A report for
Universitätsklinikum Schleswig-Holstein / Campus Kiel
on Shared Decision Making
for end-stage renal insufficiency

Kleijnen Systematic Reviews Ltd

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LIST OF ABBREVIATIONS

AE	Adverse event
APD	Automated peritoneal dialysis
CAPD	Continuous ambulatory peritoneal dialysis
CADTH	Canadian Agency for Drugs and Technologies in Health
CCPD	Continuous cycling peritoneal dialysis
CDSR	Cochrane Database of Systematic Reviews
CENTRAL	Cochrane Central Register of Controlled Trials
CI	Confidence interval
CM	Conservative management
CDSR	Cochrane Database of Systematic Reviews
CRD	Centre for Reviews and Dissemination
DARE	Database of Abstracts of Reviews of Effects
EQ-5D	European Quality of Life-5 Dimensions
FAQ	Frequently asked question
GIN	Guidelines International Network
HD	Haemodialysis
HDF	Haemodiafiltration
HRQoL	Health-related quality of life
HRs	Hazard ratios
HTA	Health Technology Assessment
KSR	Kleijnen Systematic Reviews Ltd
mths	Months
N/A	Not applicable
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NRS	Non-randomised study
PD	Peritoneal dialysis
PICO	Participants, intervention, comparators, outcomes and study design
QoL	Quality of life
RCT	Randomised controlled trial
RR	Risk ratio
RRT	Renal replacement therapy
SDM	Shared decision making
SPPB	Short Physical Performance Battery
TPx	Transplant
TTE	Time to event
UK	United Kingdom
USA	United States of America
VAS	Visual analogue scale
yrs	Years

PROJECT OBJECTIVE

One aim of the research project “Making SDM a reality” is to create interactive websites to inform patients as part of shared decision making (SDM).

For a range of topics, Kleijnen Systematic Reviews Ltd. (KSR) will prepare an evidence table of treatment options and an evidence report with a synthesis of the literature underpinning the evidence table.

The topic of this evidence report is end-stage renal disease focusing on treatment options relating to dialysis and transplantation.

METHODS

INCLUSION CRITERIA

The research question underpinning the literature searches for this topic was developed in conjunction with clinical departments at Universitätsklinikum Schleswig-Holstein / Campus Kiel. The question was framed in terms of participants, intervention, comparators and outcomes (PICO), see Table 1.

As detailed below, literature searches were carried out using a stepwise approach to identify relevant studies according to study design. In the first step, searches aimed to identify relevant systematic reviews and guidelines. For this project, no further searches were conducted as relevant results were extracted from the identified literature.

Table 1: Inclusion criteria for searches

PICO	
Patients	Patients with terminal [end-stage] renal insufficiency [kidney disease]
Interventions	• Haemodialysis (HD and HDF combined) • Peritoneal dialysis (subgroups continuous ambulatory PD (CAPD) and automated or continuous cycling PD (APD/CCPD)) • Renal transplant • Conservative care (= palliative care)
Comparators	Comparisons between interventions
Outcomes	Primary: Survival, HrQoL, symptoms, treatment efforts (e.g. time in dialysis centre etc.), Impact on [activities of] daily living (e.g. nutrition), adverse events Secondary: FAQs following scoping searches and needs assessments
Study design	Systematic reviews and guidelines

APD = automated peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; CCPD = continuous cycling peritoneal dialysis; FAQ = frequently asked question; HD = haemodialysis; HDF = haemodiafiltration; HRQoL = health-related quality of life; PD = peritoneal dialysis

In consultation with the commissioner, questions frequently asked by patients in conjunction with outcomes identified in the literature were developed into an evidence table outline.

FREQUENTLY ASKED QUESTIONS

The following research questions were identified as frequently asked questions (FAQs):

- FAQ 1: What is it and how does the treatment work?
- FAQ 2: How long will the treatment be effective?
- FAQ 3: How will I feel?
- FAQ 4: What ist the effect on health-related quality of life?
- FAQ 5: What adverse events are linked to the treatment?
- FAQ 6: What is the impact on daily life?
- FAQ 7: What is the effect on overall survival?

LITERATURE SEARCHES

Literature searches were carried out using a stepwise approach to identify relevant studies according to study design:

1. Systematic reviews and guidelines
2. Randomised controlled trials
3. Observational studies
4. Supplementary searches

Only in the event of no relevant systematic reviews or guidelines being identified were further searches to be conducted to identify randomised controlled trials (RCTs; Step 2.), and if no RCTs were identified, only then would searches be undertaken to identify observational studies (Step 3.).

The search strategies were developed specifically for each database and the keywords adapted according to the configuration of each database. Searches were limited by date range for systematic reviews and guidelines to five years (2012-2018). Where appropriate, searches were limited to remove animal studies. Searches were not limited by language or publication status.

Handling of citations

Identified references from the bibliographic database searches were downloaded into EndNote bibliographic management software for further assessment and handling. Individual records within the EndNote libraries were tagged with searching information, such as searcher, date searched, database host, database searched, strategy name and iteration, theme or search question. This enabled the information specialist to track the origin of each individual database record, and its progress through the screening and review process.

Quality assurance within the search process

For all searches undertaken by the KSR Information team, the main Embase strategy was independently peer reviewed by a second KSR Information Specialist. Strategy peer review was informed by items based on the Canadian Agency for Drugs and Technologies in Health (CADTH) checklist.[1]

SEARCH SOURCES

1. Systematic reviews and guidelines

The following systematic review specific databases were searched from 2012 to present:

- KSR Evidence (Internet): 2015 - 2018/02/23 (https://ksrevidence.com/)
- Cochrane Database of Systematic Reviews (CDSR) (Wiley): up to 2018/02/Iss2
- Database of Abstracts of Reviews of Effects (DARE) (Wiley): up to 2015/04/Iss2
- Health Technology Assessment (HTA) database (Wiley): up to 2016/4/Iss4

The following guidelines resources were searched from 2012 to present:

- Guidelines International Network (GIN) (Internet): up to 22.2.18 (http://www.g-i-n.net/library/international-guidelines-library)
- NHS Evidence (Internet): up to 22.2.18 (www.evidence.nhs.uk/)

Full details of all search strategies are presented in Appendix 1.

2. RCTs

As the search for secondary sources was sufficient, no additional searches for primary studies were undertaken.

3. Observational studies

As the search for secondary sources was sufficient, no additional searches for observational studies were undertaken.

4. Supplementary searches

In addition to the formal searches documented above, reviewers conducted supplementary hand searches to identify potentially relevant references, e.g. guidance specific to Germany and websites of patient organisations. The bibliographies of included studies and review articles were also checked for additional relevant articles.

METHODS OF STUDY SELECTION, QUALITY ASSESSMENT AND DATA EXTRACTION

Two reviewers independently inspected the title and abstract of each reference identified by the search and determined the potential relevance of each article. For potentially relevant articles, or in cases of disagreement, the full article was obtained, independently inspected, and inclusion criteria applied. Any disagreements were resolved through discussion.

Data extraction

An evidence hierarchy was used to select the most appropriate study(ies) to populate the evidence table. Where more than one study could provide evidence for the table the most relevant studies were extracted using the following criteria: recency (most recent preferred), quality (highest quality preferred), representativeness (populations representative of the general target population preferred). Where there were gaps in the evidence table (no systematic review or guideline available), as described before, relevant RCTs would have been searched for and extracted, and where no RCTs would have been identified, observational studies would have been used.

For each study, data were extracted by one reviewer and checked by another. Any disagreements were resolved by consensus.

In cases where multiple results were reported for the same outcome in a group of participants, data presenting time to effect (TTE) results were prioritized over non-TTE results as TTE data gives a more precise result than non-TTE.

RESULTS

LITERATURE SEARCHES AND INCLUSION ASSSESSMENT

For this evidence report, systematic searches for systematic reviews and guidelines were supplemented by hand searches.

Systematic searches were conducted on 22 February 2018 to identify relevant questions (frequently asked questions; FAQs) and to answer the clinical questions focusing on systematic reviews, meta-analyses and evidence-based guidelines. A total of 2,883 references were retrieved from literature searches. After de-duplication, 2,540 titles and abstracts were screened by two reviewers. Full papers were obtained for seven citations. After further review, a total of six were excluded: one reference was considered to have been superseded by other resources and five references had no usable data.

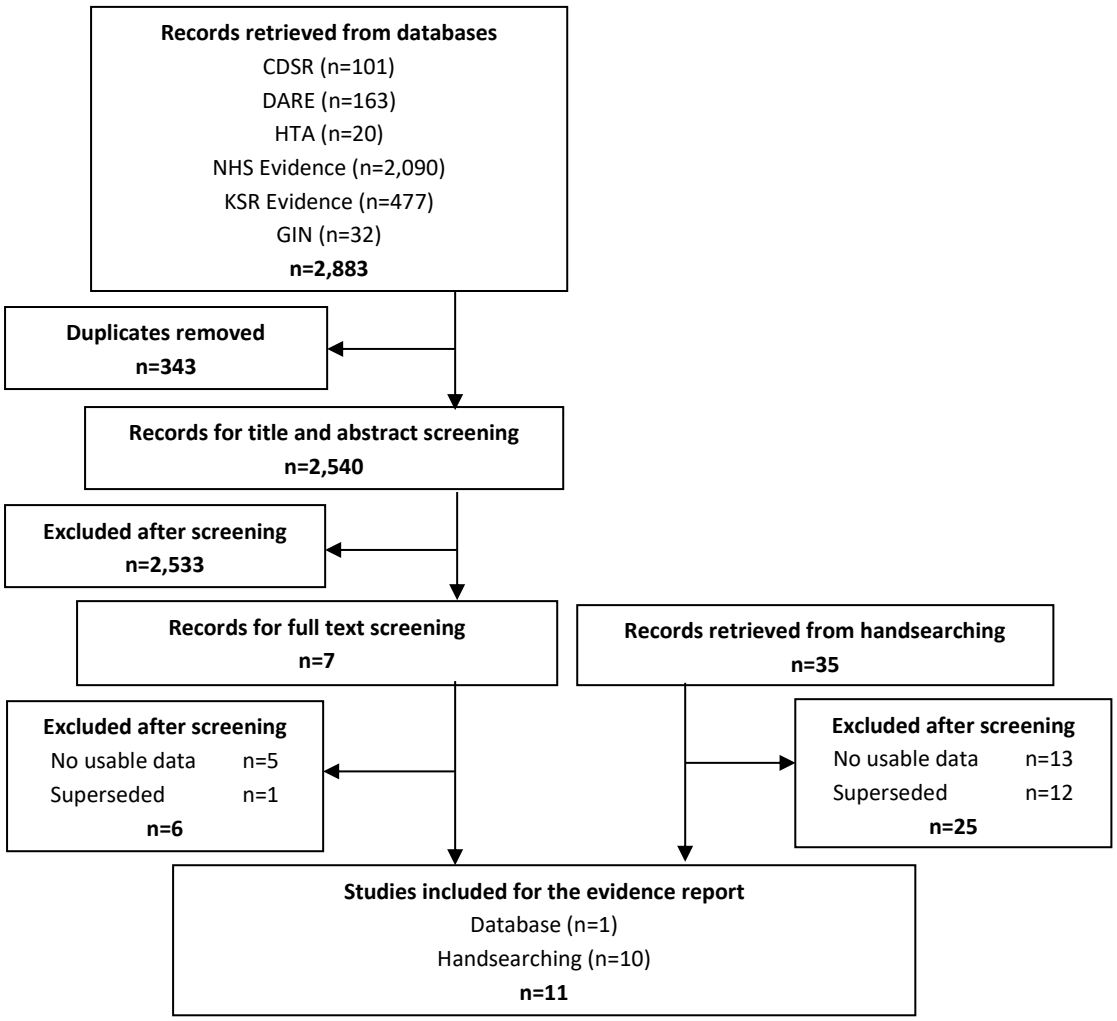
To answer the more descriptive FAQs, handsearching, concentrating on additional guidelines (in particular trying to find relevant German guidelines) and on patient organisations which identified patient-driven arguments and prioritisations, was performed. An additional 34 publications and sites were identified, of which eight were used as reference material (the rest either not containing relevant information, being less precise or being superseded by newer resources). The handsearches also picked up a new guideline which had not been published at the date of the systematic searches.

Therefore, the most updated evidence identified is coming from the NICE renal replacement and conservative management guideline to be published in September 2018. A draft of evidence report B on modalities of renal replacement therapy (RRT) was published in April 2018.[2] Guidelines of the National Institute for Health and Care Excellence are evidence based guidelines based on systematic and comprehensive literature searches of relevant databases, in this case Medline and Embase. The various outcomes are assessed using the GRADE tool, and calculations and presentations managed with Review Manager.

Depending on the FAQ, we are presenting relevant sub-sets of the evidence from NICE 2018[2] alongside additional evidence, where relevant. The numbers from the various outcomes are checked for availability of absolute numbers, which are presented whenever available. This is further amended with information from health and patient organisations.

A summary of the study selection process according to modified PRISMA reporting guidelines is reported in Figure 1.

Figure 1: Study selection process



OVERVIEW OF THE EVIDENCE

The information identified to answer the patient questions is given below organised by question and the underpinning evidence in Table 2.

Table 2: Studies populating the evidence table

Study ID	What is it and how does the treatment work?	How long will this treatment be efficient?	How will I feel?	Health related quality of life	Adverse events	Impact on daily life	Overall survival
Abbott 2004[3 a]							x
Amaral 2016[4 a]		x					
Balasubramanian 2011[5 a]		x		x			

Study ID	What is it and how does the treatment work?	How long will this treatment be efficient?	How will I feel?	Health related quality of life	Adverse events	Impact on daily life	Overall survival
Beduschi 2015[6] [a]		x					x
Bekker 2017[7]	x		x			x	x
Bro 1999[8] [a]					x		
Chandna 2011[9] [a]							x
Chertow 2010[10] [a]				x	x	x	x
de Fijter 1994[11] [a]					x	x	x
Elwyn 2015[12]		x					
Grams 2013[13] [a]		x					x
Healthwise 2017a[14]	x		x				
Healthwise 2017b[15]						x	
Healthwise 2017c[16]			x				
Jaar 2005[17] [a]							x
Jain 2009[18] [a]							x
Johnson 2009[19] [a]					x		
Katopodis 2009[20] [a]							x
Kidney Health Australia[21]	x		x			x	
Korevaar 2003[22] [a]				x			x
Manns 2009[23] [a]				x	x	x	x
McDonald 2009[24] [a]							x
Mehrotra 2011[25] [a]							x
Merion 2005[26] [a]							x
Milton 2008[27] [a]		x					
Murtagh 2007[28] [a]							x
NHS Choices 2015a[29]			x				
NHS Choices 2015b[30]						x	
NHS Direct 2016a[31]	x						
NHS Direct 2016b[32]		x					
Purnell 2013[33] [b]						x	
Rocco 2011[34] [a]				x	x	x	x
Snyder 2002[35] [a]		x					x
Termorshuizen 2003[36] [a]							x
Vonesh 2004[37] [a]							x
Weinhandl 2010[38] [a]							x
Winkelmayer 2002[39] [a]							x
Yeates 2012[40] [a]						x	x

a) This study had been extracted from NICE 2018 [2]. Further details are presented in Table 11
b) This study was identified through clinical review of this report.
NHS = National Health Service; NICE = National Institute for Health and Care Excellence

FAQ 1: What is it and how does the treatment work?

Table 3 presents details on the five treatments and how these work.

Table 3: What is it and how does the treatment work?

Haemodialysis (HD)
Blood is taken usually from your arm and into an external machine that filters it, before it is passed back into the arm along another tube.
NHS Direct 2016a[31]; Bekker 2017[7]
Automated or Continuous Cycling Peritoneal Dialysis (APD/CCPD)
The inside lining of your abdomen (the peritoneum) is used as the filter, rather than a machine. The used fluid is drained into a bag and replaced with fresh fluid. You have a machine at home which does the dialysis automatically, overnight while you sleep.
NHS Direct 2016a[31]; Bekker 2017[7]
Continuous Ambulatory Peritoneal Dialysis (CAPD)
The inside lining of your abdomen (the peritoneum) is used as the filter, rather than a machine. The used fluid is drained into a bag a few hours later and replaced with fresh fluid. You do your own dialysis and can walk and move around with the dialysis solution in your abdomen.
NHS Direct 2016a[31]; Bekker 2017[7]
Transplant (TPx)
You have surgery to receive a new kidney from someone living, or from someone who has just died. You will need to take immunosuppressant drugs for as long as you have your kidney - usually for the rest of your life.
NHS Direct 2016a[31]; Kidney Health Australia[21]
Conservative management (CM)
The aim of conservative care is to make you comfortable and relieve your symptoms, not to extend your life. The treatment does not filter extra fluid and waste products out of your blood.
Healthwise 2017a[14]
APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; CM = conservative management; HD = haemodialysis; NHS = National Health Service; TPx = transplant

FAQ 2: How long will the treatment be effective?

PD can be effective for at least a few years, HD for up to 20 years. If TPx is successful, it can be effective for many years. About 90% of TPx still function after five years, and on average, the transplanted kidney in 50-60% of people receiving a TPx will still be working at 15 years after TPx. How long CM is effective depends on the progression of your renal disease and very much on what other illnesses you may have.[7, 12, 32]

The clinical evidence for the decision matrix is presented in Table 4.

Table 4: Modality failure

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Descript.		Baseline	Risk difference (95% CI)
Evidence from non-randomised studies									
CAPD vs. APD/CCPD									
NICE 2018[2]	2[a]	2-5 years	VERY LOW due to risk of bias and imprecision	CAPD 1623	APD/CCPD 1639	Adults aged >18 to 70	TTE HR 1.03 (0.65 to 1.62)	No baseline data available	
Living donor TPx vs. deceased donor									
Snyder 2002[b]	1	5 years	VERY LOW due to risk of bias, indirectness and imprecision	Living donor TPx vs. Deceased donor n(total)=22776		Adults aged >18 to 70	Graft failure RR 0.88 (0.79 to 0.98)	No baseline data available	
Pre-emptive TPx vs. post-dialysis TPx									
NICE 2018[2]	2[c]	3 years	VERY LOW due to risk of bias and imprecision	Pre-emptive TPx n=11570	Post-dialysis TPx n=16453	Adults aged >18 to 70	Graft failure TTE HR 0.8 (0.75 to 0.85)	No baseline data available	
Amaral 2016[b]	1	5 years	VERY LOW due to	Pre-emptive TPx	Post-dialysis TPx n=5859	Children and young	Graft failure TTE HR 0.76 (0.64 to	No baseline data available	

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Descript.		Baseline	Risk difference (95% CI)
			imprecision	n=1668		people aged 2 to 18	0.9)		
Grams 2013[b]	1	Average 3 years	VERY LOW due to risk of bias and imprecision	Pre-emptive TPx n=10992	Post-dialysis TPx n=14428	Adults >70	Graft failure TTE HR 0.89 (0.74 to 1.07)	No baseline data available	

a) Balasubramanian 2011[5]; Beduschi 2015[6]; b) Information from NICE 2018[2]; c) Grams 2013[13]; Milton 2008[27]
APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; CI = confidence interval; HD = haemodialysis; HR = hazard ratio; PD = peritoneal dialysis; RCT = randomised controlled trial; RR = risk ratio; TPx = transplant; TTE = time to event

FAQ 3: How will I feel?

Table 5 presents the clinical evidence for the decision matrix on the question "How will I feel?"

Table 5: How will I feel?

	Haemodialysis (HD)	Automated or Continuous Cycling Peritoneal Dialysis (APD/CCPD)	Continuous Ambulatory Peritoneal Dialysis (CAPD)	Transplant (TPx)	Conservative management (CM)
How will I feel?	You will feel better than before you started dialysis, but side effects do include tiredness, itchy skin and muscle cramps. You may also have a sudden drop in blood pressure during haemodialysis, which can make you feel dizzy. You may get infections and blood clots in the vascular access points.	You will feel better than before you started dialysis, but side effects do include fatigue and you may put on some weight. You have more risk of a hernia. An infection of the peritoneum, called peritonitis, is more common for people having peritoneal dialysis.	You will feel better than before you started dialysis, but side effects do include fatigue and you may put on some weight. You have more risk of a hernia. An infection of the peritoneum, called peritonitis, is more common for people having peritoneal dialysis.	Your symptoms should get much better or go away completely after receiving a kidney transplant.	Weakness and tiredness are most common symptoms. A poor appetite, itching, and shortness of breath are also likely for many people on conservative care. However, it is not always easy to tell which are symptoms of kidney disease and which are caused by other illnesses.
Reference	Bekker 2017[7]; NHS Choices 2015a[29]	Bekker 2017[7]; NHS Choices 2015a[29]	Bekker 2017[7]; NHS Choices 2015a[29]	Bekker 2017[7]; Kidney Health Australia[21]	Bekker 2017[7]; Healthwise 2017a [14]; Healthwise 2017c[16]

APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; CM = conservative management; HD = haemodialysis; NHS = National Health Service; TPx = transplant

FAQ 4: What ist the effect on health-related quality of life?

The clinical evidence for the decision matrix is presented in Table 6. In addition to the evidence summarized in Table 6, one systematic review was identified comparing life participation activities among adults treated by haemodialysis, peritoneal dialysis, or kidney transplant (Purnell 2013[33]). This review suggests that individuals with a transplant are better able to take part in jactivities of daily living than individuals undergoing any other renal replacement therapy. Transplant patients seem to have better physical functioning, less limitations caused by the treatment modality itself and are more often able to go back to work.

Table 6: Health related quality of life

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Risk difference (95% CI)
				Submodalities		Description	
Evidence from RCTs							
EQ-5D VAS (0-100, higher is better)							
Korevaar 2003[22 a]	1	2.5 years	VERY LOW due to risk of bias and imprecision	PD n=20 mean 54.4 SD 21.9	HD n=18 mean 59.2 SD 11.8	Adults aged >18 to 70	Mean EQ-5D VAS in the PD groups was 4.8 lower than the HD group (15.84 lower to 6.24 higher)
SF-36 Mental Composite Score (0-100, high is good outcome)							
NICE 2018[2]	3[b]	1 year	VERY LOW due to risk of bias and indirectness	HD >3x a week n=164	HD 3x a week n=153	Adults aged >18 to 70	The mean QoL (mental) in the HD 3x a week was -0.25 change score, in the HD >3x a week group it was 3.52 higher (3.27 to 3.78 higher)
SF-36 Physical Composite Score (0-100, high is good outcome)							
NICE 2018[2]	3[b]	1 year	VERY LOW due to risk of bias and indirectness	HD >3x a week n=164	HD 3x a week n=153	Adults aged >18 to 70	The mean QoL (physical) in the HD 3x a week was 1.3 change score, in the HD >3x a week group it was 2.73 higher (2.52 to 2.95 higher)
EQ-5D (0-1.0, high is good outcome)							
Manns 2009[23 a]	1	6 months	VERY LOW due to risk of bias,	HD >3x a week n=27	HD 3x a week n=25	Adults aged >18 to 70	Mean difference 0.12 (0.00 to 0.24 higher)

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Risk difference (95% CI)
				Submodalities		Description	
			indirectness and imprecision				
Symptom/function (SPPB, 0-12, high is good outcome)							
NICE 2018[2]	2[c]	1 year	VERY LOW due to risk of bias, indirectness and imprecision	HD >3x a week n=130	HD 3x a week n=118	Adults aged >18 to 70	Mean difference 0.14 (0.09 to 0.20 higher)
Evidence from non-randomised studies							
SF-36 Mental Composite Score (0-100, high is good outcome)							
Balasubramanian 2011[5 a]	1	1 year	VERY LOW due to risk of bias and imprecision	CAPD n=178	APD/CCPD n=194	Adults aged >18 to 70	The mean QoI in the CAPD group was 1.5 lower than the APD/CCPD group (8.16 lower to 5.16 higher)
SF-36 Physical Composite Score (0-100, high is good outcome)							
Balasubramanian 2011[5 a]	1	1 year	VERY LOW due to risk of bias and imprecision	CAPD n=178	APD/CCPD n=194	Adults aged >18 to 70	The mean QoL in the CAPD group was 2.2 lower than the APD/CCPD group (8.16 lower to 3.76 higher)

a) Information from NICE 2018[2]; b) Chertow 2010[10]; Manns 2009[23]; Rocco 2011[34]; c) Chertow 2010[10]; Rocco 2011[34]
APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; EQ-5D = European Quality of Life-5 Dimensions; HD = haemodialysis; HR = hazard ratio; PD = peritoneal dialysis; RCT = randomised controlled trial; RR = risk ratio; SPPB = Short Physical Performance Battery; TTE = time to event; VAS = visual analogue scale

FAQ 5: What adverse events are linked to the treatment?

The clinical evidence for the decision matrix is presented in Table 7.

Table 7: Adverse Events

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
Evidence from RCTs									
Physical discomfort									
Bro 1999[8] [a]	1	6 months	VERY LOW due to risk of bias and imprecision	CAPD n=13 mean 2.2 SD 1.3	APD/CCPD n=12 mean 1.9 SD 1	Adults aged >18 to 70	Mean difference 0.30 (-0.61 to 1.21) [Symptom scores (physical discomfort 1-5, high is poor)]	The mean symptom scores at 6 months in the APD/CCPD group was 1.9	The mean symptom scores at 6 months in the CAPD group was 0.3 higher (0.61 lower to 1.21 higher)
Procedure required									
NICE 2018[2]	3[c]	1 year	VERY LOW due to risk of bias, indirectness and imprecision	HD >3x a week n=196 AEs=73	HD 3x a week n=187 AEs=49	Adults aged >18 to 70	Vascular access procedure required RR 1.42 (1.05 to 1.91)	With HD 3x a week: 299 per 1000	With HD >3x a week: 126 more per 1000 (from 15 more to 272 more)
Infection									
Bro 1999[8] [a]	1	6 months	VERY LOW due to risk of bias and imprecision	CAPD n=13 AEs=1	APD/CCPD n=12 AEs=1	Adults aged >18 to 70	Exit site infection RR 0.92 (0.06 to 13.18)	With APD/CCPD: 83 per 1000	With CAPD: 7 fewer per 1000 (from 78 fewer to 1000 more)
NICE 2018[2]	2[b]	0.5-1.5 years	LOW due to risk of bias and imprecision	CAPD n=51 AEs=8	APD/CCPD n=53 AEs=3	Adults aged >18 to 70	Peritonitis RR 2.61 (0.73 to 9.27)	With APD/CCPD: 66 per 1000	With CAPD: 106 more per 1000 (from 18 fewer to 546 more)
Manns 2009[23]	1	6 months	VERY LOW due to risk of	HD >3x a week n=26	HD 3x a week n=26	Adults aged >18 to 70	Bacteraemia RR 1.00 (0.28 to	With HD 3x a week: 160 per	With HD >3x a week: 0 more per

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
			bias, indirectness and imprecision	AEs=4	AEs=4		3.58)	1000	1000 (from 115 fewer to 413 more)
Evidence from non-randomised studies									
Infection									
Johnson 2009[19 a]	1	1 year	VERY LOW due to risk of bias and imprecision	PD n=6020	HD n=15916	Adults aged >18 to 70	Deaths from infection HR 0.93 (0.66 to 1.32)	No baseline data available	

a) Information from NICE 2018[2]; b) Bro 1999[8]; de Fijter 1994[11]; c) Chertow 2010[10]; Manns 2009[23]; Rocco 2011[34]
AEs = adverse events; APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; HD = haemodialysis; HR = hazard ratio; PD = peritoneal dialysis; RCT = randomised controlled trial; RR = risk ratio; TTE = time to event

FAQ 6: What is the impact on daily life?

Please see the descriptive text in Table 8 and the clinical evidence for hospitalisation in Table 9.

Table 8: Impact on daily life

Haemodialysis (HD)
You will need to make time for dialysis appointments three times per week for a minimum of four hours. You do not usually need treatment between sessions, so you should have time for days out, short holidays, and other activities. For longer holidays your treatment will need to be planned at a dialysis unit at your destination. You may need to restrict the amount of salt, potassium, and phosphate in your diet. You will also need to restrict the amount of fluid you drink.
Bekker 2017[7]; Healthwise 2017b[15]; Kidney Health Australia[21]
Automated or Continuous Cycling Peritoneal Dialysis (APD/CCPD)
You will have your dialysis every night (one session 6-10 hours daily) while you are attached to a machine. This means you don't need to schedule your work and other daytime activities around your dialysis. You can go on day trips, but it can be difficult to travel for longer, as you need to be attached to your dialysis machine at night. The equipment can however be transported by car. You may need to restrict the amount of salt and phosphate in your diet. You may also need to restrict the amount of fluid you drink but probably not as much as if you were having haemodialysis.
Bekker 2017[7]; Healthwise 2017b[15]; Kidney Health Australia[21]
Continuous Ambulatory Peritoneal Dialysis (CAPD)
You will need to fit your daily activities around your dialysis - four bag changes daily, each approx 30 minutes, no days off. If you work, your health care team can give advice on how to do dialysis exchanges in your workplace. You may be able to travel. You can take dialysis fluid and bags with you or have them delivered to your travel destination. You may need to restrict the amount of salt and phosphate in your diet. You may also need to restrict the amount of fluid you drink but probably not as much as if you were having haemodialysis.
Bekker 2017[7]; Healthwise 2017b[15]; Kidney Health Australia[21]
Transplant (TPx)
You should be able to return to your normal activities and work within 3–6 months after transplant. You can then also travel provided you bring supplies of your immunosuppressant drugs. The immunosuppressant drugs can increase appetite, but usually there are no other diet and fluid restrictions after a kidney transplant. However, some people do need to modify what they eat, because of other health problems (such as high blood pressure and high cholesterol).
Bekker 2017[7]; Healthwise 2017b[15]; Kidney Health Australia[21]; NHS Choices 2015b[30]
Conservative management (CM)
The conservative management does not in itself restrict what you can do, but your general health and symptoms may restrict what you can do. Many people say they have trouble getting around. You are likely to spend less time in hospital than if you were having dialysis. You may not need to go to hospital at all for treatment. This depends on your other illnesses and your symptoms. You can travel if your health allows you to. You may not need a restricted diet with conservative management, but this will depend on your symptoms. You only need to restrict your fluid and salt if you are getting

symptoms like puffiness from excess fluid.
Bekker 2017[7]; Healthwise 2017b[15]; Kidney Health Australia[21]
APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; CM = conservative management; HD = haemodialysis; NHS = National Health Service; TPx = transplant

Table 9: Hospitalisation

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
Evidence from RCTs									
de Fijter 1994[11]	1	1.5 years	VERY LOW due to risk of bias and imprecision	CAPD n=41	APD/CCPD n=41	Adults aged >18 to 70	Rate ratio 1.67 (1.11 to 2.52)	Risk with APD/CCPD: 488 admissions per 1000	with CAPD: 327 more per 1000 (from 54 more to 742 more)
NICE 2018[2]	3[b]	1 year	VERY LOW due to risk of bias, inconsistency, indirectness and imprecision	HD >3x a week n=195	HD 3x a week n=188	Adults aged >18 to 70	Rate Ratio 0.96 (0.78 to 1.20)	Risk with HD 3x a week: 950 admissions per 1000	With HD >3x a week: 38 fewer per 1000 (from 209 fewer to 190 more)
Evidence from non-randomised studies									
Yeates 2012[40 a]	1	2.1 years	LOW due to risk of bias	PD n=910	HD n=910	Adults aged >18 to 70	Rate Ratio 0.99 (0.94 to 1.05)	No baseline data available	

a) Information from NICE 2018[2]; b) Chertow 2010[10]; Manns 2009[23]; Rocco 2011[34]

APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; HD = haemodialysis; HR = hazard ratio; PD = peritoneal dialysis; RCT = randomised controlled trial; RR = risk ratio; TTE = time to event

FAQ 7: What is the effect on overall survival?

Your life expectancy is lower than that of people without your condition, but once on dialysis (HD or PD) it will be higher though affected by the same factors as other people not on dialysis. Cause of death for people on dialysis is usually not the kidney disease, but another illness they may have such as cardiovascular disease, diabetes or infection.[7]

There is not yet any evidence showing firm favourable survival with one mode of dialysis over another. However studies have shown better survival with TPx over dialysis and over CM. This however is not necessarily so for elderly for whom the evidence is less certain. It seems there may be better survival with dialysis over CM, however, another study showed that dialysis and TPx taken together gave no better or worse survival than CM (see Table 10).

Table 10: Mortality

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
Evidence from RCTs									
CAPD vs. APD/CCPD									
de Fijter 1994[11 a]	1	1.5 years	VERY LOW due to risk of bias and imprecision	CAPD events=2 n=41 (4.9%)	APD/CCPD events=4 n=41 (9.8%)	Adults aged >18 to 70	RR 0.5 (0.1 to 2.58)	Risk with APD/CCPD: 98 per 1000	With CAPD: 49 fewer per 1000 (from 88 fewer to 155 more)
HD >3x a week vs. HD 3x a week									
NICE 2018[2]	4[b]	3 years	VERY LOW due to risk of bias, inconsistency, indirectness and imprecision	HD >3x a week n=201 events=35	HD 3x a week n=193 events=39	Adults aged >18 to 70	Peto Odds ratio 0.83 (0.49 to 1.38)	Risk with HD 3x a week: 119 per 1000	With HD >3x a week: 30 fewer per 1000 (from 100 fewer to 50 more)
PD vs. HD									
Korevaar	1	2.5	VERY LOW	PD	HD	Adults aged	TTE	Risk with HD:	With PD: 232

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
2003[22 a]		years	due to risk of bias and imprecision	n=20	n=18	>18 to 70	HR 0.45 (0.02 to 10.13)	500 per 1000	fewer per 1000 (from 486 fewer to 499 more)
Evidence from non-randomised studies									
CAPD vs. APD/CCPD									
Beduschi 2015[6 a]	1	5 years	VERY LOW due to risk of bias and imprecision	CAPD n=1445	APD/CCPD n=1445	Adults aged >18 to 70	TTE HR 1.44 (1.21 to 1.71)	No baseline data available	
TPx vs. dialysis									
NICE 2018[2]	2[c]	3-4 years	MODERATE due to large effect	TPx n=41209	Dialysis n=109725	Adults aged >18 to 70	RR 0.28 (0.27 to 0.29)*	No baseline data available	
Abbott 2004[3 a]	1	3 years	LOW due to study design	TPx n=16495	Dialysis n=17044	Adults aged >18 to 70	TTE HR 0.47 (0.44 to 0.50)*	No baseline data available	
Abbott 2004[3 a]	1	3 years	LOW due to study design	TPx n=1443	Dialysis n=3720	Adults >70	HR 0.59 (0.51 to 0.68)	No baseline data available	
Merion 2005[26 a]	1	2.5 years	LOW due to risk of bias and indirectness	TPx n=1719	Dialysis n=5172	Adults aged >18 to 70 with BMI ≥ 30 kg/m^2	TTE HR 0.39 (0.33 to 0.46)	No baseline data available	
PD vs. HD									
NICE 2018[2]	4[d]	Average 2.5 years	VERY LOW due to risk of bias, inconsistency and imprecision	PD n=17702	HD n=23803	Adults aged >18 to 70	HR 1.21 (0.94 to 1.56)	No baseline data available	

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
Jaar 2005[17 a]	1	2.5 years	VERY LOW due to risk of bias and imprecision	PD n=274	HD n=767	Adults >70	TTE HR 1.66 (0.93 to 2.96)	No baseline data available	
Jaar 2005[17 a]	1	Average 2.5 years	VERY LOW due to risk of bias and imprecision	PD n=860	HD n=502	Adults aged >18 to 70 with residual urine output	HR 1.15 (0.80 to 1.65)	No baseline data available	
NICE 2018[2]	2[e]	Average 2.5 years	VERY LOW due to risk of bias, inconsistency and imprecision	PD n=46714	HD n=353448	Adults aged >18 to 70 with diabetes mellitus	RR 0.47 (0.08 to 2.86)*	No baseline data available	
NICE 2018[2]	2[e]	Average 2.5 years	VERY LOW due to risk of bias and imprecision	PD n=46714	HD n=353448	Adults aged >18 to 70 without diabetes mellitus	RR 0.99 (0.9 to 1.09)*	No baseline data available	
NICE 2018[2]	3[f]	2.5 years	VERY LOW due to risk of bias and imprecision	PD n=34461	HD n=266380	Adults aged >18 to 70 with diabetes mellitus	TTE HR 1.12 (1.06 to 1.19)*	No baseline data available	
NICE 2018[2]	3[f]	2.5 years	VERY LOW due to risk of bias,	PD n=34461	HD n=266380	Adults aged >18 to 70 without	TTE HR 1.04 (0.83 to 1.32)*	No baseline data available	

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
			inconsistency and imprecision			diabetes mellitus			
NICE 2018[2]	2[e]	Average 2.5 years	VERY LOW due to risk of bias and imprecision	PD n=46714	HD n=353448	Adults >70 with diabetes mellitus	RR 1.12 (0.75 to 1.66)*	No baseline data available	
NICE 2018[2]	2[e]	Average 2.5 years	VERY LOW due to risk of bias and imprecision	PD n=46714	HD n=353448	Adults >70 without diabetes mellitus	RR 1.22 (1.14 to 1.3)*	No baseline data available	
NICE 2018[2]	2[g]	Average 2.5 years	VERY LOW due to risk of bias and imprecision	PD n=34187	HD n=265613	Adults >70 with diabetes mellitus	TTE HR 1.20 (1.13 to 1.26)*	No baseline data available	
NICE 2018[2]	2[g]	Average 2.5 years	VERY LOW due to risk of bias	PD n=34187	HD n=265613	Adults >70 without diabetes mellitus	TTE HR 1.06 (1.01 to 1.11)*	No baseline data available	
Pre-emptive TPx vs. post-dialysis TPx									
Grams 2013[13 a]	1	3 years	VERY LOW due to risk of bias	Pre-emptive TPx n=10992	Post-dialysis TPx n=14428	Adults aged >18 to 70	TTE HR 0.97 (0.91 to 1.03)	No baseline data available	
Grams 2013[13 a]	1	Average 3 years	VERY LOW due to risk of bias and imprecision	Pre-emptive TPx n=10992	Post-dialysis TPx n=14428	Adults >70	HR 0.84 (0.74 to 0.95)	No baseline data available	

Study IDs	No of studies	Follow-up	GRADE Quality	No of patients			Relative effect (95% CI)	Anticipated absolute effects	
				Submodalities		Description		Baseline	Risk difference (95% CI)
Living donor TPx vs. deceased donor									
Snyder 2002[35 a]	1	5 years	VERY LOW due to risk of bias and indirectness	Living donor TPx vs. Deceased donor n(total)=22776		Adults aged >18 to 70	RR 0.71 (0.60 to 0.84)	No baseline data available	
Dialysis/TPx vs. CM									
Chandna 2011[9 a]	1	0-18 years	VERY LOW due to risk of bias, imprecision	Dialysis/TPx n=106	CM n=77	Adults >70	HR 0.85 (0.57 to 1.27)	No baseline data available	
Dialysis vs. CM									
Murtagh 2007[28 a]	1	2 years	VERY LOW due to risk of bias	Dialysis n=52	CM n=77	Adults >70	HR 2.94 (1.56 to 5.53)	No baseline data available	

a) Information from NICE 2018[2]; b) Chertow 2010[10]; Katopodis 2009[20]; Manns 2009[23]; Rocco 2011[34]; c) Jain 2009[18]; Merion 2005[26]; d) Jaar 2005[17]; McDonald 2009[24], Weinhandl 2010[38]; Winkelmayer 2002[39]; e) Termorshuizen 2003[36]; Vonesh 2004[37]; f) Jaar 2005[17]; Mehrotra 2011[25]; Yeates 2012[40]; g) Mehrotra 2011[25]; Yeates 2012[40]
APD/CCPD = automated/continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; CM = conservative management; HD = haemodialysis; HR = hazard ratio; PD = peritoneal dialysis; RCT = randomised controlled trial; RR = risk ratio; TTE = time to event
* In cases where multiple results were reported of for the same outcome for the same group of patient having more than one resultin a group of participants, data presenting time to effect (TTE) results were prioritized over non-TTE results (e.g. TTE HR results prioritized over HR results). This was a summary decision, as TTE data gives a more precise result than non-TTE.

ASSESSMENT OF THE CLINICAL REVIEW EVIDENCE

As detailed before, results from RCTs and non-randomised studies were extracted from NICE 2018[2]. Details of these 27 studies are presented in Table 11.

Table 11: Overview of studies populating the evidence table

Study ID	Participants	Interventions	Outcomes	Setting Country	Study Design	Follow-up duration
Abbott 2004[3]	Adults (general population) Adults aged 65 yrs and over	TPx from deceased donor (n = 16495) Dialysis (n = 17044)	Mortality	USA USRDS /CMS	NRS	Average 3 yrs
Amaral 2016[4]	Children and young people aged <18	Pre-emptive TPx (n=1668) Non-pre-emptive TPx (n=5859)	Time to failure RRT form	USA USRDS /CMS	NRS	Up to 5.2 yrs
Balasubramanian 2011[5]	Adults (general population)	APD/CCPD (n=194) CAPD (n=178)	Quality of life (SF36) Time to failure RRT form	UK, Study-specific	NRS	Average 2.2 yrs
Beduschi 2015[6]	Adults (general population)	APD/CCPD (n=1445) CAPD (n=1445)	Mortality Time to failure RRT form	Brazil, Study-specific	NRS	Up to 7 yrs
Bro 1999[8]	Adults (general population)	APD/CCPD (n=17) CAPD (n=17)	Symptom score Infection	Denmark	RCT	6 mths
Chandna 2011[9]	>75 yrs old adults	RRT (n=106) CM (n=77)	Mortality	UK	NRS	18 yrs
Chertow 2010[10]	Adults and young people age >12y (general population)	HD>3x a week in-centre (n=125) HD 3x a week in-centre (n=120)	Quality of life (SF36) Symptom score (SPPB) Mortality Hospitalisation	USA	RCT	Up to 3y

Study ID	Participants	Interventions	Outcomes	Setting Country	Study Design	Follow-up duration
			(count) Psychological wellbeing (BDI) Cognitive impairment Vascular access issues			
de Fijter 1994[11]	Adults (general population)	APD/CCPD (n=41) CAPD (n=41)	Mortality Hospitalisation (count) Infection	The Netherlands	RCT	Up to 2.5 yrs
Grams 2013[13]	Adults. Recipient age: under 65 yrs; 65 and older	Pre-emptive TPx (n=10992) TPx after up to a year of dialysis (n=14428)	Mortality Time to failure RRT form	USA OPTN	NRS	Up to 15 yrs
Jaar 2005[17]	Adults - under / over 65y - with / without diabetes - with residual renal function	HD (n=767) PD (n=274)	Mortality	USA, Study-specific	NRS	Average 2.4 yrs
Jain 2009[18]	Adults (general population)	TPx (n = 157) Dialysis (n = 598)	Mortality	UK, Study-specific	NRS	Average 4.5 yrs
Johnson 2009[19]	Adults (general population)	HD (n=15916) PD (n=6020)	Infection	Australia and New Zealand ANZDATA	NRS	Up to 10 yrs
Katopodis 2009[20]	Adults Without diabetes	HD >3x wk (n=8) HD 3x wk (n=8)	Mortality	Greece	RCT	1 year
Korevaar 2003[22]	Adults (general population)	HD (n=18) PD (n=20)	QoL (EQ VAS) Mortality	The Netherlands	RCT	Up to 5 yrs
Manns 2009[23]	Adults (general population)	HD >3 x wk, nocturnal home (n=27)	Quality of life (SF36, EQ5D) Symptom score	Canada	RCT	6 months

Study ID	Participants	Interventions	Outcomes	Setting Country	Study Design	Follow-up duration
		HD 3x wk in-centre or home (n=25)	(KDQ) Mortality Vascular access issues			
McDonald 2009[24]	All ages (general population)	HD (n=14,733) PD (n=10,554)	Mortality	Australia and New Zealand ANZDATA	NRS	Average 2.5 yrs
Mehrotra 2011[25]	Adults with at least one comorbidity -less/more than 65y old -with/ without diabetes	HD (n=233,082) PD (n=19,879)	Mortality	USA USRDS	NRS	Average 2.5 yrs
Merion 2005[26]	Adults (general population)	TPx (n = 41,042) Dialysis (n = 109127)	Mortality	USA USRDS/CMS	NRS	Average 3 yrs
Milton 2008[27]	Adults (general population)	Pre-emptive TPx (n=578) Non-pre-emptive TPx (n=2025)	Time to failure RRT form	Australia and New Zealand ANZDATA	NRS	Up to 10 yrs
Murtagh 2007[28]	>75 yrs old adults	RRT (n=52) CM (n=77)	Mortality	UK, Study-specific	NRS	2 yrs
Rocco 2011[34]	Adults (general population)	HD>3x week at home, nocturnal (n=45) HD 3x week at home (n=42)	Quality of life (SF36) Symptom score (SPPB) Mortality Hospitalisation (count) Vascular access issues	USA	RCT	Up to 3 yrs
Snyder 2002[35]	Adults (general	Living donor	Mortality	USA CMS	NRS	Up to 5 yrs

Study ID	Participants	Interventions	Outcomes	Setting Country	Study Design	Follow-up duration
	population)	Deceased donor Total n=252,402	Graft failure			
Termorshuizen 2003[36]	Adults -aged under/over 60y -with / without diabetes	HD (n=742) PD (n=480)	Mortality	The Netherlands NECOSAD	NRS	Up to 2 yrs
Vonesh 2004[37]	Adults aged over 45 with one or more comorbidity --aged up to / over 65 -with / without diabetes	HD (n=352,706) PD (n=46,234)	Mortality	USA CMS	NRS	3 yrs
Weinhandl 2010[38]	Adults (general population)	HD (n=6337) PD (n=6337)	Mortality	USA CMS	NRS	Average 2.3 yrs
Winkelmayer 2002[39]	Adults aged >65y	HD (n=1966) PD (n=537)	Mortality	USA Medicare / Medicaid in state of NJ	NRS	12 months
Yeates 2012[40]	Adults -aged 45-64 yrs / >65 yrs -with / without diabetes	HD (n=32,531) PD (n=14,308)	Mortality Hospitalisation (count, sub-set)	Canada CORR	NRS	Up to 5 yrs

CM = Conservative management; HD = Haemodialysis; mths = months; NRS = Non-randomised study; PD = Peritoneal dialysis; QoL = Quality of life; RCT = Randomised controlled trial; RRT = Renal replacement therapy; UK = United Kingdom; USA = United States of America; yrs = years

DISCUSSION

STRENGTHS, LIMITATIONS AND UNCERTAINTIES

This report builds on the most up to date information available in secondary publications, i.e. we are using a guideline searching primary studies in December 2017. However, it should be noted that new primary studies published between December 2017 and completion of this report (June 2018) might have been missed. No relevant and recent German guidelines were identified.

What is obvious from the report is that amount of absolute numbers available for answering the FAQs are limited. A source of potential confusion for patients might be the lack of a common baseline. All of the identified information is based on comparisons between two treatments. It is not considered ethical to compare renal replacement therapy (RRT) to placebo. The use of conservative management (CM) is limited, since the patients choosing CM are likely to be elderly and/or have multiple comorbidities. Thus the numbers in this report do not lend themselves to direct comparison between anything but the two treatments in question for a particular outcome. Comparing two different studies with different populations would mean potentially comparing two very different groups of people (e.g. in terms of age and comorbidities) as well as comparing two RRT's and thus not knowing if the resulting difference is due to the RRT mode or the difference in population groups.

This report also elucidates the lack of high quality evidence in this field. We have a few RCTs presenting limited number of patients, and a number of non-randomised studies where the outcomes are mostly assessed to be of low to very low quality in the GRADE tool. Thus a lot of the outcomes are presenting a lack of evidence for a difference between treatments rather than a shown difference. To illustrate: for outcome mortality, there seems fo be a tendency that peritoneal dialysis (PD) patients do better than haemodialysis (HD) patients, but the number of patients and events is so limited that the difference seen could be coincidental (as evidenced by the large confidence intervals).

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APPENDIX 1: SEARCH STRATEGIES

Database	Dates	Results
CDSR	2012 - Iss 2, Feb 2018	101
DARE	2012 - Iss 2, Apr 2015	163
HTA	2012 - Iss 4, Oct 2016	20
NHS Evidence	1.1.2012 – 22.2.2018	2090
KSR Evidence	2015 - 2018	477
GIN	Up to 22.2.2018	32
Total		**2883**
Total after de-duplication		**2540**

Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 2 of 12, February 2018
Database of Abstracts of Reviews of Effects (DARE) (Wiley): Issue 2 of 4, April 2015
Health Technology Assessment Database (HTA) (Wiley): Issue 4 of 4, October 2016
Searched: 22.2.18

#1 MeSH descriptor: [Kidney Failure, Chronic] explode all trees 3968
#2 ((Chronic or end-stage or end stage or "stage 5" or "stage five") near/2 (renal or kidney*) near/2 (failure* or disease* or disorder* or insufficien* or dysfunction)):ti,ab,kw 10368
#3 #1 or #2 Publication Year from 2012 to 20184768

CDSR = 101

DARE = 163

CENTRAL = 4433

HTA = 20

NHS EED = 51

NHS Evidence (www.evidence.nhs.uk): up to 2018/02/22
Searched: 22.2.18
Filtered by Guidance / Systematic reviews / Date 1.1.2012 – 22.2.2018

(Chronic OR end stage OR "end stage" OR "stage 5" OR "stage five") (renal OR kidney*) (failure* OR disease* OR disorder* OR insufficien* OR dysfunction)

2090 results

KSR Evidence: 2015 – 2018/02/22
Searched:23.2.18

Searched across any field

End stage renal or end stage kidney or stage 5 renal or stage 5 kidney or stage five renal or stage five kidney or chronic renal or chronic kidney

2015-2018 = 477 results

International Guideline Library (GIN) (www.g-i-n.net): up to 2018/02/22
Searched: 22.2.18

Chronic renal	12	11	imported (in development guidelines not imported)
Chronic kidney		31	28 imported (in development guidelines not imported)
End stage renal		1	1 imported
End stage kidney	0		
Stage 5 renal	0		
Stage 5 kidney	0		
Stage five renal		0	
Stage five kidney	0		
Total	44	40	
Duplicates removed		**32**	