (from 168 fewer to 4 more)

1 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were included.

1.5.2 Excluded studies

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

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

1.5.3 Unit costs

Relevant current UK unit costs were provided to aid consideration of cost effectiveness. Clinical evidence was identified relating to ultrasound mapping of veins prior to creation of vascular access for haemodialysis. Below is the cost of a vascular ultrasound scan occurring in an outpatient setting. Diagnostic imaging is reported separately in the NHS reference costs in this setting. The clinical evidence suggested a possible reduction in access failure. Access failure may result in an additional access-related procedure and so NHS reference costs for these are included in Table 5.

Table 4: UK NHS reference costs 2015/16 for ultrasound occurring in an outpatient setting

Currency Code	Currency Description	No. of examinations	Unit Cost		
			National Average	Lower Quartile	Upper Quartile
RD47Z	Vascular Ultrasound Scan	126,486	£58	£39	£70

Source: NHS reference costs 2015/16[1]

Table 5: 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	

Currency description	Currency code	Admission	Number of FCEs	National average unit cost	Weighted average
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 Catheter, 18 years and under	YR43B	Elective inpatient	95	£1,209	£650
		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	

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

Source: NHS reference costs 2015/16[1]

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.

1.5.4 Cost calculation

Clinical evidence was identified relating to routine ultrasound mapping of veins prior to creation of AVF for haemodialysis. Rates of ultrasound use will be higher with a routine ultrasound strategy, and so ultrasound costs will be higher; the exact difference between strategies will depend on whether the comparator is no ultrasound or selective ultrasound which varied between included clinical studies. However, the evidence suggests that the rates of AVF failure (which will require an additional procedure) are lower and this will offset the additional ultrasound costs. Below we calculate the cost of AVF failure required to completely offset the additional ultrasound costs. This is also summarised in Table 6 below.

Where the comparison is routine ultrasound versus no ultrasound (as in Nursal 2006[5] and Ferring 2010[2]) the average per person cost difference will be the cost of an ultrasound; that is £58 (see unit cost section above). Where the comparison is routine ultrasound versus selective ultrasound the rate of ultrasound in the selective arm needs to be taken into account. In Smith 2014[6] from the clinical review, 34% of people had an ultrasound in the selective arm resulting in an average ultrasound cost per person of £20 (£58 x 34%) and the difference with a routine ultrasound strategy is reduced to £38 (£58 - £20).

Downstream, the clinical evidence suggested a lower rate of AVF failure with routine ultrasound. AVF failure would result in resource use such as an additional vascular access procedure and so this would at least partially offset the higher cost with routine ultrasound. Using the absolute failure rates reported in the clinical evidence profile in section 1.44 of an absolute reduction of 97 per 1000, to offset the additional cost of ultrasound AVF failure would need to associated with a cost at least £593 (when the comparator is no ultrasound) or £391 (when the comparator is selective ultrasound with a 34% use rate).

The definition of AVF failure varied between the included clinical studies. In Ferring 2010[2] AVF failure was defined as “AVFs were unusable for dialysis, requiring a salvage intervention, new access formation or insertion of a HD catheter” while in Smith 2014[6] it was just thrombosis. The NHS references costs related to dialysis access are reported in Table 5 in the previous section. The average cost for admission for these procedures is greater than that required to offset the additional cost of ultrasound - ‘Open Arteriovenous Fistula, Graft or Shunt Procedures’ is £2012 and ‘Insertion of HD catheter’ is £1149 in adults and £2367 in children.

Even if a higher cost of ultrasound is used (£70, the upper quartile from the NHS reference costs), the cost of AVF required to offset the additional ultrasound costs is below these average admission costs.

Table 6: Routine ultrasound mapping of veins prior to creation of vascular access for haemodialysis: threshold cost calculation

	Comparator (No US / selective US)	Routine US	Difference Routine – comparator (no US / selective US)
US use[a]	0% / 34%	100%	100% / 66%
Average US cost per patient (use % x unit cost of ultrasound £58[b])	£0 / £20	£58	£58 / £38
AVF failure[a]	358 per 1000	261 per1000	97 fewer per 1000
Cost of AVF failure that would result in no difference in costs for routine US			£593 / £391
Sensitivity analysis where the cost of ultrasound is £39 (lower quartile in reference costs)[b]			*£403 / £266*
Sensitivity analysis where the cost of ultrasound is £70 (upper quartile in reference costs)[b]			*£721 / £476*

Abbreviations: AVF: arteriovenous fistula; US: ultrasound.
(a) From clinical review in Section 1.4
(b) NHS reference costs 2015/16[1]

1.6 Resource impact

The recommendations made based on this review (see section 1.9) are not expected to have a substantial impact on resources.

1.7 Evidence statements

1.7.1 Clinical evidence statements

- Moderate quality evidence from 3 studies of 333 participants showed a clinically important benefit of routine ultrasound scanning in terms of AVF success rate.

1.7.2 Health economic evidence statements

- No relevant economic evaluations were included.

1.8 Interpreting the evidence

1.8.1.1 The outcomes that matter most

Routine ultrasound mapping of veins prior to creation of vascular access

Critical outcomes were mortality and quality of life. Time to failure of RRT was defined as time until that modality of RRT was no longer working or suitable, and a modality switch occurred. Since death in a person receiving RRT could also be considered “failure”, some papers presented “death censored failure”, but we have favoured presenting both death and failure separately.

Other important outcomes were numbers of hospitalisation, measures of mental wellbeing and cognitive impairment, malignancy and adverse events, in the case of ultrasound scanning vascular access issues (including AVF failure) was a particularly important adverse event. We were also interested in outcomes representing people’s experience of care.

Cardiac assessment

No evidence was identified.

US of iliac vessels

No evidence was identified.

Psychological assessment for live donor pair or recipient

No evidence was identified

1.8.1.2 The quality of the evidence

Routine ultrasound mapping of veins prior to creation of vascular access

There was moderate quality evidence in adults, for a benefit of routine ultrasound scanning on the outcome of AVF failure. There were no other outcomes available for this comparison in any age group. There was no other evidence available for any of the other comparisons.

Cardiac assessment

No evidence was identified.

US of iliac vessels

No evidence was identified.

Psychological assessment for live donor pair or recipient

No evidence was identified.

1.8.1.3 Benefits and harms

Routine ultrasound mapping of veins prior to creation of vascular access

The point estimate for the absolute effect fell just short of the agreed upon absolute MID for dichotomous outcomes but given the magnitude of the relative and absolute effects, the impact of AVF failures and the consensus based nature of the absolute MID points, the committee agreed that the evidence represented a clinically important benefit of routine ultrasound scanning in terms of reducing AVF failure.

The committee noted that there were unlikely to be any specific harms of routine ultrasound scanning, the harms of offering the intervention therefore were only related to any possible delays in fistula formation if scanning was not immediately available. The committee agreed that the benefit in terms of failure rate outweighed concerns about delays in formation.

Cardiac assessment

The committee noted that there may be benefits of cardiac assessment in preparation for transplant in terms of preventing people with excessively high cardiovascular risk from being inappropriately exposed to the risks of surgery, allowing people to optimise their cardiovascular risk profile before surgery and promoting the most appropriate use of potential kidney transplants. However there are considerable harms involved in terms of potentially delaying the patient pathway towards transplantation (especially when the benefits of pre-emptive transplantation are considered) and the harms of each individual cardiac assessment themselves. Given the magnitude and uncertainty of these benefits and harms, as well as the current variability of service provision, this was considered an important area for a research recommendation.

The committee noted that it is current practice to undertake cardiac assessment in children and young people (up to 18 years) to identify congenital anomalies and confirm adequate function to withstand high fluid loads during transplantation

US of iliac vessels

No evidence was identified.

Psychological assessment for live donor – recipient pair or recipient

No evidence was identified.

1.8.2 Cost effectiveness and resource use

Routine ultrasound mapping of veins prior to creation of vascular access

No relevant published studies were identified.

Clinical evidence of benefit was identified for routine ultrasound mapping of veins prior to creation of an AVF for haemodialysis. Rates of ultrasound use will be higher with the routine ultrasound strategy, and so ultrasound costs will be higher; the exact difference between strategies will depend on whether the comparator is no ultrasound or selective ultrasound which varied between included clinical studies. However, the rates of AVF failure (which will require an additional procedure) were found to be higher in the clinical review and this will offset the additional ultrasound costs.

A threshold analysis based on the evidence included in the clinical review found that in order to offset the additional costs of a routine ultrasound strategy the cost of AVF failure would need to be at least £593 when the comparator was no ultrasound or £391 when the comparator was selective ultrasound. The committee considered the current UK average costs for procedures that would be required in the case of AVF failure (for example, a salvage procedure, new AVF creation procedure or insertion of an HD catheter), and concluded that as these were well in excess of the threshold value required to offset the cost of routine ultrasound it was reasonable to conclude that this was likely to be cost saving. The average cost for admission for 'Open Arteriovenous Fistula, Graft or Shunt Procedures' is £2012 and 'Insertion of HD catheter' is £1149 in adults and £2367 in children.

Given the clinical benefit to the patient of avoiding procedures and the likely cost savings the committee concluded that routine ultrasound mapping prior to creation of AVF was likely to be cost effective and so this supported a recommendation for its use.

The committee believe that currently practice is variable regarding whether a selective or routine strategy is employed but agreed that a recommendation for routine ultrasound scanning would not involve a large change in practice. The recommendation is not expected to result in a substantial resource impact to the NHS in England.

Cardiac assessment

No relevant published studies were identified. Undertaking cardiac assessment will involve resource use and this will vary depending on what assessments are undertaken, although plausibly there may be downstream cost or health benefits that offset this. However, given the lack of clinical evidence the committee was unable to make a judgement regarding cost effectiveness.

US of iliac vessels

No relevant published studies were identified. Undertaking ultrasound of iliac vessels will involve resource use, although there may be cost or health benefits that offset this. Given the lack of clinical evidence the committee was unable to make a judgement regarding cost effectiveness.

Psychological assessment for live donor – recipient pair or recipient

No relevant published studies were identified. Undertaking psychological assessment for live donor pairs or recipients will involve resource use and may delay treatment. The committee agreed that there were likely benefits to patients but also potential harms due to delays in treatment. Given this and the lack of clinical or cost effectiveness evidence the committee agreed that a recommendation for assessment in specific high risk groups was appropriate. Psychological assessment in high risk people was considered current practice in many areas. The recommendation was considered likely to better target psychological assessment in other areas. The recommendation was not considered likely to have a substantial resource impact overall.

1.8.3 Other factors the committee took into account

The committee also recognised that an assessment should involve preparing people for renal replacement therapy for example procedures to create vascular access. Preparing a person psychologically is important for reducing non-adherence and improving outcomes. The committee also highlighted the importance of discussing a person's individual preferences and understanding how decisions on renal replacement therapy or conservative management are likely to impact on a person's everyday life.

Routine ultrasound mapping of veins prior to creation of vascular access

The committee discussed how ultrasound scanning may take place. Current clinical practice is variable but typically involves at minimum a selective ultrasound scanning program, for those in whom a physical examination alone is insufficient or impractical (CT or angiography may also be required). In some centres this scanning is done by the consultant who will be responsible for subsequent AVF creation, whereas in others people are referred to ultrasound departments. The studies including in the review involved duplex ultrasound scanning.

The committee discussed whether there would be any implementation issues for a routine ultrasound strategy and concluded that there should not be any significant issues as ultrasound is already widely used within hospitals.

Psychological assessment for live donor pair or recipient
The committee noted that as part of the initial assessment for RRT other members of the MDT and psychosocial team may assess for psychosocial issues and provide support as appropriate. Further assessment by a clinical psychologist or psychiatrist is only for those people who are considering transplant and where complex risk factors have been previously identified in order plan appropriate support/psychological intervention. These issues are usually complex, and assessment should be carried out a specially trained mental health professional

The committee discussed that the purpose of this assessment of the transplant recipient is to identify any potential risk factors for example substance abuse, non-adherence to treatment or a previous or current mental health condition that may result in post-operative non-adherence or morbidity, and to advise on or provide support and intervention as appropriate. The psychological assessment of young people and children covers psycho-social factors, quality of life, knowledge of the condition, worries and concerns and readiness for transplant. How the person processes information and any barriers to learning are also assessed.

The committee noted that living donors have to undergo a Human Tissue Authority Independent Assessment. This explores capacity, checks the person is not being pressured and will not receive any payment. The committee discussed whether donors should undergo additional psychological assessment but agreed that this should be based on individual circumstances.

The committee noted the importance of adhering to the Mental Capacity Act (2005).

The guideline committee was aware of NICE's guideline on information and education in CG182 Chronic Kidney Disease in adults: assessment and management.

References

1. 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.

2. Ferring M, Claridge M, Smith SA, Wilmink T. Routine preoperative vascular ultrasound improves patency and use of arteriovenous fistulas for hemodialysis: a randomized trial. Clinical Journal of the American Society of Nephrology. 2010; 5(12):2236-44

3. Mihmanli I, Besirli K, Kurugoglu S, Atakir K, Haider S, Ogut G et al. Cephalic vein and hemodialysis fistula: surgeon's observation versus color Doppler ultrasonographic findings. Journal of Ultrasound in Medicine. 2001; 20(3):217-22

4. 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/

5. Nursal TZ, Oguzkurt L, Tercan F, Torer N, Noyan T, Karakayali H et al. Is routine preoperative ultrasonographic mapping for arteriovenous fistula creation necessary in patients with favorable physical examination findings? Results of a randomized controlled trial. World Journal of Surgery. 2006; 30(6):1100-7

6. Smith GE, Barnes R, Chetter IC. Randomized clinical trial of selective versus routine preoperative duplex ultrasound imaging before arteriovenous fistula surgery. British Journal of Surgery. 2014; 101(5):469-74

7. Zhang Z, Wang XM. Hemodynamic evaluation of native arteriovenous fistulas for chronic hemodialysis with color Doppler ultrasound. Chinese Journal of medical imaging technology. 2006; 22(5):718-21

Appendices

Appendix A: Review protocols

Table 7: Review protocol: how to assess people for RRT

Field	Content
Review question	How should people progressing through later stages of CKD be assessed for RRT?
Type of review question	Intervention
Objective of the review	Provide evidence for recommendations about what should occur during the "assessment" for RRT period
Eligibility criteria – population / disease / condition / issue / domain	Children, young people and adults with CKD stage 3 to 5 Stratified by: • Age (<2, 2 to <18, 18 to <70, ≥70) • BAME vs non-BAME • DM vs no DM
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Assessment: • Cardiac assessment (as minimum stress test/echocardiogram) • US of iliac vessels • US mapping of vascular access sites • Psychological assessment for live donor pair or recipient only(including checking for adherence)
Eligibility criteria – comparator(s) / control or reference (gold) standard	Any of the above strategies (alone or in combination) compared with any other or usual care/sham
Outcomes and prioritisation	Critical • Patient, family/carer health-related QoL (continuous) • Symptom scores and functional measures (continuous) • Mortality (dichotomous and time to event) • Hospitalisation (rates or continuous) • Time to failure of RRT form (time to event) Important • Psychological distress and mental wellbeing (continuous) • Cognitive impairment (dichotomous) • Patient, family/carer experience of care (continuous) • Growth (continuous) • Malignancy (dichotomous) • Adverse events o Infections (dichotomous) o Vascular access issues (dichotomous) o Dialysis access issues (dichotomous) o Acute transplant rejection episodes (dichotomous) When outcomes are reported at multiple timepoints, the later timepoints will be prioritised. All outcomes must be reported after at least 4 weeks of the intervention under investigation. The outcomes of mortality and

	hospitalisation must be reported after at least 6 months. For quality of life, symptom scores/functional measures, psychological distress/mental wellbeing and experience of care, any validated measures will be accepted. Absolute MIDs of 30 per 1000 will be used for mortality and modality failure. Absolute MIDs of 100 per 1000 will be used for all other outcomes dichotomous outcomes. Where relative MIDs are required (if absolute effects are unavailable), 0.90 to 1.11 will be used for mortality and modality failure. The default relative MIDs of 0.8 to 1.25 will be used for all other dichotomous outcomes. Default continuous MIDs of 0.5x SD will be used for all continuous outcomes, except where published, validated MIDs exist.
Eligibility criteria – study design	RCTs will be prioritised. If insufficient evidence is found, 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	
Proposed sensitivity / subgroup analysis, or meta-regression	• Different modalities of RRT
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 the separate search strategy appendix for the guideline.
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	For details please see evidence tables in Appendix D (clinical evidence

variables to be collected	tables) or H (health economic evidence tables) of the evidence report.
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 report.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by 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 guideline in collaboration with the committee. For details please see the separate Methods report for this guideline.
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 the NHS in England.
PROSPERO registration number	Not registered

Table 8: 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.[4] Each included study is summarised in an economic evidence profile and an evidence table. Any excluded studies are detailed in the excluded studies table with the reason for exclusion in Appendix I. **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the Committee if required. The ultimate aim is to include economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the Committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. For example, if a high quality study from a UK perspective is available a similar study from another country's perspective may be excluded. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will have been excluded before being assessed for applicability and methodological limitations. *Economic study type:* • Cost-utility analysis (most applicable). • Other type of full economic evaluation (cost-benefit analysis, cost-effectiveness analysis, cost-consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will have been excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2001 or later but that depend on unit costs and resource data entirely or predominantly from before 2001 will be rated as 'Not applicable'. • Studies published before 2001 will have been excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the economic analysis:* • The more closely the clinical effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more

	useful the analysis will be for decision-making in the guideline. • The following will be rated as 'Very serious limitations' and excluded: economic analyses undertaken as part of clinical studies that are excluded from the clinical review; economic models where relative treatment effects are based entirely on studies that are excluded from the clinical review; comparative costing analyses that only look at the cost of delivering dialysis (as current UK NHS reference costs are considered a more relevant estimate of this for the guideline); within-trial economic analyses based on non-randomised studies that do not meet the minimum adjustment criteria outlined in the main review protocol.

Appendix B: Literature search strategies

B.1 Clinical search literature search strategy

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

For more detailed information, please see the Methodology Review.

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

Table 9: 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 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 10: 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

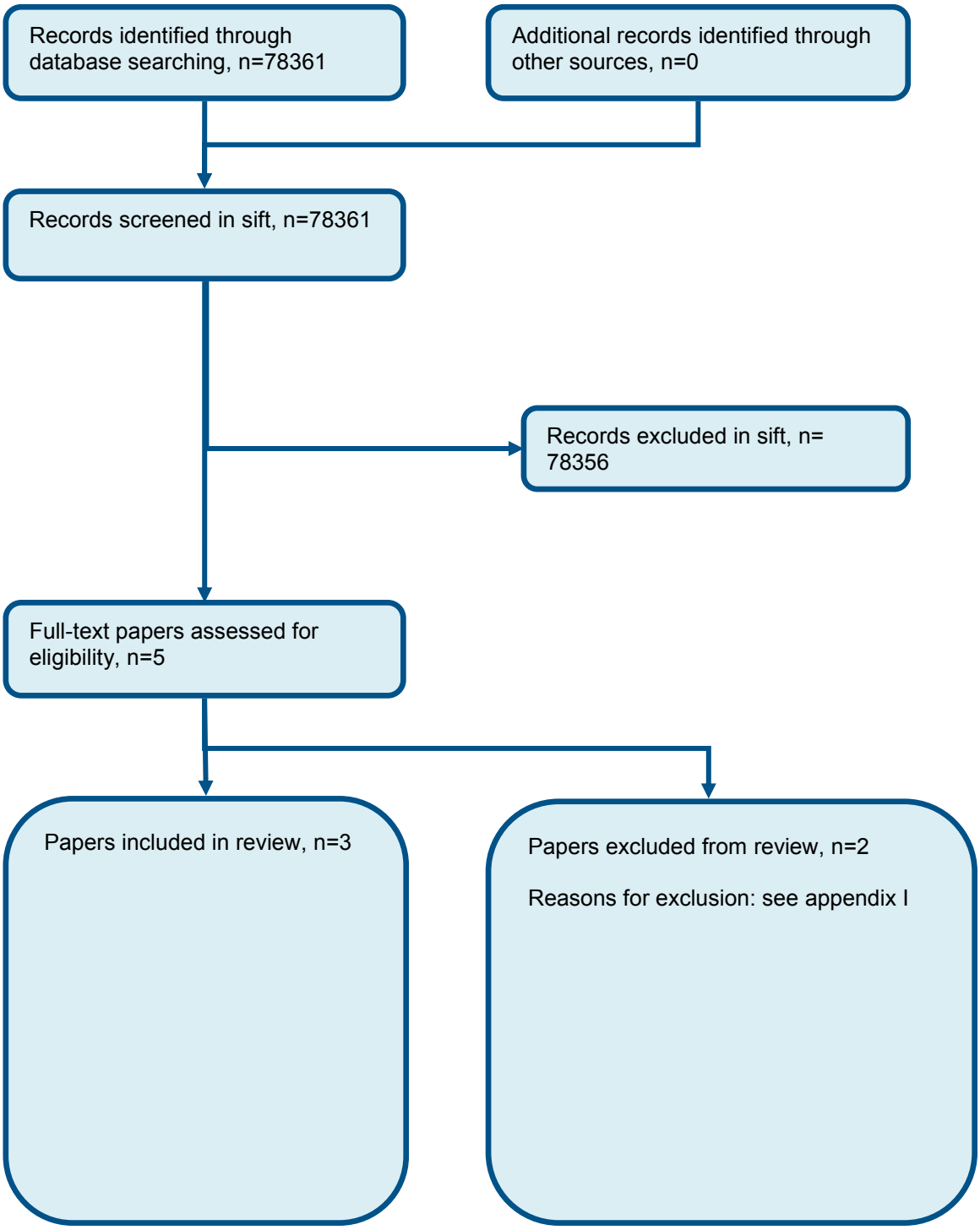
1.	exp renal replacement therapy/
2.	((renal or kidney) adj2 replace*).ti,ab.
3.	(hemodiafilt* or haemodiafilt* or (biofilt* adj1 acetate-free)).ti,ab.
4.	(hemodialys* or haemodialys*).ti,ab.
5.	((kidney* or renal) adj3 (transplant* or graft*)).ti,ab.
6.	capd.ti,ab.
7.	dialys*.ti,ab.
8.	(artificial adj1 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



Appendix D: Clinical evidence tables

Study	Ferring 2010[2]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=218)
Countries and setting	Conducted in United Kingdom; Setting: UK, clinic based assessments
Line of therapy	1st line
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients with end-stage kidney disease at Heart of England Hospital (Birmingham, United Kingdom) who were referred for formation of AVF were invited to take part in the study. Included were all with either none or one previous AVF.
Exclusion criteria	Patients who had already participated in the study, who had more than one previous AVF, or had a previous upper-arm arteriovenous graft were excluded.
Recruitment/selection of patients	Not specified
Age, gender and ethnicity	Age - Median (range): 68 (20 to 89). Gender (M:F): Define. Ethnicity: 70% Caucasian, 20% Indo-Asian, 5% African
Further population details	
Indirectness of population	No indirectness
Interventions	(n=112) Intervention 1: US mapping of access sites. Done by nephrology trainee or vascular access nurse specialist, used portable US scanner, 5-10MHz linear probe, standardised scan protocol used and most distal site that was suitable was recommended for AVF formation. Duration 1 month. Concurrent medication/care: All patients also got preoperative physical assessment by one of four vascular surgeons with experience in AVF formation, assessed pulses in elbows, wrists and assessed superficial veins in forearm and upper arm

	(n=106) Intervention 2: No specific intervention. Patients also received ultrasound but surgeons were not informed of the ultrasound results. Duration 1 month. Concurrent medication/care: All patients also got preoperative physical assessment by one of four vascular surgeons with experience in AVF formation, assessed pulses in elbows, wrists and assessed superficial veins in forearm and upper arm
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: US MAPPING OF ACCESS SITES versus CLINICAL EXAMINATION ONLY Protocol outcome 1: AEs - vascular access issues - Actual outcome for General population: All primary AVF failures at 1 month; Group 1: 24/95, Group 2: 33/91; Comments: All AVF that were never adequate for haemodialysis after initial surgical formation, including immediate failure on the day of surgery, early thrombosis and failure to mature Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17; Group 2 Number missing: 16	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; 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 ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Nursal 2006[5]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in Turkey; Setting: Turkey, hospital nephrology department
Line of therapy	1st line
Duration of study	--: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Only those fulfilling physical examination criteria (minimum venous diameter 1 mm without tourniquet, visible vein length at least 5 cm, adequate arterial pulse, adequate hand circulation, absence of venous collateral circulation in shoulder, absence of oedema)
Exclusion criteria	Did not meet PE criteria
Recruitment/selection of patients	Consecutive referrals to nephrology department for creation of haemodialysis access
Age, gender and ethnicity	Age - Mean (SD): 57 (14). Gender (M:F): Define. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: US mapping of access sites. High resolution 7.5MHz transducer US, at least 3 cardiac cycles included for automatic mapping, roughly 30 minute duration, sites were chosen if preoperative diameters of radial artery and cephalic vein were at least 1.6mm. Duration Median follow-up 217 days. Concurrent medication/care: Physical examination to select most distal suitable site for AVF (n=35) Intervention 2: No specific intervention. Physical examination as for the US arm but without additional US investigation. Duration Median follow-up 217 days. Concurrent medication/care: Nil else
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: US MAPPING OF ACCESS SITES versus PE ONLY

Protocol outcome 1: AEs - vascular access issues
- Actual outcome for General population: Proportion without patent AVFs at end of follow-up at Median follow-up 217 days; Group 1: 12/35, Group 2: 12/35

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; 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 ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

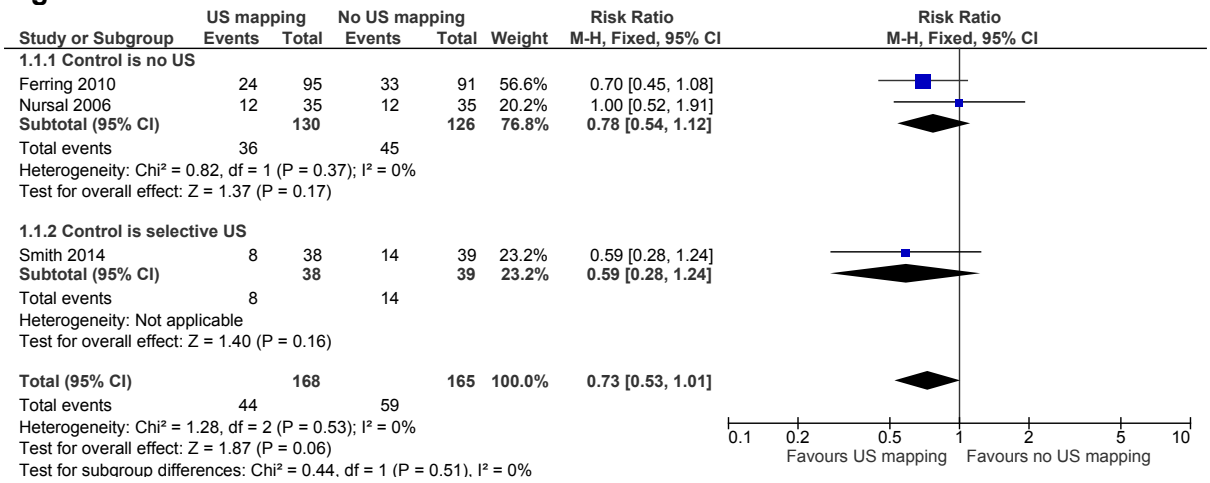
Study	Smith 2014[6]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=94)
Countries and setting	Conducted in United Kingdom; Setting: UK, vascular department
Line of therapy	1st line
Duration of study	Intervention + follow up: 1 month
Method of assessment of guideline condition	Adequate method of assessment/diagnosis:
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Referred for creation of AVF for HD
Exclusion criteria	Unable to consent, age less than 18, inability to attend follow-up
Recruitment/selection of patients	All referrals
Age, gender and ethnicity	Age - Mean (range): 65 (23-85). Gender (M:F): Not stated. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness:
Interventions	(n=47) Intervention 1: US mapping of access sites. Ultrasound for all participants. Duplex mapping by vascular scientist. Transverse view imaging the length of artery from the axilla to the anatomical snuffbox including both forearm branches; measurement of the AP diameter of arteries at the antecubital fossa, and at the level of the wrist and anatomical snuffbox (min diameter of 2mm for AVF formation), measurement of arterial peak systolic velocity at the antecubital fossa and in the radial artery at the level of the wrist; application of a proximal venous tourniquet to the wrist with measurement of the AP vein diameters in the mid upper arm, AC fossa, mid forearm and at the level of the wrist and the snuffbox (min diameter 2mm). Colour flow and compression used to confirm patency. Subclavian vein patency and waveform was also assessed. Proposed site for AVF formation was the most distal site on the non-dominant arm at which either PE or US criteria for suitability were present. Duration 1 month. Concurrent medication/care: Physical examination by vascular consultant or trainee, including: palpation of brachial, radial and ulnar pulses, assessment of collateral supply to hand with Allen's test, visual assessment of superficial veins with tourniquet, palpation and manual compression of veins, tap test (n=47) Intervention 2: US mapping of access sites. Only those with unsatisfactory physical examination

	received ultrasound, ultrasound as for routine group. Satisfactory PE defined as following criteria met for either wrist or antecubital sites: easily palpable pulse, collateral flow via the ulnar artery for the wrist (Allen's test), adequate diameter and length of superficial vein potentially available for cannulation and transmitted pulse present using the tap test. Duration 1 month . Concurrent medication/care: As for routine US group
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ROUTINE US versus SELECTIVE US Protocol outcome 1: AEs - vascular access issues - Actual outcome for General population: Primary AVF failure (thrombosis within 30 days of formation) at 1 month; Group 1: 8/38, Group 2: 14/39 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; 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; Psychological distress and mental wellbeing; Preferred location of death; Cognitive impairment; Patient/family/carer experience of care; Growth; Malignancy; AEs - infections; AEs - dialysis access issues; AEs - acute transplant rejection episodes

Appendix E: Forest plots

E.1 Ultrasound versus physical examination

Figure 1: AVF failure



Appendix F: GRADE tables

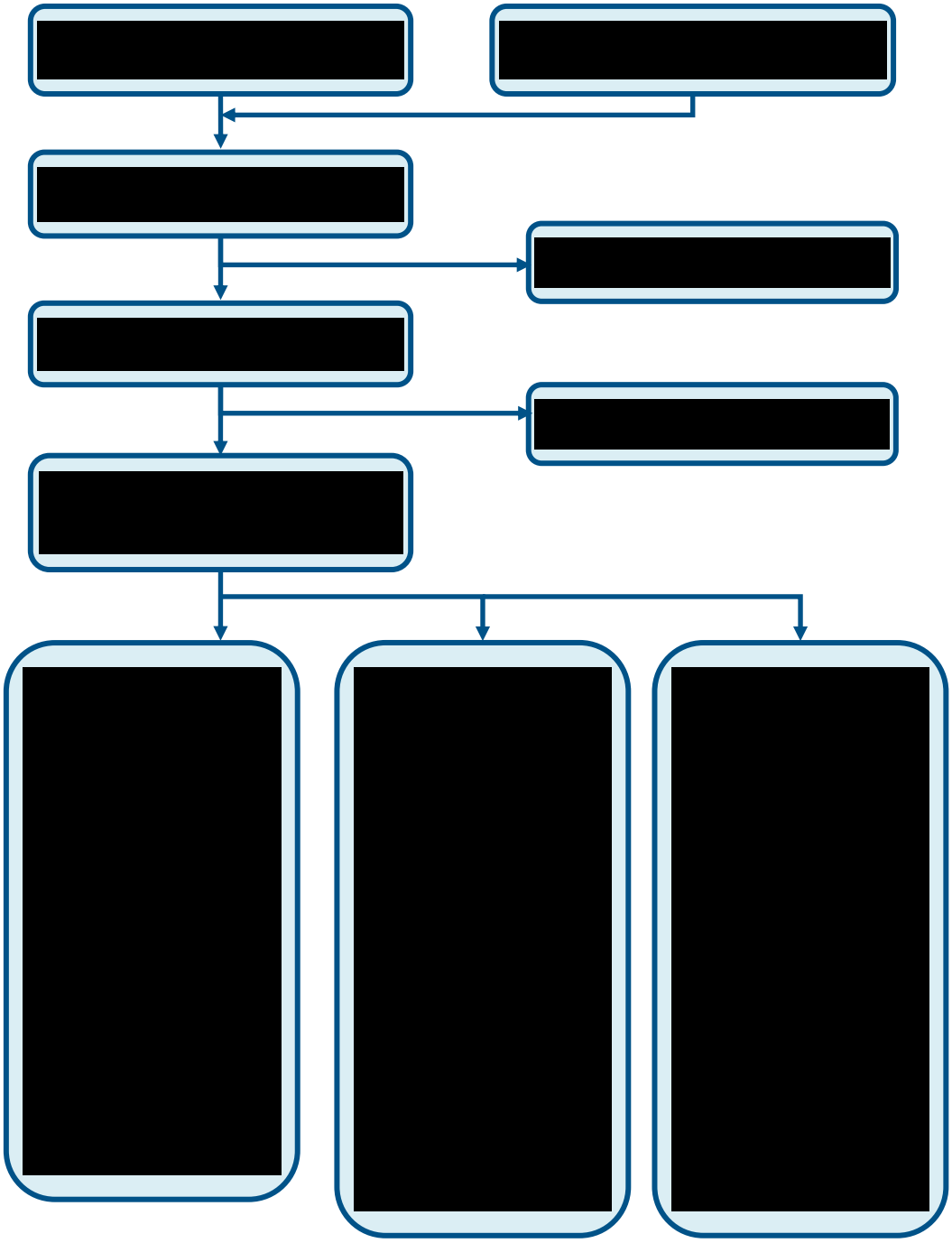
Table 11: Clinical evidence profile: US vs PE

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ultrasound	Physical examination	Relative (95% CI)	Absolute		
AVF failure (follow-up 1 to 6 months)												
3	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	44/168 (26.2%)	35.8%	RR 0.73 (0.53 to 1.01)	97 fewer per 1000 (from 168 fewer to 4 more)	⊕⊕⊕O MODERATE	IMPORTANT

1 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 57: 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

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

Appendix H: Health economic evidence tables

None.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 12: Studies excluded from the clinical review

Study	Exclusion reason
Mihmanli 2001[3]	Less than minimum duration
Zhang 2006[7]	Not in English

I.2 Excluded health economic studies

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

Table 13: Studies excluded from the health economic review

Reference	Reason for exclusion
None	

Appendix J: Research recommendations

J.1 Cardiac assessment before transplantation

Research question: What is the clinical and cost effectiveness of cardiac assessment before transplantation?

Why this is important:

There was no evidence for cardiac assessment identified in this review so the committee could not form a recommendation regarding its effectiveness. It is important to form recommendations in this area so that assessment of people prior to transplantation is done in the most clinical and cost effective manner.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Children young people and adults with CKD stage 3 to 5 being assessed for possible renal transplant Intervention/comparison: • Cardiac assessment (including at least a cardiac stress test or echocardiogram) before transplantation • No/low intensity cardiac assessment (e.g. ECG only) before transplantation Outcomes: Patient, family/carer health-related QoL, proportion going on to receive renal transplant, proportion of pre-emptive transplants, mortality, cardiovascular events, resource use, time to failure of RRT form, psychological distress and mental wellbeing, patient, family/carer experience of care
Importance to patients or the population	Research in this area could establish if there is a justification for intensive cardiac assessment prior to transplant, if that is the case it could help reduce the cardiac risk of people who receive renal transplants and potentially prevent people in whom cardiac risk is too high from undergoing the additional risk of transplantation. If cardiac assessment is found to have no clinically important benefit, this could remove a barrier to timely transplantation
Relevance to NICE guidance	There is current uncertainty about the clinical and cost effectiveness of cardiac assessment before transplantation.
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 specifically assessing the impact of cardiac assessment before transplantation
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.