National Institute for Health and Care Excellence

Final

RRT and conservative management

Evidence reviews for when to create access formation and/or list for transplantation

NICE guideline

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Final

This evidence review was developed by the National Guideline Centre

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1 Decision support

1.1 Review question: What is the most clinical and cost effective way of planning dialysis access formation and/or list for transplantation?

1.2 Introduction

For people who have agreed to proceed to RRT after appropriate assessment, consideration should be given to the most appropriate timing of dialysis access and listing for transplantation.

Access for dialysis should be created in time to ensure people can use their preferred dialysis modality and access route and avoid an 'unplanned start' which would often require hospital admission. This must be balanced against avoiding problems of creating access too early for example in people who may never require dialysis. The aim of this review is to look at the optimal timing to create access for dialysis and when to list for transplant.

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.
Intervention(s)	• Early preparation by eGFR (e.g. 15-20/20-25/25-30ml/min) • Late preparation by eGFR (e.g. 10-15ml/min) • Early preparation by time from start of dialysis/transplantation (either actual or estimated from risk tool – e.g. Tangri score) • Late preparation by time from start of dialysis/transplantation (either actual or estimated from risk tool – e.g. Tangri score) Preparation to include creation of HD access, PD access or transplant listing. Results to be reported separately by type of preparation.
Comparison	Any early strategy compared with any late strategy
Outcomes	Critical • Patient, family/carer health-related QoL (continuous) • Mortality (dichotomous and time to event) Important • Pre-emptive transplantation rates (rates or dichotomous) • Proportion starting on modality of choice (rates or dichotomous) • Proportion with access created/transplant listed who do not go on to require or use RRT (rates or dichotomous) • Psychological distress and mental wellbeing (continuous) • Symptom scores and functional measures (continuous) • Hospitalisation (rates or continuous) • Time to failure of RRT form (time to event) • Patient, family/carer experience of care (continuous) • Adverse events ○ Infections (dichotomous)

	○ Vascular access issues (dichotomous) ○ Dialysis access issues (dichotomous) ○ Acute transplant rejection episodes (dichotomous)
Study design	RCTs only NRS included if insufficient RCT evidence with adjustment for key confounders (age, ethnicity, comorbidities and baseline health)

1.4 Clinical evidence

1.4.1 Included studies

Four studies were included in the review;[22, 24, 45, 47] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 4).

One NRS compared time between access placement and HD initiation, one NRS compared fistula placement within one month before initiation to fistula placement 1-2 months before initiation and one NRS compared time from creation to use less than 30 days to time from creation to use over 30 days. Two studies[22, 24] reported results from overlapping although not identical cohorts of the USRDS, these results were extracted separately as the two studies reported different outcomes.

One RCT study compared time between access placement and PD initiation.

No evidence was found assessing the optimum time to list people for transplant.

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
Haemodialysis				
Hod 2015[22]	Time between access placement and HD initiation: 1-3 months (n = 4519) 3-6 months (n = 4300) 6-9 months (n = 2579) 9-12 months (n = 1739)	USA Adults >70 (at least 67 years old, mean 76) Excluded those with an AVF created <1 month before initiation of dialysis	AVF success (initiation of HD using AVF initially placed) Reported for general population and DM, black subgroups	NRS Adjusted for duration of nephrology care prior to dialysis AVF success rate for total population was 55% Type of AVF not

Study	Intervention and comparison	Population	Outcomes	Comments
	>12 months (n = 4374)			specified
Ishani 2014[24]	Fistula placement within 1 month before initiation Fistula placement 1-2 months before initiation n = 14,459	USA Adults >70 (at least 67 years old, mean 77) 88% had seen a nephrologist in year preceding initiation of HD	Mortality	NRS Adjusted for types of care prior to dialysis including number of nephrology visits Only included those with a functioning fistula Type of AVF not specified
Ravani 2004[47]	Time from creation to use <30 days Time from creation to use >30 days n = 414	Italy Adults over 18 Did not exclude unplanned starters. 75% had received some form of predialysis care	Time to AVF failure (intervention free period to first failure; failure defined as failure to mature, definitive clotting or malfunction caused by stenosis or partial thrombosis)	NRS Adjusted for pre-dialysis including number of visits Prescribed interval time before cannulation 2 to 4 weeks 86% of population used their AVF although 47% were using a catheter at HD initiation Type of AVF not specified
Peritoneal dialysis				
Ranganathan 2017[45]	Time from creation to use 1 week (n=39) Time from creation to use 2 weeks (n=42) Time from creation to use 4 weeks (n=41) n = 122	Australia Adults over 18 (mean age 57) Those planning to start PD within 4 weeks	Modality failure (switch to HD) Infections (PD-related including tunnel and peritonitis) Leak Outcomes reported at 6 months (modality failure) and 2 months (infections, leak)	RCT Terminated early due to worse outcomes in 1 week group

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

1.4.4.1 Haemodialysis access

Table 3: Clinical evidence summary: Late vascular access creation versus early vascular access creation, adults 18-70, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early HD access creation, 18-70	Risk difference with Late HD access creation (95% CI)
AVF failure (time from creation to use <30 days vs >30 days)	414 (1 study) 5 years	LOW[1] due to risk of bias	HR 1.94 (1.34 to 2.82)	-[2]	
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias. 2 Control group risk unavailable					

Table 4: Clinical evidence summary: Late vascular access creation versus early vascular access creation, adults >70, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early HD access creation, >70	Risk difference with Late HD access creation (95% CI)
Successful AVF creation (1-3 months from placement to initiation vs >12 months)	8893 (1 study) 3 years	LOW[1] due to risk of bias	OR 0.49 (0.44 to 0.55)	-[3]	
Successful AVF creation (3-6 months from placement to initiation vs >12 months)	8674 (1 study) 3 years	LOW[1] due to risk of bias	OR 0.93 (0.85 to 1.02)	-[3]	
Successful AVF creation (6-9 months from placement to	6953	LOW[1]	OR	-[3]	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early HD access creation, >70	Risk difference with Late HD access creation (95% CI)
initiation vs >12 months)	(1 study) 3 years	due to risk of bias	0.99 (0.88 to 1.11)		
Successful AVF creation (9-12 months from placement to initiation vs >12 months)	6113 (1 study) 3 years	LOW[1] due to risk of bias	OR 1 (0.9 to 1.11)	-[3]	
Successful AVF creation (1-3 months from placement to initiation vs >12 months) in BAME	3224* (1 study) 3 years	LOW[1] due to risk of bias	OR 0.49 (0.39 to 0.61)	-[3]	
Successful AVF creation (3-6 months from placement to initiation vs >12 months) in BAME	3224* (1 study) 3 years	VERY LOW[1,2] due to risk of bias, imprecision	OR 0.89 (0.72 to 1.10)	-[3]	
Successful AVF creation (6-9 months from placement to initiation vs >12 months) in BAME	3224* (1 study) 3 years	VERY LOW[1,2] due to risk of bias, imprecision	OR 0.94 (0.74 to 1.20)	-[3]	
Successful AVF creation (9-12 months from placement to initiation vs >12 months) in BAME	3224* (1 study) 3 years	VERY LOW[1,2] due to risk of bias, imprecision	OR 0.93 (0.71 to 1.21)	-[3]	
Successful AVF creation (1-3 months from placement to initiation vs >12 months) in patients with diabetes	9810* (1 study) 3 years	LOW[1] due to risk of bias	OR 0.5 (0.44 to 0.56)	-[3]	
Successful AVF creation (3-6 months from placement to initiation vs >12 months) in patients with diabetes	9810* (1 study) 3 years	LOW[1] due to risk of bias	OR 0.93 (0.82 to 1.05)	-[3]	
Successful AVF creation (6-9 months from placement to	9810*	LOW[1]	OR	-[3]	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early HD access creation, >70	Risk difference with Late HD access creation (95% CI)
initiation vs >12 months) in patients with diabetes	(1 study) 3 years	due to risk of bias	1.08 (0.94 to 1.24)		
Successful AVF creation (9-12 months from placement to initiation vs >12 months) in patients with diabetes	9810* (1 study) 3 years	VERY LOW[1,2] due to risk of bias, imprecision	OR 1.06 (0.90 to 1.24)	-[3]	
Mortality (fistula placement within 1 month before initiation vs 1-2 months before initiation)	12102 (1 study) 4 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 1.26 (1.03 to 1.54)	-[3]	

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.
3 Control group risk unavailable
*Not total for each outcome, only overall total for sub groups recorded

1.4.4.2 Peritoneal dialysis access

Table 5: Clinical evidence summary: Late (1 week) peritoneal access creation versus early (4 week) peritoneal access creation, adults 18-70, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early PD access creation (4 weeks)	Risk difference with Late PD access creation (1 week) (95% CI)
Modality failure (switch to HD because PD catheter dysfunction)	80 (1 study) 6 months	LOW[1,2] due to risk of bias, imprecision	RR 0.15 (0.02 to 1.17)	171 per 1000	145 fewer per 1000 (from 167 fewer to 29 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early PD access creation (4 weeks)	Risk difference with Late PD access creation (1 week) (95% CI)
Infections (PD-related/tunnel/peritonitis)	80 (1 study) 2 months	VERY LOW[1,2] due to risk of bias, imprecision	RR 5.26 (0.64 to 43)	24 per 1000	104 more per 1000 (from 9 fewer to 1000 more)
Leak	80 (1 study) 2 months	MODERATE[1] due to risk of bias	RR 11.56 (1.57 to 85.42)	24 per 1000	258 more per 1000 (from 14 more to 1000 more)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 6: Clinical evidence summary: Late (1 week) peritoneal access creation versus early (2 week) peritoneal access creation, adults 18-70, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early PD access creation (2 weeks)	Risk difference with Late PD access creation (1 week) (95% CI)
Modality failure (switch to HD because PD catheter dysfunction)	81 (1 study) 6 months	LOW[1] due to imprecision	RR 1.08 (0.07 to 16.63)	24 per 1000	2 more per 1000 (from 22 fewer to 372 more)
Infections (PD-related/tunnel/peritonitis)	81 (1 study) 2 months	LOW[1] due to imprecision	RR 5.38 (0.66 to 44.07)	24 per 1000	104 more per 1000 (from 8 fewer to 1000 more)
Leak	81 (1 study) 2 months	MODERATE[1] due to imprecision	RR 2.96 (1.03 to 8.53)	95 per 1000	187 more per 1000 (from 3 more to 717 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early PD access creation (2 weeks)	Risk difference with Late PD access creation (1 week) (95% CI)
1 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 7: Clinical evidence summary: Late (2 weeks) peritoneal access creation versus early (4 weeks) peritoneal access creation, adults 18-70, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Early PD access creation (4 weeks)	Risk difference with Late PD access creation (2 week) (95% CI)
Modality failure (switch to HD because PD catheter dysfunction)	83 (1 study) 6 months	LOW[1,2] due to risk of bias, imprecision	RR 0.14 (0.02 to 1.08)	171 per 1000	147 fewer per 1000 (from 167 fewer to 14 more)
Infections (PD-related/tunnel/peritonitis)	83 (1 study) 2 months	VERY LOW[1,2] due to risk of bias, imprecision	RR 0.98 (0.06 to 15.09)	24 per 1000	0 fewer per 1000 (from 23 fewer to 344 more)
Leak	83 (1 study) 2 months	VERY LOW[1,2] due to risk of bias, imprecision	RR 3.9 (0.46 to 33.48)	24 per 1000	71 more per 1000 (from 13 fewer to 792 more)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were included.

1.5.2 Excluded studies

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

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

1.5.3 **Summary of studies included in the economic evidence review**

None.

1.5.4 Unit costs

Relevant current UK unit costs were provided to the committee to aid consideration of cost effectiveness. Clinical evidence was identified relating to timing of vascular access creation for haemodialysis. NHS reference costs for access-related procedures are included in Table 8 below.

Table 8: UK NHS reference costs 2015/16 for dialysis access-related inpatient and outpatient procedures

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

Currency description	Currency code	Admission	Number of FCEs	National average unit cost	Weighted average
Venous Catheter, 18 years and under		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	
		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					

Currency description	Currency code	Admission	Number of FCEs	National average unit cost	Weighted average
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[13]

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.

1.5.5 **Exploratory cost calculation**

Evidence from the clinical review in a study of over 70 year olds suggested that earlier AVF creation may increase the rate of AVF success compared to later creation (success defined in the study as initiation of HD using the AVF initially placed; failure as dialysis initiated using access other than AVF – catheter or graft; those who initiated dialysis using an AVF other than that initially placed were excluded) which may translate to a reduction in procedure costs associated with AVF failure.

The potential procedure cost differences from such a change in AVF failure as defined in the Hodd study are summarised in Table 9 below. The biggest difference is seen when moving from AVF creation 1-3 months before initiation of dialysis to 3-6 month before; an estimated reduction in initiation of dialysis by catheter or graft rather than the initial AVF placed of 157 per 1000, translated to a saving of between £317 and £181 per person. Note that this is based only on the additional procedure that would result from AVF failure as defined by the study, that is for creation of a graft or insertion of a catheter. It is likely there would be additional costs associated with failure where a graft or catheter is used for dialysis such as increased infections or potentially another procedure to try and establish an AVF subsequent to starting dialysis.

It should be noted that earlier creation of dialysis access may result in an increase in vascular access procedures as it is likely that there will be an increase in access that is created but never used as the patient has a transplant or dies before needing to start dialysis. In addition, it is unknown whether more procedures might be required between creation of the AVF and initiation of dialysis to maintain patency of the AVF. No clinical evidence was available regarding either of these outcomes.

Table 9: Exploratory cost calculation based on Hod 2015[22] clinical study

AVF placement to HD initiation	AVF success[a]				AVF failure[a]			
	OR vs >12[b]	RR vs >12[c]	Rate[d]	No. per 1000	Rate[e]	No. per 1000	Incremental per 1000[f]	Average incremental cost saving per person[g]
1-3 months	0.49	0.68	37%	373	63%	627		
3-6 months	0.93	0.97	53%	531	47%	469	-157	-£317 to -£181
6-9 months	1.00	1.00	55%	549	45%	451	-18	-£36 to -£21
9-12 months	0.99	1.00	55%	546	45%	454	2	£3 to £5
>12 months			55%	549	45%	451	-2	-£5 to -£3

(a) In Hod 2015[22]: AVF success was defined as initiation of HD using the AVF initially placed; AVF failure was defined as dialysis initiated using access other than AVF, despite an AVF being the initial access planned; people were excluded where dialysis was initiated using an AVF other than that initially placed, that is, the initial AVF failed but another was inserted. See clinical evidence sections for more details.

(b) Odds ratios (OR) from Hod 2015[22]

(c) Relative risk (RR) calculated using an estimated control event rate (CER) for >12 months of 55% based on the unadjusted success rate across the whole study. RR = OR/(1-CER(1-OR)).*

(d) Estimated control event rate for >12 months of 55% based on the unadjusted success rate across the whole study. Rates for other groups calculated using this rate and the relevant relative risk (RR).

(e) AVF failure rate is calculate as 100% – AVF success rate %.

(f) Difference in no. per 1000 with this group compared to the previous group e.g. 3-6 vs 1-3 months, 6-9 vs 3-6 months etc

(g) AVF failure was defined as dialysis initiated using access other than AVF, despite an AVF being the initial access planned therefore this is estimated by applying either the average cost of admission for catheter insertion (£1,149; NHS reference costs 2015/16, YR41A, Insertion of Tunnelled Central Venous Catheter; weighted average of all admission categories) or cost of admission for graft procedure (£2012; NHS reference costs 2015/16, YQ42Z, Open Arteriovenous Fistula, Graft or Shunt Procedures; weighted average of all admission categories).[13]

1.6 Resource impact

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

1.7 Evidence statements

1.7.1 Clinical evidence statements

Late vascular access creation versus early vascular access creation

Adults 18-70

No evidence for patient, family/carer health-related QoL, mortality, symptom scores and functional measures, pre-emptive transplantation rates, proportion starting on modality of choice, proportion with access created/transplant listed who do not go on to require or use RRT, psychological distress and mental wellbeing, hospitalisation, patient, family/carer experience of care and adverse events.

There was a clinical harm of intervention for time to failure of RRT (time from creation to use <30 days vs >30 days, 1 study low quality).

Adults >70

No evidence for patient, family/carer health-related QoL, pre-emptive transplantation rates, proportion starting on modality of choice, proportion with access created/transplant listed who do not go on to require or use RRT, time to failure of RRT, psychological distress and mental wellbeing, hospitalisation, patient, family/carer experience of care and adverse events.

There was no clinical benefit for symptom scores and functional measures of successful AVF creation (3-6 months vs >12 months, 1 study low quality) (3-6 months vs >12 months, BAME subgroup, 1 study low quality) (3-6 months vs >12 months, diabetes present, 1 study very low quality) (6-9 months vs >12 months, 1 study low quality) (6-9 months vs >12 months, BAME subgroup, 1 study very low quality) (6-9 months vs >12 months, diabetes present, 1 study low quality) (9-12 months vs >12 months, 1 study low quality) (9-12 months vs >12 months, BAME subgroup, 1 study very low quality) (9-12 months vs >12 months, diabetes present, 1 study very low quality).

There was a clinical harm of late access creation for symptom scores and functional measures of successful AVF creation (1-3 months vs >12 months, 1 study low quality) (1-3 months vs >12 months, BAME subgroup, 1 study low quality) (1-3 months vs >12 months, diabetes present, 1 study low quality) and mortality (fistula placement within 1 month before initiation vs 1-2 months before initiation, 1 study very low quality).

Late peritoneal dialysis access creation versus early peritoneal dialysis access creation

No evidence for patient, family/carer health-related QoL, mortality, symptom scores and functional measures, pre-emptive transplantation rates, proportion starting on modality of choice, proportion with access created/transplant listed who do not go on to require or use RRT, psychological distress and mental wellbeing, hospitalisation, patient, family/carer experience of care.

1 week vs 4 weeks

There was a clinically important benefit of creation at 1 week from use for modality failure (1 study, low quality).

There was a clinically important harm of creation at 1 week from use for infections (1 study, very low quality) and leak (1 study moderate quality).

1 week vs 2 weeks

There was no clinically important difference in creation at 1 week from use for modality failure (1 study, low quality).

There was a clinically important harm of creation at 1 week from use for infections (1 study, low quality) and leak (1 study moderate quality).

2 weeks vs 4 weeks

There was a clinically important benefit in creation at 2 weeks from use for modality failure (1 study, low quality).

There was no clinically important difference in creation at 2 weeks from use for infections (1 study, very low quality).

There was a clinically important harm of creation at 2 weeks from use for leaks (1 study, very low quality).

1.7.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.7.3 The committee's discussion of the evidence

1.7.4 Interpreting the evidence

1.7.4.1 The outcomes that matter most

The committee considered quality of life and mortality to be critical outcomes. The committee considered pre-emptive transplantation rates, proportion starting on modality of choice, proportion with access created/transplant listed who do not go on to RRT, psychological distress/mental wellbeing, symptom scores/functional measures, hospitalisation, time to failure of RRT form, experience of care and adverse events to be important outcomes.

1.7.4.2 The quality of the evidence

No evidence was available for timing of transplant listing.

No randomised evidence was available for timing of vascular access creation. The only outcomes available for the timing of vascular access creation were mortality and variants of fistula success rate. Evidence quality was in general low or very low. No studies were available that prospectively assessed cohorts following two different timing strategies. No studies were available in children or young people under the age of 18.

One randomised controlled trial was available for the timing of peritoneal dialysis access creation. The outcomes ranged from moderate to very low quality, mostly due to imprecision

and risk of bias. There was only evidence available for open surgical creation of peritoneal dialysis access creation.

1.7.4.3 Benefits and harms

Vascular access

The evidence in this review showed a clinically important benefit for creating an arteriovenous fistula for vascular access more than 1 month from initiation of dialysis in terms of both mortality (in people aged over 70) and success rate (in people aged 18 to 70). There was also a clinically important harm, in terms of success rate, of creating vascular access 1-3 months from initiation of dialysis vs >12 months from initiation of dialysis (in people aged over 70), whereas there was no clinically important difference between 3-6 months vs >12 months, 6-9 months vs >12 months or 9-12 months vs >12 months (in people aged over 70). These effects were seen in the general population and in the diabetes mellitus and black and ethnic minority subgroups. There appeared to be some evidence of a dose response effect, with the latest creation being associated with the worse outcomes. Overall the evidence suggested that the minimum desired time from vascular access creation to initiation of dialysis would be 3-6 months.

The available evidence did not capture all of the benefits and harms of various timing strategies. The committee noted that benefits of earlier creation include reducing the number of unplanned starters but harms include the creation of fistulae that are never required, either because the person dies before requiring RRT or because they receive a transplant in the interim period. The committee agreed that the consequence of a fistula being created too late (for example, additional number of access procedures and hospital admissions) was of more concern than the consequence of creating an unused fistula in a person with kidney disease. In general aiming to promote fistula creation earlier in the treatment pathway may increase the total number of fistulae created by surgeons but this may be offset by reducing the urgency of each creation.

Peritoneal dialysis access

The evidence in the review showed a clinically important harm of creating access 4 weeks vs either 2 weeks or 1 week from use in terms of modality failure by the end of 6 months. The evidence in the review also showed a clinically important harm of creating access 1 week vs either 2 weeks or 4 weeks from use in terms of leaks and infections. No other outcomes were reported in the evidence.

The committee noted that aiming to create access 2 weeks from use would not be large shift in current practice although it may help to standardise approaches. Any recommendation in this area needs interpretation in terms of the availability of local services and the timing of local treatment pathways, so while it may be appropriate to aim to create access 2 weeks from first use.

The committee discussed the fact that in the UK there are a variety of options for creating peritoneal dialysis access including open surgery (as appeared to be done in the included study), laparoscopic surgery and percutaneous insertion. The availability and use of these options varies across the country and this is largely dictated by what services and skills are available locally. The committee agreed that the evidence in the review was only directly relevant to open surgical access creation. The committee agreed that the recommendation could not cover percutaneous or laparoscopic insertion. The committee chose to make a research recommendation in this area.

Transplant listing

No evidence was available for timing of transplant listing.

The committee discussed how earlier transplant listing may increase the likelihood of pre-emptive transplant which was found to have better health outcomes in the modalities review. Although it was noted that if listing earlier results in an earlier pre-emptive transplant you will use up more of the transplant longevity at a time when you did not actually need RRT. The committee also highlighted that kidneys available to those on the transplant list are limited and it was important not to list people too early so as to optimise longevity and direct them at the people who will derive most benefit. They concluded that there was no evidence to guide a recommendation for a specific timepoint at which people should be listed for transplant and that a research recommendation should be made.

1.7.5 Cost effectiveness and resource use

Vascular access

No published economic evaluations were included.

A study from the clinical evidence review suggested that earlier AVF creation may increase the rate of AVF success compared to later creation (success defined in the study as initiation of HD using the AVF initially placed; failure as dialysis initiated using access other than AVF – catheter or graft; those who initiated dialysis using an AVF other than that initially placed were excluded) which may translate to a reduction in procedure costs associated with AVF failure. It was estimated that when moving from AVF creation 1-3 months before initiation of dialysis to 3-6 month before initiation of dialysis, there would be a reduction in dialysis by catheter or graft rather than the initial AVF placed of 157 per 1000 and this translated to a saving of between £317 and £181 per person. The committee highlighted that there also would be other costs associated with failure where a graft or catheter is used for dialysis such as potentially another procedure to try and establish an AVF subsequent to starting dialysis and additional hospital admissions.

It is noted that people who started dialysis on AVF but not on the initial AVF placed were excluded from the study. It may be that there would be more of these people in the earlier access creation group because of the extra time to undertake a second procedure which could also result in a difference in resource use – this information is however not provided in the study. Earlier creation of dialysis access may result in an increase in vascular access procedures as it may be that there will be an increase in access that is created but never used as the patient has a transplant or dies before needing to start dialysis. In addition, it is unknown whether more procedures might be required between creation of the AVF and initiation of dialysis to maintain patency of the AVF. No clinical evidence was available regarding either of these outcomes.

The committee highlighted that earlier access creation was likely to result in better planning of dialysis initiation and this may mean that there was improved efficiency.

While the evidence was incomplete to fully assess differences in cost, overall the committee concluded that it was likely that creation of AVF access around 6 months prior to initiation of HD/HDF would be likely to be cost saving compared to later access creation. Given this and the benefits to patients in terms of improved AVF success they felt it was likely to be cost effective and thus supported a recommendation for access creation around 6 months.

Although there is considered to be some variability, the committee noted that the recommendation does not represent a large shift from current practice and was not considered likely to have a substantial resource impact.

Peritoneal access

No published economic evaluations were included.

The clinical evidence suggested that there was an increase in modality failure with creation of PD access at 4 weeks compared to 2 or 1 week – this would therefore be likely to also have increased resource use. The evidence in the review also showed a clinically important harm of creating access 1 week vs either 2 weeks or 4 weeks from use in terms of leaks and infections and it is likely that there would be some resource implications of dealing with this. The committee therefore concluded that this supports creation of PD access by open surgical technique at 2 weeks prior to use. There was no clinical or economic evidence for other types of PD access creation.

Although there is some variability, the committee noted that the recommendation was generally in line with current practice and was not considered likely to have a substantial resource impact. Where a change in practice was required there was potential for cost savings.

Transplant listing

No published economic evaluations were included.

Listing earlier is unlikely to increase costs compared to listing later as it is unlikely to change the number of people listed. However, a transplant will have a limited life and so if listing earlier results in earlier pre-emptive transplants you may use up some of the transplant longevity at a time when you did not actually need RRT, and more second transplants may be required. However, if rates of pre-emptive transplant were increased by earlier listing there would likely be cost savings due to dialysis avoided and have improved health outcomes for patients. In addition, the committee highlighted that kidneys available to those on the transplant list are limited and it was important not to list people too early as there would be potential to deprive someone who really needed it.

Given the lack of evidence to assess the clinical and economic trade-offs the committee felt a recommendation could not be made about timing of listing but a research recommendation was made.

1.7.6 Other factors the committee took into account

Vascular access

The guideline committee highlighted the importance of discussing with the person the different types of access and the implications of these, for example restrictions on activities. The committee noted that some types of vascular access, for example brachio-basilic arteriovenous fistula formation, may require two operations (including the initial anastomosis procedure and subsequent superficialisation & translocation procedure) and time needs to be allowed for this. In addition, only approximately half of fistulae created in primary patency. Further interventions may be required before the fistula can be used for example balloon assisted maturation of an AVF if there are stenosis higher up the arm or selected ligation of tributaries to improve flow up the main vein.

The committee noted that the evidence on creation of vascular access related to use of haemodialysis rather than haemodiafiltration, however they agreed that the recommendations were equally appropriate to the use of haemodiafiltration.

Transplant listing

The committee reinforced current practice that all patients who will benefit from a transplant should be assessed. Whether or not a person is placed on the transplant waiting list depends on a number of individual factors, for example co-morbidities and prognosis. When

a person is place on the waiting list also depends on a variety of factors for example current renal function and expected rate of deterioration.

The committee confirmed that the recommendations on vascular access and transplant listing were applicable to children and young people.

Peritoneal access

The committee emphasised that the aim of this review was to determine the optimal time of access creation but not the optimal form of access to create, therefore the recommendations on timing of peritoneal access creation do not address alternative methods of creation (for example the Moncrieff method) that may involve multiple procedures at different timepoints.

References

1. Al-Balas A, Lee T, Young CJ, Barker-Finkel J, Allon M. Predictors of initiation for predialysis arteriovenous fistula. Clinical Journal of the American Society of Nephrology. 2016; 11(10):1802-1808

2. Al-Jaishi AA, Lok CE, Garg AX, Zhang JC, Moist LM. Vascular access creation before hemodialysis initiation and use: a population-based cohort study. Clinical Journal of the American Society of Nephrology. 2015; 10(3):418-27

3. Alencar de Pinho N, Coscas R, Metzger M, Labeeuw M, Ayav C, Jacquelinet C et al. Predictors of nonfunctional arteriovenous access at hemodialysis initiation and timing of access creation: A registry-based study. PloS One. 2017; 12(7):e0181254

4. Almasi-Sperling V, Galiano M, Lang W, Rother U, Rascher W, Regus S. Timing of first arteriovenous fistula cannulation in children on hemodialysis. Pediatric Nephrology. 2016; 31(10):1647-57

5. Asano M, Thumma J, Oguchi K, Pisoni RL, Akizawa T, Akiba T et al. Vascular access care and treatment practices associated with outcomes of arteriovenous fistula: international comparisons from the Dialysis Outcomes and Practice Patterns Study. Nephron. 2013; 124(1-2):23-30

6. Astor BC, Eustace JA, Powe NR, Klag MJ, Sadler JH, Fink NE et al. Timing of nephrologist referral and arteriovenous access use: The CHOICE study. American Journal of Kidney Diseases. 2001; 38(3):494-501

7. Bansal N, He C, Murphy DP, Johansen KL, Hsu CY. Timing of preemptive vascular access placement: do we understand the natural history of advanced CKD?: an observational study. BMC Nephrology. 2013; 14:115

8. Bashar K, Zafar A, Elsheikh S, Healy DA, Clarke-Moloney M, Casserly L et al. Predictive parameters of arteriovenous fistula functional maturation in a population of patients with end-stage renal disease. PloS One. 2015; 10(3):e0119958

9. Beuscart JB, Pagniez D, Boulanger E, Duhamel A. Registration on the renal transplantation waiting list and mortality on dialysis: an analysis of the French REIN registry using a multi-state model. Journal of Epidemiology. 2015; 25(2):133-41

10. Cass A, Cunningham J, Snelling P, Ayanian JZ. Late referral to a nephrologist reduces access to renal transplantation. American Journal of Kidney Diseases. 2003; 42(5):1043-9

11. Chan MR, Dall AT, Fletcher KE, Lu N, Trivedi H. Outcomes in patients with chronic kidney disease referred late to nephrologists: a meta-analysis. American Journal of Medicine. 2007; 120(12):1063-70

12. Collins J, Cooper B, Branley P, Bulfone L, Craig J, Fraenkel M et al. Outcomes of patients with planned initiation of hemodialysis in the IDEAL trial. Contributions to Nephrology. 2011; 171:1-9

13. 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.

14. Diehm N, van den Berg JC, Schnyder V, Buhler J, Willenberg T, Widmer M et al. Determinants of haemodialysis access survival. Vasa. 2010; 39(2):133-9

15. Elhassan E, Teitelbaum I. Time between peritoneal dialysis catheter insertion and use. Contributions to Nephrology. 2012; 178:228-31

16. Farooq Z, Mehmood A, Saeed S, Raja KM, Khan MN, Murtaza B. Early versus late arterio-venous fistulae: impact on failure rate. Journal of Ayub Medical College. 2010; 22(3):179-81

17. Feldman HI, Joffe M, Rosas SE, Burns JE, Knauss J, Brayman K. Predictors of successful arteriovenous fistula maturation. American Journal of Kidney Diseases. 2003; 42(5):1000-1012

18. Fissell RB, Srinivas T, Fatica R, Nally J, Navaneethan S, Poggio E et al. Preemptive renal transplant candidate survival, access to care, and renal function at listing. Nephrology Dialysis Transplantation. 2012; 27(8):3321-9

19. Grams ME, Li L, Greene TH, Tin A, Sang Y, Kao WH et al. Estimating time to ESRD using kidney failure risk equations: results from the African American Study of Kidney Disease and Hypertension (AASK). American Journal of Kidney Diseases. 2015; 65(3):394-402

20. Heaf JG. Algorithm for optimal dialysis access timing. Clinical Nephrology. 2007; 67(2):95-104

21. Hiremath S, Knoll G, Weinstein MC. Should the arteriovenous fistula be created before starting dialysis?: a decision analytic approach. PloS One. 2011; 6(12):e28453

22. Hod T, Patibandla BK, Vin Y, Brown RS, Goldfarb-Rumyantzev AS. Arteriovenous fistula placement in the elderly: when is the optimal time? Journal of the American Society of Nephrology. 2015; 26(2):448-56

23. Hodges TC, Fillinger MF, Zwolak RM, Walsh DB, Bech F, Cronenwett JL. Longitudinal comparison of dialysis access methods: risk factors for failure. Journal of Vascular Surgery. 1997; 26(6):1009-19

24. Ishani A, Gilbertson DT, Kim D, Bradbury BD, Collins AJ. Predialysis care and dialysis outcomes in hemodialysis patients with a functioning fistula. American Journal of Nephrology. 2014; 39(3):238-47

25. Jeffrey RF, Akbani H, Scally AJ, Peel R. Comparison of transplant listing strategy in two renal dialysis centers within a regional transplant alliance. Clinical Nephrology. 2005; 64(6):438-43

26. Jungers P, Zingraff J, Albouze G, Chauveau P, Page B, Hannedouche T et al. Late referral to maintenance dialysis: detrimental consequences. Nephrology Dialysis Transplantation. 1993; 8(10):1089-93

27. Kaygin MA, Talay S, Dag O, Erkut B. An experience of arteriovenous fistulas created for hemodialysis in the largest health center in eastern Turkey. Renal Failure. 2012; 34(3):291-6

28. Lee KG, Chong TT, Goh N, Achudan S, Tan YL, Tan RY et al. Outcomes of arteriovenous fistula creation, effect of preoperative vein mapping and predictors of fistula success in incident haemodialysis patients: A single-centre experience. Nephrology. 2017; 22(5):382-387

29. Lee T, Barker J, Allon M. Associations with predialysis vascular access management. American Journal of Kidney Diseases. 2004; 43(6):1008-13

30. Lee T, Thamer M, Zhang Q, Zhang Y, Allon M. Reduced cardiovascular mortality associated with early vascular access placement in elderly patients with chronic kidney disease. American Journal of Nephrology. 2016; 43(5):334-340

31. Lopez-Vargas PA, Craig JC, Gallagher MP, Walker RG, Snelling PL, Pedagogos E et al. Barriers to timely arteriovenous fistula creation: A study of providers and patients. American Journal of Kidney Diseases. 2011; 57(6):873-882

32. Lorenzo V, Martin M, Rufino M, Hernandez D, Torres A, Ayus JC. Predialysis nephrologic care and a functioning arteriovenous fistula at entry are associated with better survival in incident hemodialysis patients: An observational cohort study. American Journal of Kidney Diseases. 2004; 43(6):999-1007

33. Magalhaes LP, Dos Reis LM, Graciolli FG, Pereira BJ, De Oliveira RB, De Souza AAL et al. Predictive factors of one-year mortality in a cohort of patients undergoing urgent-start Hemodialysis. PloS One. 2017; 12(1):0167895

34. Marinovich S, Perez-Loredo J, Lavorato C, Rosa-Diez G, Bisigniano L, Fernandez V et al. Initial glomerular filtration rate and survival in hemodialysis. The role of permanent vascular access. Nefrologia. 2014; 34(1):76-87

35. Marron B, Ostrowski J, Torok M, Timofte D, Orosz A, Kosicki A et al. Type of referral, dialysis start and choice of renal replacement therapy modality in an international integrated care setting. PloS One. 2016; 11(5):e0155987

36. Miyamoto M, Kurita N, Suemitsu K, Murakami M. Fistula and survival outcomes after fistula creation among predialysis chronic kidney disease stage 5 patients. American Journal of Nephrology. 2017; 45(4):356-364

37. 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/

38. O'Hare AM, Bertenthal D, Walter LC, Garg AX, Covinsky K, Kaufman JS et al. When to refer patients with chronic kidney disease for vascular access surgery: should age be a consideration? Kidney International. 2007; 71(6):555-61

39. Ocak G, Rotmans JI, Vossen CY, Rosendaal FR, Krediet RT, Boeschoten EW et al. Type of arteriovenous vascular access and association with patency and mortality. BMC Nephrology. 2013; 14 79

40. Oliver MJ, Quinn RR, Garg AX, Kim SJ, Wald R, Paterson JM. Likelihood of starting dialysis after incident fistula creation. Clinical Journal of the American Society of Nephrology. 2012; 7(3):466-71

41. Oniscu GC, Schalkwijk AA, Johnson RJ, Brown H, Forsythe JL. Equity of access to renal transplant waiting list and renal transplantation in Scotland: cohort study. BMJ. 2003; 327(7426):1261

42. Ortega T, Ortega F, Diaz-Corte C, Rebollo P, Ma Baltar J, Alvarez-Grande J. The timely construction of arteriovenous fistulae: a key to reducing morbidity and mortality and to improving cost management. Nephrology Dialysis Transplantation. 2005; 20(3):598-603

43. Patzer RE, Plantinga LC, Paul S, Gander J, Krisher J, Sauls L et al. Variation in dialysis facility referral for kidney transplantation among patients with end-stage renal disease in Georgia. JAMA. 2015; 314(6):582-594

44. Plantinga LC, Pastan SO, Wilk AS, Krisher J, Mulloy L, Gibney EM et al. Referral for kidney transplantation and indicators of quality of dialysis care: A cross-sectional study. American Journal of Kidney Diseases. 2016; 20:20

45. Ranganathan D, John GT, Yeoh E, Williams N, O'Loughlin B, Han T et al. A randomized controlled trial to determine the appropriate time to initiate peritoneal dialysis after insertion of catheter (Timely PD Study). Peritoneal Dialysis International. 2017; 37(4):420-428

46. Ravani P, Barrett B, Mandolfo S, Brunori G, Cancarini G, Imbasciati E et al. Factors associated with unsuccessful utilization and early failure of the arterio-venous fistula for hemodialysis. Journal of Nephrology. 2005; 18(2):188-96

47. Ravani P, Brunori G, Mandolfo S, Cancarini G, Imbasciati E, Marcelli D et al. Cardiovascular comorbidity and late referral impact arteriovenous fistula survival: A prospective multicenter study. Journal of the American Society of Nephrology. 2004; 15(1):204-209

48. Saran R, Dykstra DM, Pisoni RL, Akiba T, Akizawa T, Canaud B et al. Timing of first cannulation and vascular access failure in haemodialysis: an analysis of practice patterns at dialysis facilities in the DOPPS. Nephrology Dialysis Transplantation. 2004; 19(9):2334-40

49. Slinin Y, Greer N, Ishani A, MacDonald R, Olson C, Rutks I et al. Timing of dialysis initiation, duration and frequency of hemodialysis sessions, and membrane flux: a systematic review for a KDOQI clinical practice guideline. American Journal of Kidney Diseases. 2015; 66(5):823-36

50. Solid CA, Carlin C. Timing of arteriovenous fistula placement and medicare costs during dialysis initiation. American Journal of Nephrology. 2012; 35(6):498-508

51. Stoumpos S, Stevens KK, Aitken E, Kingsmore DB, Clancy MJ, Fox JG et al. Predictors of sustained arteriovenous access use for haemodialysis. American Journal of Nephrology. 2014; 39(6):491-8

52. Tonelli M, Klarenbach S, Rose C, Wiebe N, Gill J. Access to kidney transplantation among remote- and rural-dwelling patients with kidney failure in the United States. JAMA. 2009; 301(16):1681-90

53. Weber CL, Djurdjev O, Levin A, Kiaii M. Outcomes of vascular access creation prior to dialysis: building the case for early referral. ASAIO Journal. 2009; 55(4):355-60

54. Wilmink T, Hollingworth L, Stevenson T, Powers S. Is early cannulation of an arteriovenous fistula associated with early failure of the fistula? Journal of Vascular Access. 2017; 18(1 Suppl):S92-S97

55. Zhang JC, Al-Jaishi A, Perl J, Garg AX, Moist LM. Hemodialysis arteriovenous vascular access creation after kidney transplant failure. American Journal of Kidney Diseases. 2015; 66(4):646-54

Appendices

Appendix A: Review protocols

Table 10: Review protocol: planning dialysis access formation, transplant listing and/or conservative management

Review protocol for timing of access creation and transplant listing

Field	Content
Review question	What is the most clinical and cost effective way of planning dialysis access formation, transplant listing and/or conservative management?
Type of review question	Intervention
Objective of the review	Identify evidence of clinical and cost effectiveness of different timing strategies for RRT access creation and transplant listing
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)	• Early preparation by eGFR (e.g. 15-20/20-25/25-30ml/min) • Late preparation by eGFR (e.g. 10-15ml/min) • Early preparation by time from start of dialysis/transplantation (either actual or estimated from risk tool – e.g. Tangri score) • Late preparation by time from start of dialysis/transplantation (either actual or estimated from risk tool – e.g. Tangri score) Preparation to include creation of HD access, PD access or transplant listing. Results to be reported separately by type of preparation.
Eligibility criteria – comparator(s) / control or reference (gold) standard	Any early strategy compared with any late strategy
Outcomes and prioritisation	Critical • Patient, family/carer health-related QoL (continuous) • Mortality (dichotomous and time to event) Important • Pre-emptive transplantation rates (rates or dichotomous) • Proportion starting on modality of choice (rates or dichotomous) • Proportion with access created/transplant listed who do not go on to require or use RRT (rates or dichotomous) • Psychological distress and mental wellbeing (continuous) • Symptom scores and functional measures (continuous) • Hospitalisation (rates or continuous) • Time to failure of RRT form (time to event) • Patient, family/carer experience of care (continuous) • Adverse events

	○ Infections (dichotomous) ○ Vascular access issues (dichotomous) ○ Dialysis access issues (dichotomous) ○ Acute transplant rejection episodes (dichotomous) When outcomes are reported at multiple timepoints, the later timepoints will be prioritised. All outcomes must be reported after at least 4 weeks of the intervention under investigation. The outcomes of mortality and hospitalisation must be reported after at least 6 months. For quality of life, symptom scores/functional measures, psychological distress/mental wellbeing and experience of care, any validated measures will be accepted. Absolute MIDs of 30 per 1000 will be used for mortality and modality failure. Absolute MIDs of 100 per 1000 will be used for all other outcomes dichotomous outcomes. Where relative MIDs are required (if absolute effects are unavailable), 0.90 to 1.11 will be used for mortality and modality failure. The default relative MIDs of 0.8 to 1.25 will be used for all other dichotomous outcomes. Default continuous MIDs of 0.5x SD will be used for all continuous outcomes, except where published, validated MIDs exist.
Eligibility criteria – study design	RCTs only, if insufficient RCT evidence, NRS that adjust for key confounders (age, ethnicity, comorbidities and baseline health) will be included
Other inclusion exclusion criteria	
Proposed sensitivity / subgroup analysis, or meta-regression	Living vs deceased transplantation
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 variables to be collected	For details please see evidence tables in Appendix D (clinical evidence 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 11: 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.[37] 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 12: 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 13: 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/

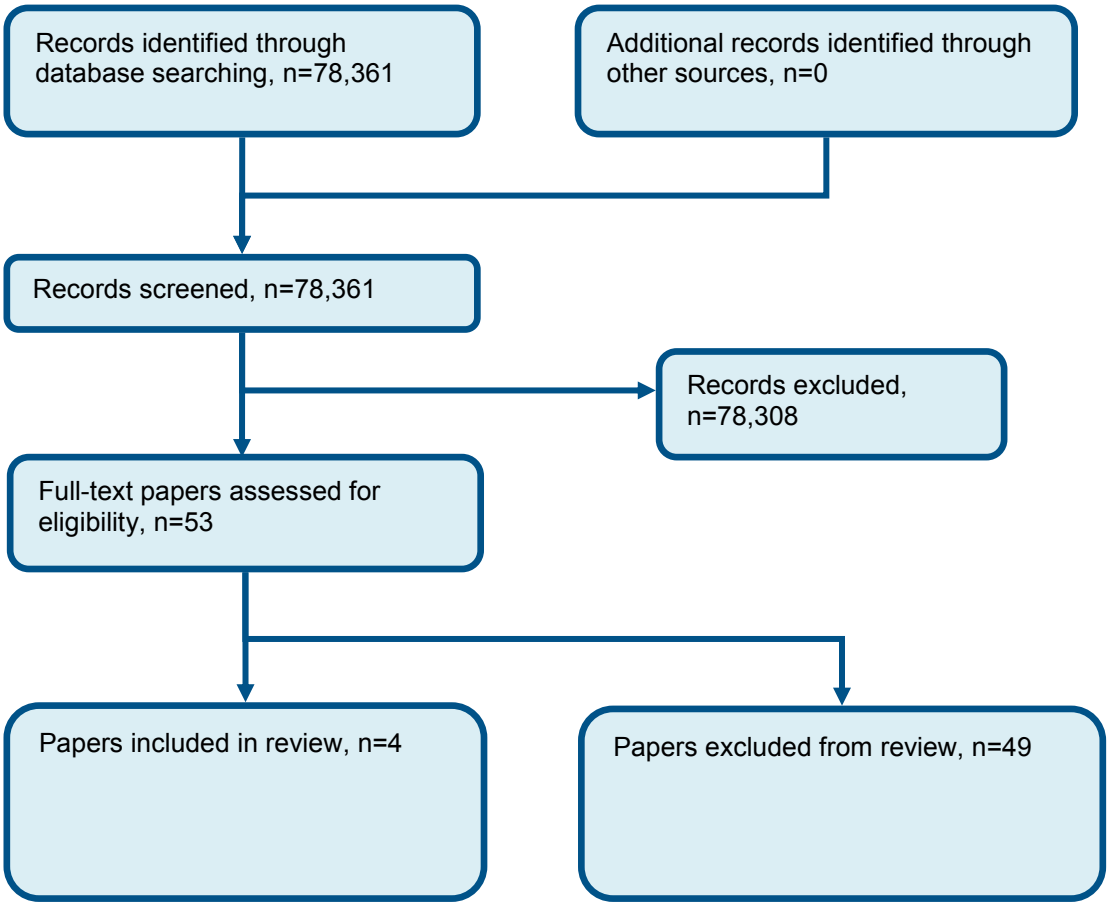
21.	exp Animal Experiment/
22.	exp Experimental Animal/
23.	animal model/
24.	exp Rodent/
25.	(rat or rats or mouse or mice).ti.
26.	or/18-25
27.	10 not 26
28.	*health economics/
29.	exp *economic evaluation/
30.	exp *health care cost/
31.	exp *fee/
32.	budget/
33.	funding/
34.	budget*.ti,ab.
35.	cost*.ti.
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 RRT modalities



Appendix D: Clinical evidence tables

Study	Hod 2015[22]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=17,511)
Countries and setting	Conducted in USA; Setting:
Line of therapy	1st line
Duration of study	Intervention time: 3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall:
Subgroup analysis within study	Not stratified but pre-specified: Age at HD initiation, race, sex, comorbidities, primary cause of ESRD, BMI and duration of nephrology care.
Inclusion criteria	Consists of patients with ESRD on HD started between January 1, 2005 and December 31, 2008, in whom an AVF was the initial access placed before dialysis initiation. We used the US renal data system (USRDS) linked with Medicare claims data to identify our retrospective cohort of interest. The USRDS dataset provided patients' clinical data that described baseline characteristics and comorbidities (as derived from CMS Form 2728), vascular access actually used at HD initiation, and time of death or transplantation. We used a minimum age of 67 years old, because we combined Medicare data from 2003 to make all study patients potentially Medicare eligible 2 years preceding dialysis initiation. Geographic population distribution divided into metropolitan, micropolitan, and rural areas was determined by the Rural–Urban Commuting Area database linked to USRDS by the zip code of the patient's residence. In addition, we used information from the US Census Bureau of median income stratified by race, which was linked to the study dataset by patient's zip codes
Exclusion criteria	Patients were excluded from the study if information regarding the outcome (dialysis access during the first outpatient treatment) was missing. In addition, those patients who changed to peritoneal dialysis or received transplantation before initiation of dialysis were also excluded. Patients who died after AVF placement but before HD

Study	Hod 2015[22]
	initiation are not included in the USRDS, and therefore, they were not a part of this study. Also, 1067 patients in whom the initially placed AVF had failed and a new AVF had been created and used for dialysis were also excluded. That decision was on the basis of uncertainty of how to classify the successful outcome of the consequent AVF, and because the initial AVF did, in fact, fail, including this group might be potentially misleading. Finally, because there is a minimal time needed for AVF maturation, patients in whom the AVF was created, 1 month before HD initiation were excluded as well.
Recruitment/selection of patients	US renal data system linked with Medicare claims
Age, gender and ethnicity	Age - Mean (SD): 76.1 (6.0). Gender (M:F): 58.3% male and 41.7% female . Ethnicity: 77.6% non-Hispanic white, 18.4% non-Hispanic black, 3.23% Asian, 0.8% native American and 0.03% other.
Further population details	
Extra comments	
Indirectness of population	No indirectness
Interventions	(n=4519) Intervention 1: Late listing/access creation - Late HD access creation. 1-3 months between access placement and HD initiation . Duration 1-3 months . Concurrent medication/care: N/A. Indirectness: No indirectness (n=4300) Intervention 2: Late listing/access creation - Late HD access creation. 3-6 months between access placement and HD initiation . Duration 3-6 months. Concurrent medication/care: N/A. Indirectness: No indirectness (n=2579) Intervention 3: Late listing/access creation - Late HD access creation. 6-9 months between access placement and HD initiation . Duration 6-9 months. Concurrent medication/care: N/A. Indirectness: No indirectness (n=1739) Intervention 4: Late listing/access creation - Late HD access creation. 9-12 months between access placement and HD initiation . Duration 9-12 months. Concurrent medication/care: N/A. Indirectness: No indirectness (n=4374) Intervention 5: Early listing/access creation - Early TPx listing. 12 months and above between access placement and HD initiation . Duration 12+ months. Concurrent medication/care: N/A. Indirectness: No indirectness

Study	Hod 2015[22]
Funding	No funding (The study was funded from departmental funds and did not have any outside sponsor or funding agency.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LATE HD ACCESS CREATION - 1-3 MONTHS versus EARLY TPX LISTING

Protocol outcome 1: Symptom scores/functional measures
- Actual outcome: Success rate from AVF creation to HD initiation at 3 years PT; OR; 0.49 (95%CI 0.44 to 0.53, Comments: Compared to >12 months);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for DM: Success rate from AVF creation to HD initiation in patients with diabetes at 3 years PT; OR; 0.5 (95%CI 0.44 to 0.56);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with diabetes n=9810; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for BAME: Success rate from AVF creation to HD initiation in blacks at 3 years PT; OR; 0.49 (95%CI 0.39 to 0.61);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with blacks n=3224; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LATE HD ACCESS CREATION 3-6 MONTHS versus EARLY TPX LISTING

Protocol outcome 1: Symptom scores/functional measures
- Actual outcome: Success rate from AVF creation to HD initiation at 3 years PT; OR; 0.93 (95%CI 0.85 to 1.02);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for DM: Success rate from AVF creation to HD initiation in patients with diabetes at 3 years PT; OR; 0.93 (95%CI 0.82 to 1.05);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with diabetes n=9810; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for BAME: Success rate from AVF creation to HD initiation in blacks at 3 years PT; OR; 0.89 (95%CI 0.72 to 1.1);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with blacks n=3224; Key confounders: age,

Study	Hod 2015[22]
ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LATE HD ACCESS CREATION 6-9 MONTHS versus EARLY TPX LISTING Protocol outcome 1: Symptom scores/functional measures - Actual outcome: Success rate from AVF creation to HD initiation at 3 years PT; OR; 1.00 (95%CI 0.9 to 1.11); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for DM: Success rate from AVF creation to HD initiation in patients with diabetes at 3 years PT; OR; 1.08 (95%CI 0.94 to 1.24); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with diabetes n=9810; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for BAME: Success rate from AVF creation to HD initiation in blacks at 3 years PT; OR; 0.94 (95%CI 0.74 to 1.2); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with blacks n=3224; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LATE HD ACCESS CREATION 9-12 MONTHS versus EARLY TPX LISTING Protocol outcome 1: Symptom scores/functional measures - Actual outcome: Success rate from AVF creation to HD initiation at 3 years PT; OR; 0.99 (95%CI 0.88 to 1.11); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for DM: Success rate from AVF creation to HD initiation in patients with diabetes at 3 years PT; OR; 1.06 (95%CI 0.9 to 1.24); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with diabetes n=9810; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for BAME: Success rate from AVF creation to HD initiation in blacks at 3 years PT; OR; 0.93 (95%CI 0.71 to 1.21); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: patients with blacks n=3224; Key confounders: age, ethnicity, co-morbidities, baseline health; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the	Quality of life ; Mortality ; Pre-emptive TPx rate ; Proportion starting on modality of choice ; Proportion with

Study	Hod 2015[22]
study	access created/TPx listed who do not go on to require RRT ; Psychological distress/mental wellbeing ; Hospitalisation ; Time to failure of RRT form ; Experience of care ; Infections ; Vascular access issues ; PD access issues ; Acute transplant rejection episodes

Study	Ishani 2014[24]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=14,459)
Countries and setting	Conducted in USA; Setting:
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: 4 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not stratified but pre-specified: age, ethnicity, co-morbidities
Inclusion criteria	To be included in the final cohort, patients were required to be aged 67 years and over at initiation. We required part A and part B coverage in the 2 years preceding initiation and a diagnosis of CKD in the 1-2 years preceding initiation. We required haemodialysis initiation with a functioning fistula, as indicated on the Medical evidence report form CMS-2728. The date of fistula placement was identified using medicare claims from the 2 years preceding haemodialysis initiation.
Exclusion criteria	Under 67 years of age.
Recruitment/selection of patients	Medicare data for patients who initiated haemodialysis between January 1, 2005 and December 31, 2009 with 2 or more years of prior medicare coverage.
Age, gender and ethnicity	Age - Mean (SD): 77.0 (6.1). Gender (M:F): 63% male, 37% female. Ethnicity: 80.7% white, 15.6% black and 3.7% Asian/other
Further population details	
Indirectness of population	No indirectness
Interventions	(n=419) Intervention 1: Early listing/access creation - Early HD access creation. Fistula placement within 1 month before initiation. Duration 4 years. Concurrent medication/care: Patients interacted substantially with the health care system in the year preceding dialysis initiation. Specialist referral was fairly common. .

Study	Ishani 2014[24]
	Indirectness: No indirectness (n=11683) Intervention 2: Late listing/access creation - Late HD access creation. Fistula placement after 1 month before initiation. Duration 4 years. Concurrent medication/care: Patients interacted substantially with the health care system in the year preceding dialysis initiation. Specialist referral was fairly common. . Indirectness: No indirectness
Funding	Academic or government funding (Supported by a research contract with Amgen, inc, thousand oaks, California, USA.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY HD ACCESS CREATION versus LATE HD ACCESS CREATION Protocol outcome 1: Mortality - Actual outcome: Mortality at 4 years pt ; HR; 1.26 (95%CI 1.03 to 1.55, Comments: Fistula placement within 1 month before initiation was associated with increased risk of mortality compared with placement 1-2 months before initiation.); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: age, gender, ethnicity, comorbidities ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Pre-emptive TPx rate ; Proportion starting on modality of choice ; Proportion with access created/TPx listed who do not go on to require RRT ; Psychological distress/mental wellbeing ; Symptom scores/functional measures ; Hospitalisation ; Time to failure of RRT form ; Experience of care ; Infections ; Vascular access issues ; PD access issues ; Acute transplant rejection episodes

Study	Ranganathan 2017[45]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=122)
Countries and setting	Conducted in Australia; Setting: Australia, two renal centres
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis

Study	Ranganathan 2017[45]
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 18, will be receiving CAPD or APD within 4 weeks of insertion of a PD catheter
Exclusion criteria	History of psychological illness, acute infectious episode in month before enrolment
Recruitment/selection of patients	All consecutive patients screened for inclusion
Age, gender and ethnicity	Age - Mean (SD): 57 (16). Gender (M:F): 56:44. Ethnicity:
Further population details	
Extra comments	35% diabetic, 85% non-Aboriginal and Torres Strait Islander
Indirectness of population	No indirectness
Interventions	(n=41) Intervention 1: Early listing/access creation - Early PD access creation. 4 weeks from creation to initiation. Duration 6 months. Concurrent medication/care: 5 cm transverse incision over anterior rectus sheath, double-cuff curled catheter, curl placed in pelvis, deep cuff within the rectus sheath. Catheter tunnelled to exterior using a trocar matched for diameter. No anchoring suture. Inflow and outflow tested before incision closed and dressings applied. AB prophylaxis an hour before procedure, bowel preparation to avoid constipation. Initiated on CAPD, automated PD not used during initial training. Formal PD training for all. Day 1 PD initiated at low intra-peritoneal volume, 1L 60-minute dwell, 4 manual exchanges, 4 manual exchanges on day 2 and 3 with daily increments of 500ml in volume and 30 minutes dwell time. Exit site examined at weekly intervals for first 4 weeks. Indirectness: No indirectness (n=42) Intervention 2: Early listing/access creation - Early PD access creation. 2 weeks from insert to initiate. Duration 6 months. Concurrent medication/care: As for 4 weeks. Indirectness: No indirectness (n=39) Intervention 3: Late listing/access creation - Late PD access creation. 1 week from insert to initiate. Duration 6 months. Concurrent medication/care: As for 4 weeks. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 2 WEEKS FROM INSERT TO INITIATE versus 4 WEEKS FROM INSERT TO INITIATE

Protocol outcome 1: Time to failure of RRT form
- Actual outcome: Switch to HD because of PD catheter dysfunction at 6 months; Group 1: 1/42, Group 2: 7/41
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4, Reason: 3 unable to start on randomisation date, 1 improved

Study	Ranganathan 2017[45]
	and did not need dialysis; Group 2 Number missing: 11, Reason: 4 symptomatic requiring earlier dialysis, 2 unable to start on date, 2 opted for palliation, 1 improved did not need dialysis, 1 catheter did not function, 1 withdrew from study Protocol outcome 2: Infections - Actual outcome: PD-related/tunnel infection/peritonitis at 2 months; Group 1: 1/42, Group 2: 1/41 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4, Reason: 3 unable to start on randomisation date, 1 improved and did not need dialysis; Group 2 Number missing: 11, Reason: 4 symptomatic requiring earlier dialysis, 2 unable to start on date, 2 opted for palliation, 1 improved did not need dialysis, 1 catheter did not function, 1 withdrew from study Protocol outcome 3: PD access issues - Actual outcome: Leak (appearance of dialysate at exit site or loss from cavity, two nurses had to concur, positive glucose dipstick confirmation) at 2 months; Group 1: 4/42, Group 2: 1/41 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 4, Reason: 3 unable to start on randomisation date, 1 improved and did not need dialysis; Group 2 Number missing: 11, Reason: 4 symptomatic requiring earlier dialysis, 2 unable to start on date, 2 opted for palliation, 1 improved did not need dialysis, 1 catheter did not function, 1 withdrew from study RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 1 WEEK FROM INSERT TO INITIATE versus 4 WEEKS FROM INSERT TO INITIATE Protocol outcome 1: Time to failure of RRT form - Actual outcome: Switch to HD because of PD catheter dysfunction at 6 months; Group 1: 1/39, Group 2: 7/41 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 3 unable to start on randomisation date, 2 pre-dialysis infection; Group 2 Number missing: 11, Reason: 4 symptomatic requiring earlier dialysis, 2 unable to start on date, 2 opted for palliation, 1 improved did not need dialysis, 1 catheter did not function, 1 withdrew from study Protocol outcome 2: Infections - Actual outcome: PD-related/tunnel infection/peritonitis at 2 months; Group 1: 5/39, Group 2: 1/41 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 3 unable to start on randomisation date, 2 pre-dialysis infection; Group 2 Number missing: 11, Reason: 4 symptomatic requiring earlier dialysis, 2 unable to start on date, 2 opted for palliation, 1 improved did not need dialysis, 1 catheter did not function, 1 withdrew from study Protocol outcome 3: PD access issues - Actual outcome: Leak (appearance of dialysate at exit site or loss from cavity, two nurses had to concur, positive glucose dipstick confirmation) at 2

Study	Ranganathan 2017[45]
months; Group 1: 11/39, Group 2: 1/41 Risk of bias: All domain - ; Indirectness of outcome: No indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 1 WEEK FROM INSERT TO INITIATE versus 2 WEEKS FROM INSERT TO INITIATE Protocol outcome 1: Time to failure of RRT form - Actual outcome: Switch to HD because of PD catheter dysfunction at 6 months; Group 1: 1/39, Group 2: 1/42 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: 5, Reason: 3 unable to start on randomisation date, 2 pre-dialysis infection; Group 2 Number missing: 4, Reason: 3 unable to start on date, 1 did not require dialysis Protocol outcome 2: Infections - Actual outcome: PD-related/tunnel infection/peritonitis at 2 months; Group 1: 5/39, Group 2: 1/42 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: 5, Reason: 3 unable to start on randomisation date, 2 pre-dialysis infection; Group 2 Number missing: 4, Reason: 3 unable to start on date, 1 did not require dialysis Protocol outcome 3: PD access issues - Actual outcome: Leak (appearance of dialysate at exit site or loss from cavity, two nurses had to concur, positive glucose dipstick confirmation) at 2 months; Group 1: 11/39, Group 2: 4/42 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: 5, Reason: 3 unable to start on randomisation date, 2 pre-dialysis infection; Group 2 Number missing: 4, Reason: 3 unable to start on date, 1 did not require dialysis	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Pre-emptive TPx rate ; Proportion starting on modality of choice ; Proportion with access created/TPx listed who do not go on to require RRT ; Psychological distress/mental wellbeing ; Symptom scores/functional measures ; Hospitalisation ; Experience of care ; Vascular access issues ; Acute transplant rejection episodes

Study	Ravani 2004[47]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=535)

Study	Ravani 2004[47]
Countries and setting	Conducted in Italy; Setting:
Line of therapy	Adjunctive to current care
Duration of study	Intervention time: 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall:
Subgroup analysis within study	Not applicable
Inclusion criteria	Data collected by means of a computerized database containing demographic and clinical information on all consecutive ESRD patients who were older than 18 years old, receiving a new AVF, and entering maintenance HD treatment programs at 3 dialysis units in Northern Italy from January 1, 1997 to December 31, 2002.
Exclusion criteria	Data for these analyses were restricted to patients who received the VA placement for the first time and by one of the local renal physicians in charge of the VA-related procedures.
Recruitment/selection of patients	Data collected by means of a computerized database containing demographic and clinical information on all consecutive ESRD patients.
Age, gender and ethnicity	Age - Mean (SD): 66.5 (14.2). Gender (M:F): 58% male, 42% female. . Ethnicity: 98% white, 2% other.
Further population details	
Indirectness of population	No indirectness
Interventions	(n=184) Intervention 1: Early listing/access creation - Early HD access creation. Time from creation to use <30 days. Duration 0-3 months. Concurrent medication/care: Not stated. (n=230) Intervention 2: Late listing/access creation - Late HD access creation. Time from creation to use >30 days. Duration 3+ months. Concurrent medication/care: Not stated. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY HD ACCESS CREATION versus LATE HD ACCESS CREATION

Protocol outcome 1: Time to failure of RRT form
- Actual outcome: AVF failure at 5 years PT; HR; 1.941 (95%CI 1.337 to 2.817, Comments: Time to use, <30 vs >30 days);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: Age, ethnicity, gender and comorbid conditions. ; Group

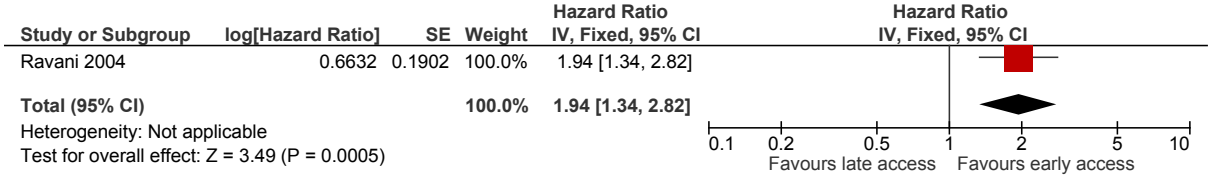
Study	Ravani 2004[47]
1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Mortality ; Pre-emptive TPx rate ; Proportion starting on modality of choice ; Proportion with access created/TPx listed who do not go on to require RRT ; Psychological distress/mental wellbeing ; Symptom scores/functional measures ; Hospitalisation ; Experience of care ; Infections ; Vascular access issues ; PD access issues ; Acute transplant rejection episodes

Appendix E: Forest plots

E.1 Late vascular access creation versus early vascular access creation

1.1 Adults 18-70

Figure 2: AVF failure (time from creation to use <30 days vs >30 days)



1.2 Adults >70

Figure 3: Successful AVF creation (1-3 months vs >12 months)

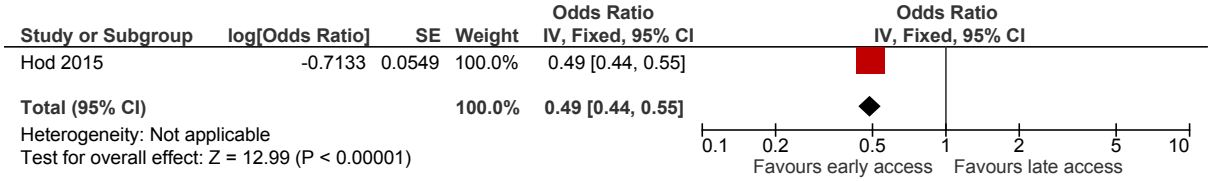


Figure 4: Successful AVF creation (3-6 months vs >12 months)

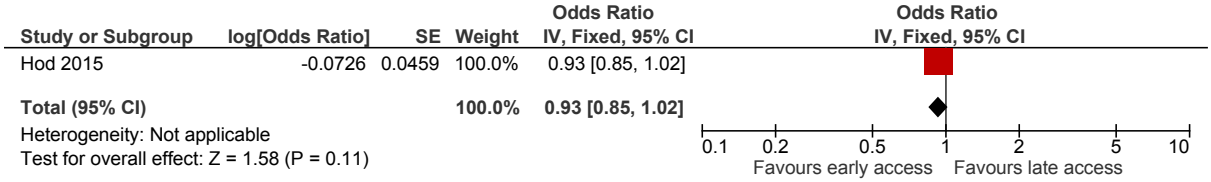


Figure 5: Successful AVF creation (6-9 months vs >12 months)

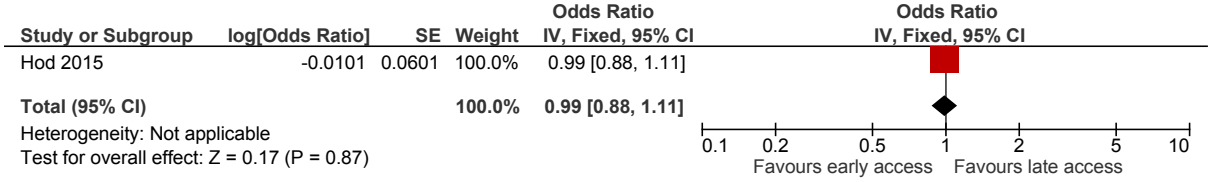


Figure 6: Successful AVF creation (9-12 months vs >12 months)

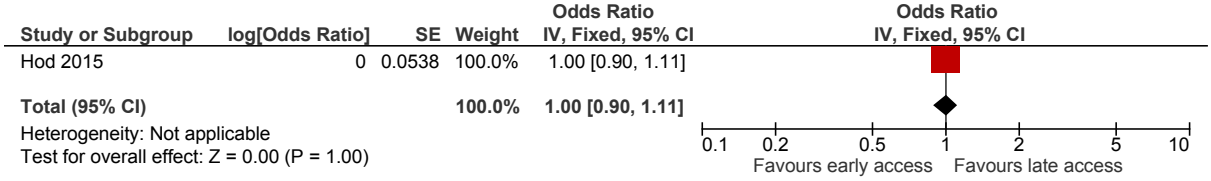


Figure 7: Successful AVF creation (1-3 months vs >12 months) in BAME

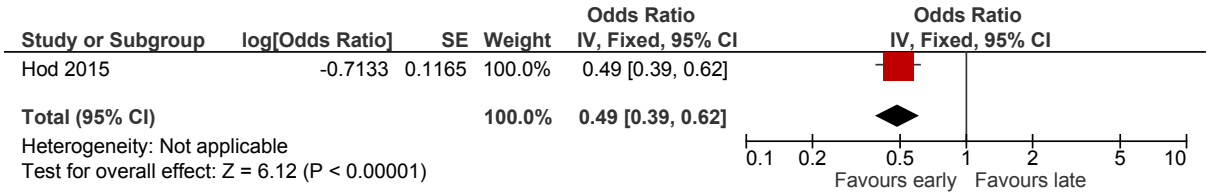


Figure 8: Successful AVF creation (3-6 months vs >12 months) in BAME

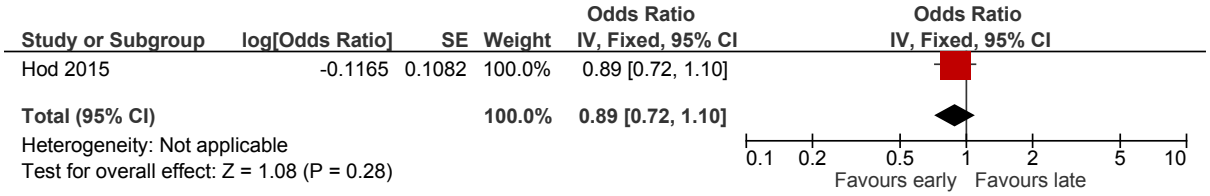


Figure 9: Successful AVF creation (6-9 months vs >12 months) in BAME

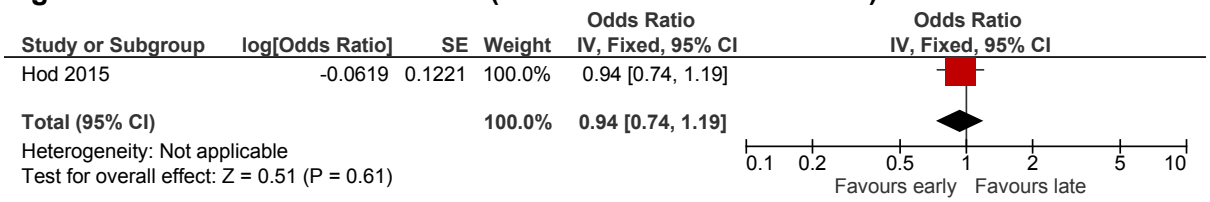


Figure 10: Successful AVF creation (9-12 months vs >12 months) in BAME

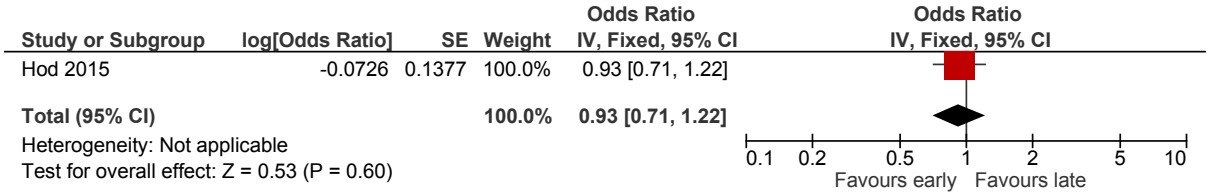


Figure 11: Successful AVF creation (1-3 months vs >12 months) in patients with diabetes

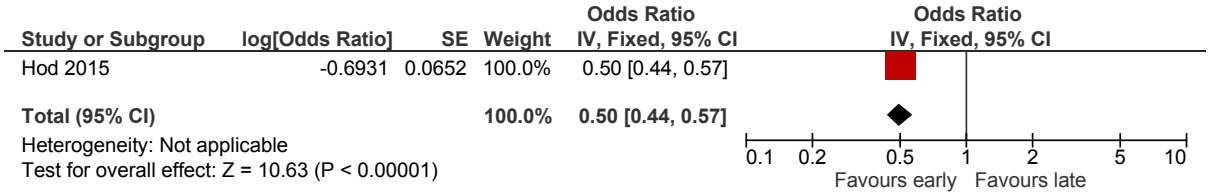


Figure 12: Successful AVF creation (3-6 months vs >12 months) in patients with diabetes

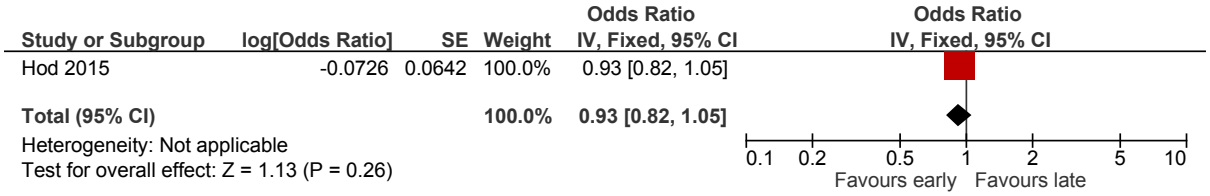


Figure 13: Successful AVF creation (6-9 months vs >12 months) in patients with diabetes

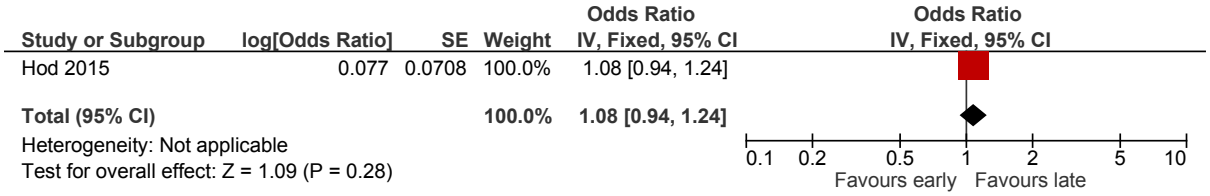


Figure 14: Successful AVF creation (9-12 months vs >12 months) in patients with diabetes

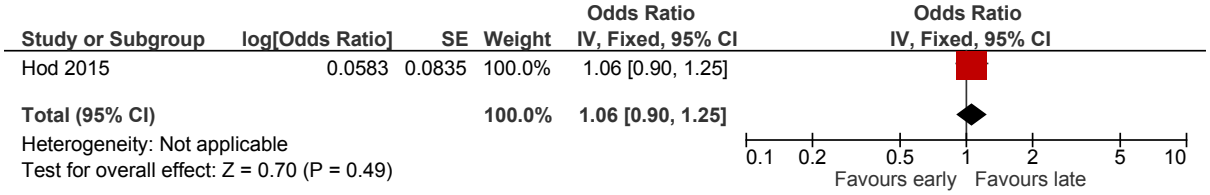
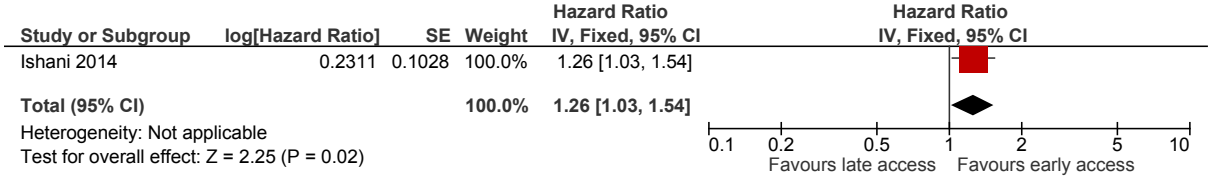


Figure 15: Mortality (fistula placement within 1 month before initiation vs 1-2 months before initiation)



E.2 Late PD access creation versus early PD access creation

Figure 16: 1 week vs 4 weeks, modality failure

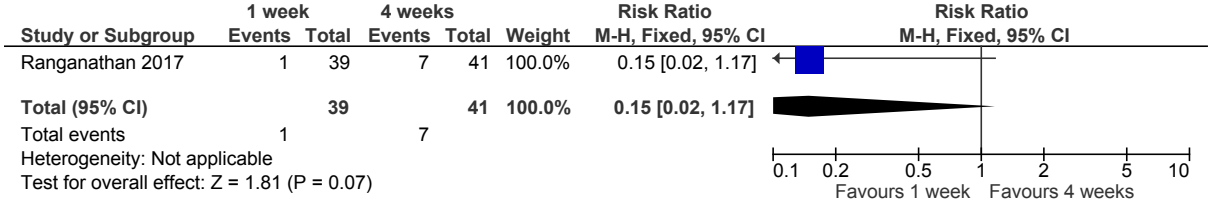


Figure 17: 1 week vs 4 weeks, infections

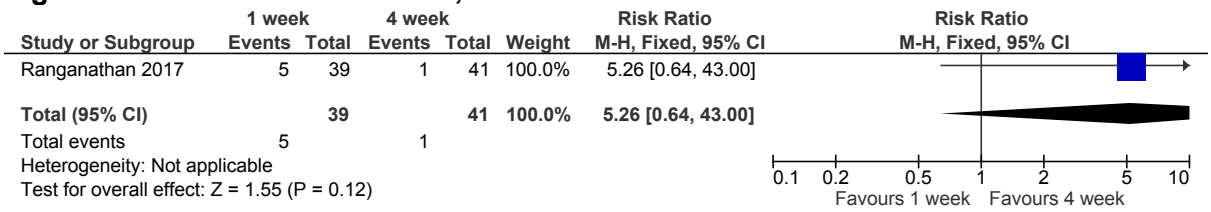


Figure 18: 1 week vs 4 weeks, leaks

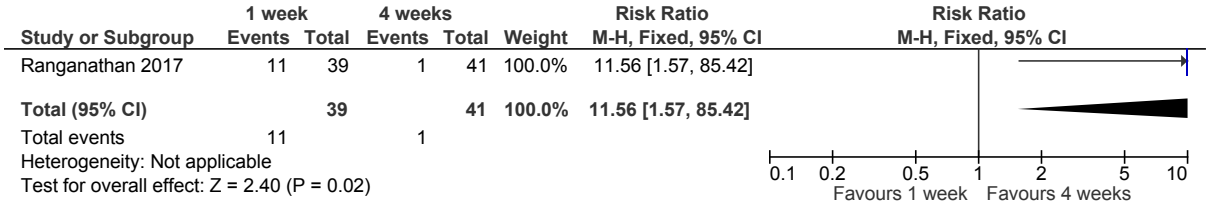


Figure 19: 1 week vs 2 weeks, modality failure

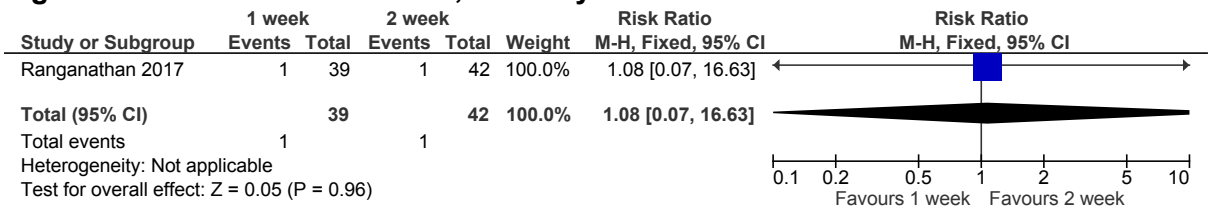


Figure 20: 1 week vs 2 weeks, infections

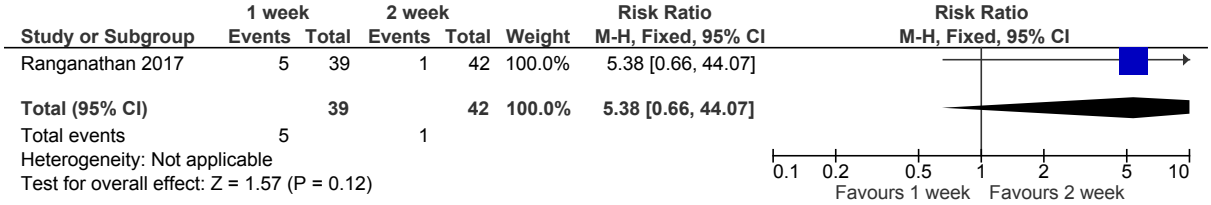


Figure 21: 1 week vs 2 weeks, leaks

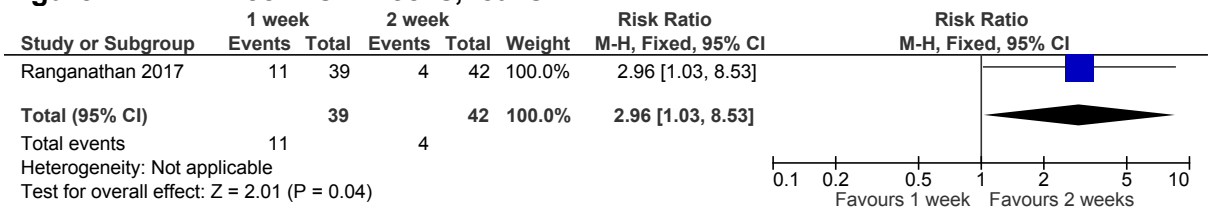


Figure 22: 2 weeks vs 4 weeks, modality failure

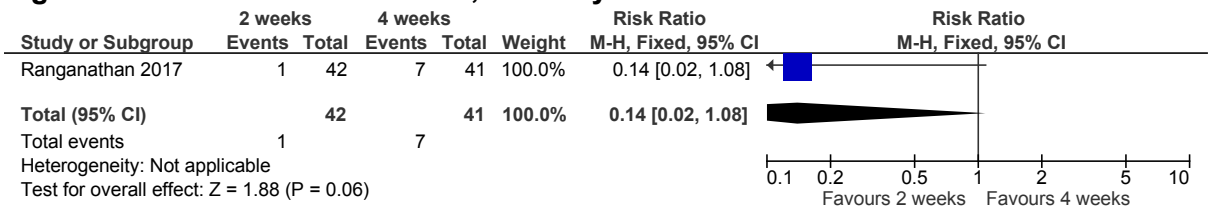


Figure 23: 2 weeks vs 4 weeks, infections

Study or Subgroup	2 week Events	Total	4 week Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ranganathan 2017	1	42	1	41	100.0%	0.98 [0.06, 15.09]
Total (95% CI)		**42**		**41**	**100.0%**	**0.98 [0.06, 15.09]**
Total events	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.99)

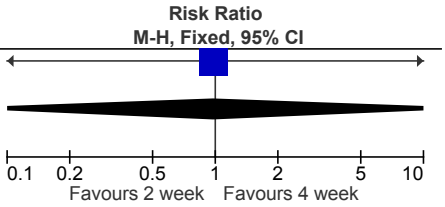
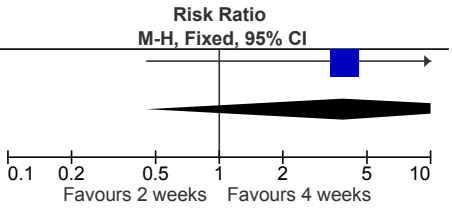


Figure 24: 2 weeks vs 4 weeks, leaks

Study or Subgroup	2 weeks Events	Total	4 weeks Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ranganathan 2017	4	42	1	41	100.0%	3.90 [0.46, 33.48]
Total (95% CI)		**42**		**41**	**100.0%**	**3.90 [0.46, 33.48]**
Total events	4		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.21)



Appendix F: GRADE tables

F.1 Haemodialysis access

Table 14: Clinical evidence profile: Late access versus early access adults, 18-70 years

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Late HD access creation	Early HD access creation, 18-70	Relative (95% CI)	Absolute		
AVF failure (time from creation to use <30 days vs >30 days) (Copy) (follow-up 5 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/184 (0%)	0%	HR 1.94 (1.34 to 2.82)	-	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.

Table 15: Clinical evidence profile: Late access versus early access adults, >70 years

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Late HD access creation	Early HD access creation, >70	Relative (95% CI)	Absolute		
Successful AVF creation (1-3 months vs >12 months) (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/4519 (0%)	0%	OR 0.49 (0.44 to 0.55)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (3-6 months vs >12 months) (follow-up 3 years)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/4300 (0%)	0%	OR 0.93 (0.85 to 1.02)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (6-9 months vs >12 months) (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/2579 (0%)	0%	OR 0.99 (0.88 to 1.11)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (9-12 months vs >12 months) (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/1739 (0%)	0%	OR 1 (0.9 to 1.11)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (1-3 months vs >12 months) in BAME (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/3224 (0%)[2]	0%	OR 0.49 (0.39 to 0.61)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (3-6 months vs >12 months) in BAME (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	0/3224 (0%)[2]	0%	OR 0.89 (0.72 to 1.10)	-	⊕OOO VERY LOW	CRITICAL
Successful AVF creation (6-9 months vs >12 months) in BAME (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	0/3224 (0%)[2]	0%	OR 0.94 (0.74 to 1.20)	-	⊕OOO VERY LOW	CRITICAL
Successful AVF creation (9-12 months vs >12 months) in BAME (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	0/3224 (0%)[2]	0%	OR 0.93 (0.71 to 1.21)	-	⊕OOO VERY LOW	CRITICAL
Successful AVF creation (1-3 months vs >12 months) in patients with diabetes (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/9810 (0%)[2]	0%	OR 0.5 (0.44 to 0.56)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (3-6 months vs >12 months) in patients with diabetes (follow-up 3 years)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/9810 (0%)[2]	0%	OR 0.93 (0.82 to 1.05)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (6-9 months vs >12 months) in patients with diabetes (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/9810 (0%)[2]	0%	OR 1.08 (0.94 to 1.24)	-	⊕⊕OO LOW	CRITICAL
Successful AVF creation (9-12 months vs >12 months) in patients with diabetes (follow-up 3 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	0/9810 (0%)[2]	0%	OR 1.06 (0.90 to 1.24)	-	⊕OOO VERY LOW	CRITICAL
Mortality (fistula placement within 1 month before initiation vs 1-2 months before initiation) (follow-up 4 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	0/419 (0%)	0%	HR 1.26 (1.03 to 1.54)	-	⊕OOO VERY LOW	CRITICAL

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2] Not total for each outcome, only overall total for sub groups recorded
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.

F.2 Peritoneal dialysis access

Table 16: 1 week from access creation to use vs 4 weeks from access creation to use, adults 18-70 years

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Late PD access creation (1 week)**	**Early PD access creation (4 weeks)**	**Relative (95% CI)**	**Absolute**		
Modality failure (switch to HD because PD dysfunction) (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1/39 (2.6%)	7/41 (17.1%)	RR 0.15 (0.02 to	145 fewer per 1000 (from 167 fewer to	⊕⊕OO LOW	IMPORTANT

									1.17)	29 more)		
Infections (PD-related/tunnel/peritonitis) (follow-up 2 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/39 (12.8%)	1/41 (2.4%)	RR 5.26 (0.64 to 43)	104 more per 1000 (from 9 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Leak (follow-up 2 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/39 (28.2%)	1/41 (2.4%)	RR 11.56 (1.57 to 85.42)	258 more per 1000 (from 14 more to 1000 more)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 17: 1 week from access creation to use vs 2 weeks from access creation to use, adults 18-70 years

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Late PD access creation (1 week)**	**Early PD access creation (2 weeks)**	**Relative (95% CI)**	**Absolute**		
Modality failure (switch to HD because PD dysfunction) (follow-up 6 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/39 (2.6%)	1/42 (2.4%)	RR 1.08 (0.07 to 16.63)	2 more per 1000 (from 22 fewer to 372 more)	⊕⊕OO LOW	IMPORTANT
Infections (PD-related/tunnel/peritonitis) (follow-up 2 months)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	5/39 (12.8%)	1/42 (2.4%)	RR 5.38 (0.66 to 44.07)	104 more per 1000 (from 8 fewer to 1000 more)	⊕⊕OO LOW	IMPORTANT
Leak (follow-up 2 months)												
1	randomised	no serious	no serious	no serious	serious[1]	none	11/39	4/42	RR 2.96	187 more per 1000	⊕⊕⊕O	IMPORTANT

	trials	risk of bias	inconsistency	indirectness			(28.2%)	(9.5%)	(1.03 to 8.53)	(from 3 more to 717 more)	MODERATE	

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

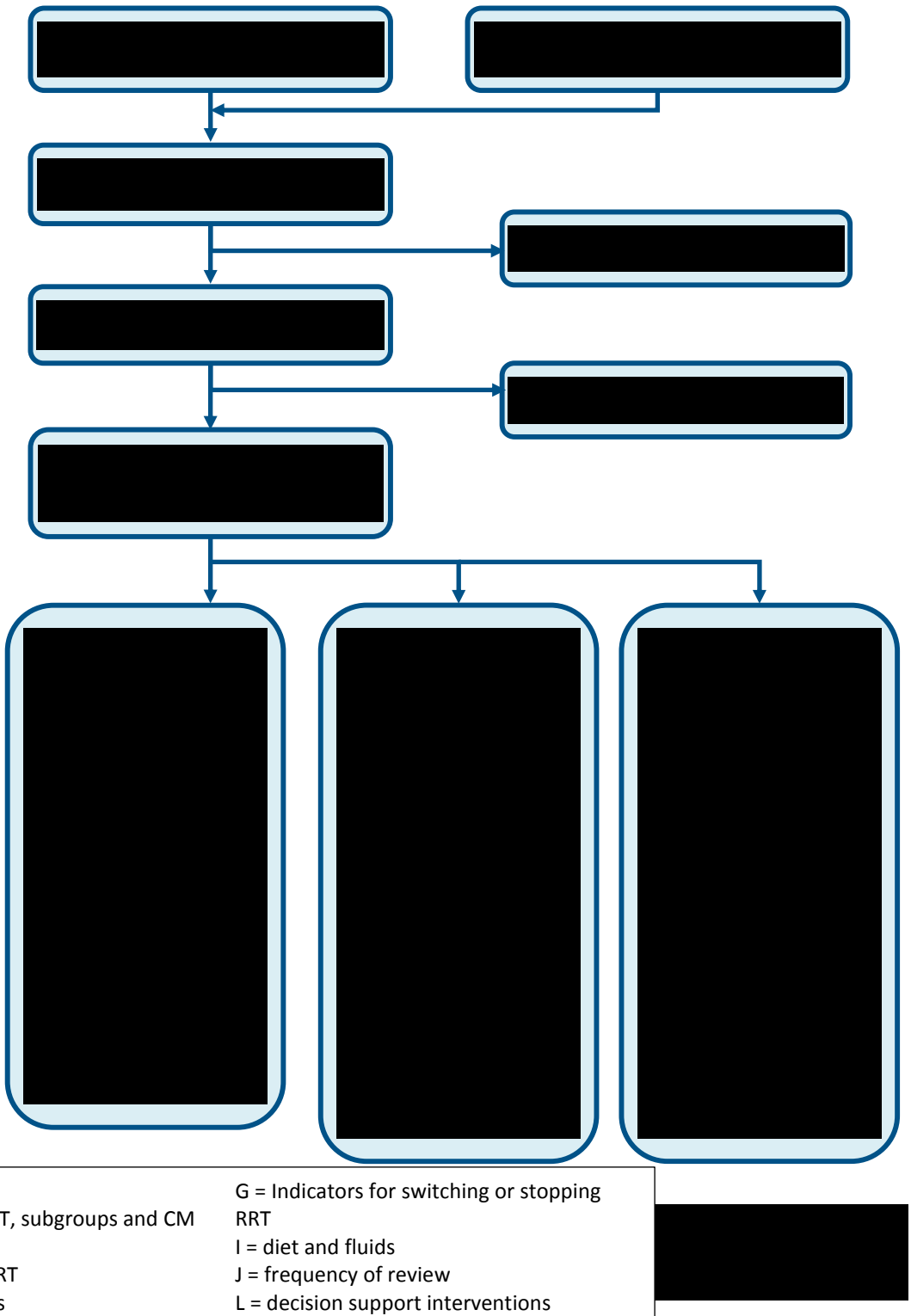
Table 18: 2 weeks from access creation to use vs 4 weeks from access creation to use, adults 18-70 years

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Late PD access creation (2 week)**	**Early PD access creation (4 weeks)**	**Relative (95% CI)**	**Absolute**		
Modality failure (switch to HD because PD dysfunction) (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	1/42 (2.4%)	7/41 (17.1%)	RR 0.14 (0.02 to 1.08)	147 fewer per 1000 (from 167 fewer to 14 more)	⊕⊕OO LOW	IMPORTANT
Infections (PD-related/tunnel/peritonitis) (follow-up 2 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/42 (2.4%)	1/41 (2.4%)	RR 0.98 (0.06 to 15.09)	0 fewer per 1000 (from 23 fewer to 344 more)	⊕OOO VERY LOW	IMPORTANT
Leak (follow-up 2 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/42 (9.5%)	1/41 (2.4%)	RR 3.9 (0.46 to 33.48)	71 more per 1000 (from 13 fewer to 792 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Appendix G: Health economic evidence selection

Figure 25: 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 19: Studies excluded from the clinical review

Study	Exclusion reason
Al-Balas 2016[1]	NRS without adequate adjustment
Al-Jaishi 2015[2]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Alencar de Pinho 2017[3]	NRS without adequate adjustment
Almasi-Sperling 2016[4]	NRS without adequate adjustment
Asano 2013[5]	No usable outcomes
Astor 2001[6]	No usable outcomes
Bansal 2013[7]	Qualitative study
Bashar 2015[8]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Beuscart 2015[9]	No usable outcomes
Cass 2003[10]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Chan 2007[11]	Incorrect interventions
Collins 2011[12]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Diehm 2010[14]	No usable outcomes
Elhassan 2012[15]	Review (not systematic)
Farooq 2010[16]	No usable outcomes
Feldman 2003[17]	No usable outcomes
Fissell 2012[18]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Grams 2015[19]	No usable outcomes
Heaf 2007[20]	NRS without adequate adjustment
Hiremath 2011[21]	No usable outcomes
Hodges 1997[23]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Jeffrey 2005[25]	NRS without adequate adjustment
Jungers 1993[26]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Kaygin 2012[27]	No usable outcomes
Lee 2004[29]	No usable outcomes
Lee 2016[30]	No usable outcomes
Lee 2017[28]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Lopez-Vargas 2011[31]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Lorenzo 2004[32]	No usable outcomes
Magalhaes 2017[33]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Marinovich 2014[34]	Inappropriate comparison – no outcomes comparing access

Study	Exclusion reason
	creation or TPx listing strategies
Marron 2016[35]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Miyamoto 2017[36]	NRS without adequate adjustment
Ocak 2013[39]	Incorrect interventions
O'Hare 2007[38]	NRS without adequate adjustment
Oliver 2012[40]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Oniscu 2003[41]	No usable outcomes
Ortega 2005[42]	No usable outcomes
Patzer 2015[43]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Plantinga 2016[44]	No usable outcomes
Ravani 2005[46]	No usable outcomes
Saran 2004[48]	No usable outcomes
Slinin 2015[49]	SR, references checked
Solid 2012[50]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Stoumpos 2014[51]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Tonelli 2009[52]	Inappropriate comparison – no outcomes comparing access creation or TPx listing strategies
Weber 2009[53]	No usable outcomes
Wilmink 2017[54]	NRS without adequate adjustment
Zhang 2015[55]	No usable outcomes

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 20: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	

Appendix J: Research recommendations

J.1 Optimal timing in PD

Research question: What is the optimum timing of laparoscopic and percutaneous PD access creation?

Why this is important:

The committee did not make recommendations on the optimal timing for laparoscopic or percutaneous PD access creation as no evidence for these strategies was identified in this review. Recommendations in this area are important to optimise the treatment pathway for people requiring RRT and to enable services to efficiently provide clinically effective treatment.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Children, young people and adults with CKD stage 3 to 5, in whom initiation of RRT, within 1 month, has been deemed appropriate Intervention/comparison: 1 - Laparoscopic PD access creation 4 weeks before use of access, laparoscopic PD access creation 2 weeks before use of access, laparoscopic PD access creation 1 week before use of access 2 – Percutaneous PD access creation 4 weeks before use of access, percutaneous PD access creation 2 weeks before use of access, percutaneous PD access creation 1 week before use of access Outcomes: Patient, family/carer health-related QoL, mortality, proportion starting on modality of choice, proportion with access created who do not go on to require or use RRT, psychological distress and mental wellbeing, symptom scores and functional measures, hospitalisation, time to failure of RRT form, patient, family/carer experience of care, adverse events (infections, dialysis access issues)
Importance to patients or the population	If effective and cost-effective, such an intervention could potentially provide significant benefits in terms of health-related quality of life, access function and reducing complications such as infections or leaks.
Relevance to NICE guidance	There is current uncertainty about what the optimal timing of PD access creation is.
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 optimum timing of laparoscopic and percutaneous PD access creation. It is important to have sufficient information on the optimal timing of creating PD access so more evidence based information can be given in regards to the different RRT options.
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	• Low: the research is of interest and will fill existing evidence gaps.

J.2 Clinical and cost effectiveness of acute dialysis

Research question: What is the clinical and cost effectiveness of initial haemodialysis versus initial peritoneal dialysis (PD) for people who start dialysis in an unplanned way?

Why this is important:

The committee did not make recommendations on the clinical and cost effectiveness of initial PD and initial HD as no evidence for these strategies was identified in this review or the modalities of RRT review. Recommendations in this area are important to ensure unplanned starters are efficiently provided with the most clinical and cost effective treatment. Unplanned starters are often begun on HD by default and may never get the opportunity to consider PD as an option. Evidence establishing acute PD as a viable option may prevent people inappropriately being committed to a treatment modality that is not optimal for them in the long run.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Children, young people and adults with CKD stage 3 to 5, in whom the need for RRT was not identified to allow for optimum planning and treatment choice (likely <90 days between identification and need for RRT) Intervention/comparison: 1. Initial PD for unplanned starters 2. Initial HD for unplanned starters Outcomes: Patient, family/carer health-related QoL, mortality, psychological distress and mental wellbeing, symptom scores and functional measures, hospitalisation, time to failure of RRT form, 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 most effective form of acute dialysis.
Relevance to NICE guidance	There is current uncertainty about the clinical and cost effectiveness of acute PD and HD for unplanned starters.
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 comparison of acute PD to acute HD. It is important to have sufficient information on initial forms of dialysis so further evidence based information can be given in regards to the different RRT options.
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.

J.3 Optimum timing of listing for transplantation

Research question: What is the optimum timing of listing for transplantation?

Why this is important:

No evidence was identified for the timing of transplant listing, resulting in the committee being unable to form a recommendation for a specific time point at which people should be listed for transplant. It is important to have recommendations in this area so people with RRT are efficiently provided with clinically effective treatment. Other evidence reviews established that pre-emptive transplant is more effective than transplant after dialysis, it would be useful for healthcare professionals to know at what stage in the treatment pathway people should be transplant listed in order to insure they eventually experience the most clinical and cost effective treatment.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Children, young people and adults with CKD stage 3 to 5, in whom transplantation within 1 year has been deemed appropriate Intervention/comparison: 1. Transplant listing 2 years before likely requirement for RRT 2. Transplant listing 1 year before likely requirement for RRT 3. Transplant listing 6 months before likely requirement for RRT Timing potentially dictated by eGFR, risk score or other validated measure Outcomes: Patient, family/carer health-related QoL, mortality, psychological distress and mental wellbeing, symptom scores and functional measures, hospitalisation, time to failure of RRT form, patient, family/carer experience of care, pre-emptive transplantation rates, proportion transplant listed who do not go on to require RRT
Importance to patients or the population	If a particular strategy could be identified that is most clinically and cost effective, it could increase the number of people able to receive pre-emptive transplants without incurring unnecessary treatment burden or wasting resource
Relevance to NICE guidance	There is current uncertainty about the optimal timing for transplant listing.
Relevance to the NHS	Research in this area will inform NICE recommendations for service delivery and provide information about optimal transplant listing timing.
Current evidence base	There is no evidence on the optimal timing of listing for transplantation. Sufficient information is needed to give evidence based information and to identify the best timing for transplant listing for those on RRT considering transplantation.
Equality	Not applicable
Study design	Due to feasibility concerns, most likely study design would be 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), potentially interrogating large existing registries and determining the impact of people being listed at various timepoints from transplantation/eGFRs
Feasibility	The difficulty in predicting need for RRT at the timepoints considered relevant to transplant listing may make this area very difficult to conduct RCTs in
Other comments	Not applicable
Importance	• Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future

updates.