National Institute for Health and Care Excellence

Final

RRT and conservative management

Modalities of RRT

NICE guideline NG107

Evidence review

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Final

This evidence review was developed by the National Guideline Centre

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1RRT modalities

1.1 Review questions:

1.1.1 What is the clinical and cost effectiveness of different modalities of renal replacement therapies and conservative management for people who have progressed to later stages of CKD?

1.1.2 Are there factors which suggest that certain forms of renal replacement therapy may be more appropriate for certain groups of people?

1.1.3 Are there groups of people in which conservative management is more appropriate than RRT?

1.2 Introduction

When people approach or have progressed to later stages CKD they need to decide whether to undergo renal replacement therapy or to choose conservative management. Renal replacement therapy is a term used to encompass life-supporting treatments for severe acute kidney injury or for people who have progressed to later stages of chronic kidney disease. It includes the following modalities: haemodialysis, haemodiafiltration, peritoneal dialysis and renal transplantation. Haemodialysis can be delivered at home, in a satellite unit or in hospital. Peritoneal dialysis can be continuous ambulatory (e.g. four sessions x 40 minutes daily) or automated (e.g. one session x 9 hrs daily). Transplantation may be pre-emptive (before dialysis) or not and may be from a living or deceased donor

Conservative management is the full supportive management (including the control of symptoms and complications and advance care planning) for those in the later stages of CKD who, in conjunction with carers and the clinical team, decide against renal replacement therapy. Conservative management will generally (although not always) be less appropriate for younger, healthier people. Conservative management is rarely an option for children

There is considerable variation in the proportion of people receiving each modality. Data from the UK renal registry show that there were 61,256 adult patients receiving renal replacement therapy (RRT) in the UK on 31st December 2015. Transplantation was the most common treatment modality (53.1%) followed closely by centre-based HD (39.0%) in either hospital centre (17.8%) or satellite unit (21.2%). The proportion on continuous ambulatory peritoneal dialysis (CAPD) and automated PD (APD) was 2.5% and 3.4% respectively. There were 941 children and young people aged 18 years who have progressed to later stages of CKD. 75.3% of paediatric patients aged 16 years and under had a functioning kidney transplant, 13.0% were receiving HD and 11.7% were receiving PD. There is variation across the country with respect to the proportion of people using each modality.

When considering the option of haemodialysis or haemodiafiltration, the optimum frequency needs to be considered. For example, in-centre haemodialysis or haemodiafiltration is typically delivered three times a week but home treatment may be more frequent.

It is also important to consider that certain factors (e.g. age, ethnicity, diabetes) may influence people's response to renal replacement therapy modalities or conservative management.

The purpose of these questions is to explore the clinical and cost effectiveness of renal replacement therapy, including different frequencies of dialysis and conservative

management. Secondly, it will aim to identify the clinical and cost effectiveness of renal replacement therapy or conservative management in specific groups of people.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People with CKD requiring RRT
Interventions	Transplant – including pre-emptive, post-dialysis, live donor, deceased donor Peritoneal dialysis – including CAPD, APD/CCPD, assisted PD Haemodialysis – including HDF, HD, in centre, at home, 3 days a week, >3 days a week Conservative management
Comparisons	Any modality compared to any other modality Transplant vs non-specific dialysis Conservative management vs non-specific renal replacement therapy Any submodality compared to any other submodality
Outcomes	Critical: • Quality of life • Mortality • Hospitalisation • Time to failure of RRT modality Important: • Mental wellbeing • Cognitive impairment • Experience of care • Growth • Malignancy • Adverse events
Study design	RCTs Non-randomised studies (NRS) to be considered if insufficient RCT evidence found on a comparison basis, only if adjusted for key confounders: • Age • Ethnicity • Comorbidities • Health at baseline

1.4 Clinical evidence

1.4.1 Included studies

Forty two studies were included in the review;[1, 15, 36, 43, 53, 65, 70, 87, 92, 97, 98, 110, 133, 139, 140, 143, 145, 172, 173, 183, 192, 196, 204, 211, 220, 224, 252, 254, 262, 271, 276, 288, 290, 293, 296, 301, 322, 330, 364, 365, 386, 402, 407, 408, 426, 447, 451, 455, 457, 463, 468] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

RCT evidence was considered sufficient for the comparisons of HDF vs HD and HD 3x a week vs HD >3x a week in adults. For all other comparisons and age strata, NRS were considered. No relevant clinical studies comparing transplant or conservative management with any other form of RRT were found.

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

Reference	Intervention	Study type	Country (Data source for NRS)	Population strata	Follow-up duration	Outcome(s)
Abbott 2004[1]	Transplant, deceased donor (n = 16495) Dialysis (n = 17044)	NRS	USA USRDS /CMS	Adults (general population) Adults aged 65 and over	Average 3y	Mortality
Amaral 2016[15]	Pre-emptive transplant (n=1668) Non-pre-emptive transplant (n=5859)	NRS	USA USRDS /CMS	Children and young people aged <18	Up to 5.2y	Time to failure RRT form
ANZDATA (dialysis) trial: Johnson 2009[183]	Haemodialysis (n=15916) Peritoneal dialysis (n=6020)	NRS	Australia and New Zealand ANZDATA	Adults (general population)	Up to 10y	Infection
ANZDATA (transplant) trial: Milton 2008[293]	Pre-emptive transplant (n=578) Non-pre-emptive transplant (n=2025)	NRS	Australia and New Zealand ANZDATA	All age (general population)	Up to 10y	Time to failure RRT form
Balasubramanian 2011[36]	APD/CCPD (n=194) CAPD (n=178)	NRS	United Kingdom Study-specific	Adults (general population)	Average 2.2y	Quality of life (SF36) Time to failure RRT form
BRAZPD II trial: Beduschi 2015[43]	APD/CCPD (n=1334) CAPD (n=1556)	NRS	Brazil Study-specific	Adults (general population)	Up to 7y	Mortality Time to failure RRT form
Bro 1999[53]	APD/CCPD (n=17) CAPD (n=17)	RCT	Denmark	Adults (general population)	6 months	Symptom score Infection
Chandna 2011[65]	RRT (n=106) CM (n=77)	NRS	UK Study-specific	Adults aged >75y	18y	Mortality
CONvective	HDF (n=358)	RCT	Canada,	Adults	Average	Mortality

Reference	Intervention	Study type	Country (Data source for NRS)	Population strata	Follow-up duration	Outcome(s)
TRAnsport STudy (CONTRAST) trial: Grooteman 2012[140] (Den hoedt 2014[97], Den hoedt 2015[98], Mazairac 2013[276])	HD (n=356)		the Netherlands, Norway	(general population)	3.0y	Infection Quality of life
De fijter 1994[92]	APD/CCPD (n=41) CAPD (n=41)	RCT	The Netherlands	Adults (general population)	Up to 2.5y	Mortality Hospitalisation (count) Infection
Estudio de Supervivencia de Hemodiafiltración On-Line (ESHOL) trial: Maduell 2013[262]	HDF (n=456) HD (n=450)	RCT	Spain	Adults general with diabetes	Average 1.9y	Mortality Hospitalisation (count)
Frequent Hemodialysis Network (Daily) trial: FHN trial group 2010[110] (Chertow 2016[70], Hall 2012[145], Kurella tamura 2013[220], Suri 2013[408], Unruh 2013[426])	HD>3x a week in-centre(n=125) HD 3x a week in-centre (n=120)	RCT	USA	Adults and young people age >12y (general population)	Up to 3y	Quality of life (SF36) Symptom score (SPPB) Mortality Hospitalisation (count) Psychological wellbeing (BDI) Cognitive impairment Vascular access issues
Frequent Hemodialysis Network Nocturnal trial: Rocco 2011[365] (Rocco 2015[364])	HD>3x week at home, nocturnal (n=45) HD 3x week at home (n=42)	RCT	USA	Adults (general population)	Up to 3y	Quality of life (SF36) Symptom score (SPPB) Mortality Hospitalisation (count) Vascular access issues
Glanton 2003[133]	HD (n=5250) TPx (n=1719)	NRS	USA USRDS	All age BMI>30kg.m^2 on waiting list for TPx	4y	Mortality
Grams 2013[139]	Pre-emptive transplant (n=10992) Transplant after up to a year of dialysis (n=14428)	NRS	USA OPTN	Adults. Recipient age: under 65y 65 and older	Up to 15y	Mortality Time to failure RRT form
Jaar 2005[172]	HD (n=767) PD (n=274)	NRS	USA Study-	Adults - under /	Average 2.4y	Mortality

Reference	Intervention	Study type	Country (Data source for NRS)	Population strata	Follow-up duration	Outcome(s)
			specific	over 65y - with / without diabetes - with residual renal function		
Jain 2009[173]	Transplant (n = 157) Dialysis (n = 598)	NRS	UK Study-specific	Adults (general population)	Average 4.5 years	Mortality
Kantartzi 2013[192]	HDF (n=24) HD (n=24)	RCT xover	Greece	Adults (general population)	Four blocks of 3m	Quality of life (SF36 Physical)
Katopodis 2009[196]	HD >3x wk (n=8) HD 3x wk (n=8)	RCT	Greece	Adults Without diabetes	12m	Mortality
Korevaar 2003[211]	HD (n=18) PD (n=20)	RCT	The Netherlands	Adults (general population)	Up to 5y	Quality of life (EQ VAS) Mortality
Locatelli 1996[254]	HDF (n=50) HD (n=105)	RCT	Italy	Adults Up to 70y	2y	Mortality Hospitalisation (count) Vascular access issues
Locatelli 2010[252]	HDF (n=40) HD (n=70)	RCT	Italy	Adults Up to 80y	2y	Mortality Infection Vascular access issues
Manns 2009[271] (Culleton 2007[87]; [204]))	HD >3 x wk, nocturnal home (n=27) HD 3x wk in-centre or home (n=25)	RCT	Canada	Adults (general population)	6m	Quality of life (SF36, EQ5D) Symptom score (KDQ) Mortality Vascular access issues
Mcdonald 2009[278]	HD (n=14,733) PD (n=10,554)	NRS	Australia, New Zealand ANZDATA	All ages (general population)	Average 2.5y	Mortality
Merion 2005[288]	Transplant (n = 41,042) Dialysis (n = 109127)	NRS	USA USRDS/CMS	Adults general population	Average 3 years	Mortality
Mehrotra 2011[284]	HD (n=233,082) PD	NRS	USA USRDS	Adults with at least one	Average 2.5y	Mortality

Reference	Intervention	Study type	Country (Data source for NRS)	Population strata	Follow-up duration	Outcome(s)
	(n=19,879)			comorbidity --less/more than 65y old --with/ without diabetes		
Mesaros-devcic 2013[290]	HDF (n=42) HD (n=43)	RCT	Croatia	Adults	3y	Mortality
Morena 2017[296]	HDF (n=190) HD (n=191)	RCT	France	Adults aged >75y	2y	Mortality Hospitalisation
Murtagh 2007[301]	RRT (n=52) CM (n=77)	NRS	UK Study-specific	Adults aged >75y	2y	Mortality
Park 2013[330]	HDF (n=20) HD (n=20)	RCT	South Korea	Adults (general population)	Up to 7y	Mortality
Schiffl 2007[386]	HDF (n=76) HD (n=76)	RCT xover	Germany	Adults (general population)	Two blocks of 2y	Mortality
Snyder 2002[402]	Living donor Deceased donor Total n=252,402	NRS	USA CMS	Adults (general population)	Up to 5 yrs	Mortality Graft failure
Stefansson 2012[407]	HDF (n=20) HD (n=20)	RCT xover	Sweden	Adults (general population)	Two blocks of 2m	Quality of life (SF36)
Termorshuizen 2003[416]	HD (n=742) PD (n=480)	NRS	The Netherlands NECOSAD	Adults --aged under/over 60y --with / without diabetes	Up to 2y	Mortality
Turkish HDF study trial: Ok 2013[322]	HDF (n=391) HD (n=391)	RCT	Turkey	Adults --general population --with diabetes	Average 2y	Mortality Hospitalisation (count) Vascular access issues
Vonesh 2004[438]	HD (n=352,706) PD (n=46,234)	NRS	USA CMS	Adults aged over 45 with one or more comorbidity --aged up to/over 65 --with / without diabetes	3y	Mortality

Reference	Intervention	Study type	Country (Data source for NRS)	Population strata	Follow-up duration	Outcome(s)
Ward 2000[447]	HDF (n=24) HD (n=21)	RCT	Germany	Adults (general population)	12m	Symptom score (KDQ) Psychological wellbeing (KDQ)
Weinhandl 2010[451]	HD (n=6337) PD (n=6337)	NRS	USA CMS	Adults (general population)	Average 2.3y	Mortality
Winkelmayer 2002[455]	HD (n=1966) PD (n=537)	NRS	USA Medicare / Medicaid in state of NJ	Adults aged >65y	12m	Mortality
Wizemann 2000[457]	HDF (n=23) HD (n=21)	RCT	Germany	Adults (general population)	2y	Mortality
Woods 1996[463]	HD at home (n=70) HD in centre (n=3102)	NRS	USA USRDS, Medicare	Adults aged 49-59y	Up to 4y	Mortality
Yeates 2012[468] and LeFrance 2012[224]	HD (n=32,531) PD (n=14,308)	NRS	Canada CORR	Adults --aged 45-64y --aged >65y --with diabetes --without diabetes	Up to 5y	Mortality Hospitalisation (count, sub-set)

Abbreviations:
APD/CCPD = automated or continuous cycling peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; CM = conservative management; HD = haemodialysis; HDF = haemodiafiltration; NRS = non-randomised study; PD = peritoneal dialysis; RCT = randomised controlled trial; RRT = renal replacement therapy; xover = crossover study

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

1.4.4.1 Children and young people aged 2 to 18

Table 3: Clinical evidence summary: Pre-emptive transplantation vs transplant after dialysis, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with TPx after dialysis,	Risk difference with TPx - pre-emptive (95% CI)
Graft failure, time to event (TTE)	7527 (1 study) 5 years	VERY LOW[1] due to imprecision	HR 0.76 (0.64 to 0.9)	No control event rate available	
1 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

1.4.4.2 Adults aged >18 to 70

Table 4: Clinical evidence summary: Transplant vs dialysis, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with dialysis	Risk difference with TPx (95% CI)
Mortality, TTE, general population	33539 (1 study) 3 years	LOW	HR 0.47 (0.44 to 0.50)	No control event rate available	
Mortality, TTE, BMI ≥ 30 kg/m^2	6891 (1 study) 2.5 years	LOW[1,2] due to risk of bias, indirectness	HR 0.39 (0.33 to 0.46)	No control event rate available	
Mortality, RR, general population	150934 (2 studies) 3-4 years	MODERATE[3] due to large effect	RR 0.28 (0.27 to 0.29)	No control event rate available	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with dialysis	Risk difference with TPx (95% CI)
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 evidence was at very high risk of bias 2 Downgraded by one increment due to indirectness of intervention (those receiving transplant were not RRT naïve) 3 Upgraded due to large effect (ratio < 0.5 or > 2) and consistent across multiple studies					

Table 5: Clinical evidence summary: PD vs HD, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with PD (95% CI)
Mortality, TTE	38 (1 study) 2.5 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 0.45 (0.02 to 10.13)	500 per 1000	232 fewer per 1000 (from 486 fewer to 499 more)
QoL (EuroQoL VAS, 0-100, higher is better)	38 (1 study) 2.5 years	VERY LOW[1,2] due to risk of bias, imprecision			The mean EQ5D VAS (0-100, higher is better) in the intervention groups was 4.8 lower (15.84 lower to 6.24 higher)
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: PD vs HD, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with PD (95% CI)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with PD (95% CI)
Mortality, TTE, general population	41505 (4 studies) 2.5 years	VERY LOW[1,2,3] due to risk of bias, inconsistency, imprecision	HR 1.21 (0.94 to 1.56)	No control event rate available	
Mortality, TTE, diabetes mellitus	300841* (3 studies) 2.5 years	VERY LOW[1,3] due to risk of bias, imprecision	HR 1.12 (1.06 to 1.19)	No control event rate available	
Mortality, TTE, no diabetes mellitus	300841* (3 studies) 2.5 years	VERY LOW[1,2,3] due to risk of bias, inconsistency, imprecision	HR 1.04 (0.83 to 1.32)	No control event rate available	
Mortality, TTE, residual urine output	1362 (1 study) 2.5 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 1.15 (0.80 to 1.65)	No control event rate available	
Mortality, RR, diabetes mellitus	400162** (2 studies) 2-3 years	VERY LOW[1,2,3] due to risk of bias, inconsistency, imprecision	RR 0.47 (0.08 to 2.86)	No control event rate available	
Mortality, RR, no diabetes mellitus	400162** (2 studies) 2-3 years	VERY LOW[1,3] due to risk of bias, imprecision	RR 0.99 (0.9 to 1.09)	No control event rate available	
All-cause hospitalisation, count rate	1820 (1 study) 2.1 years	LOW[1] due to risk of bias	Rate Ratio 0.99 (0.94-1.05)	No control event rate available	
AE (deaths from infection) between 6m and 2y after starting dialysis	21936 (1 study) 1 years	VERY LOW[1,3] due to risk of bias, imprecision	HR 0.93 (0.66 to 1.32)	No control event rate available	

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 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with PD (95% CI)
analysis 3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

(and ** total study size. Size of DM:non-DM subgroup approx. 1:3)*

Table 7: Clinical evidence summary: Transplant – pre-emptive vs after dialysis, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with TPx after dialysis	Risk difference with pre-emptive TPx (95% CI)
Mortality, TTE, general population	25420 (1 study) 3 years	VERY LOW[1] due to risk of bias	HR 0.97 (0.91 to 1.03)	No control event rate available	
Modality failure, TTE, general population	28023 (2 studies) 3 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 0.8 (0.75 to 0.85)	No control event rate available	
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 8: Clinical evidence summary: Transplant – living vs deceased donor, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with deceased donor	Risk difference with living donor (95% CI)
Mortality	22776 (1 study) 5 years	VERY LOW[1,2] due to risk of bias, indirectness	RR 0.71 (0.60 to 0.84)	No control event rate available	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with deceased donor	Risk difference with living donor (95% CI)
Graft failure	22776 (1 study) 5 years	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision	RR 0.88 (0.79 to 0.98)	No control event rate available	

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 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 9: Clinical evidence summary: HD – HDF vs HD, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with HDF (95% CI)
Mortality, TTE, general population	1620 (2 studies) 2-3 years	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision	HR 0.82 (0.61 to 1.11)	330 per 1000	50 fewer per 1000 (from 113 fewer to 29 more)
Mortality, RR, general population	2964 (9 studies) 2-3 years	VERY LOW[1,2,3,4] due to risk of bias, inconsistency, indirectness, imprecision[◊]	RR 0.82 (0.64 to 1.05)	179 per 1000	30 fewer per 1000 (from 60 fewer to 8 more)
Mortality, TTE, diabetes mellitus population	226 (1 study) 2 years	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision	HR 0.75 (0.46 to 1.22)	271 per 1000	60 fewer per 1000 (from 136 fewer to 49 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with HDF (95% CI)
population	(1 study) 2 years	due to risk of bias, indirectness, imprecision	(0.47 to 1.16)	369 per 1000	96 fewer per 1000 (from 196 fewer to 59 more)
QoL (SF-36 Physical Composite Score, 0-100, high is good outcome)	64 (2 studies) 2-3 months	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision		The mean QoL (SF-36 pcs, 0-100, high is good outcome) in the control groups was 41	The mean QoL (physical) in the intervention groups was 1.08 higher (6.57 lower to 8.73 higher)
QoL (SF-36 Mental Composite Score, 0-100, high is good outcome)	40 (1 study) 2 months	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision		The mean qol (sf-36 mcs, 0-100, high is good outcome) in the control groups was 65	The mean QoL (mental) in the intervention groups was 2 lower (8.52 lower to 4.52 higher
QoL (EQ5D, 0-1.0, high is good outcome)	367 (1 study) 3 years	LOW[1,2] due to risk of bias, indirectness		The mean qol (EQ5D, 0-1.0, high is good outcome) in the control groups was 0.73	The mean QoL in the intervention groups was 0.01 higher (0.03 lower to 0.05 higher)
Hospitalisation, rate ratio, general population	1843 (3 studies) 2 years	VERY LOW[1,2,3,4] due to risk of bias, inconsistency, indirectness, imprecision	Rate Ratio 1.03 (0.73 to 1.46)	695 per 1000	21 more per 1000 (from 188 fewer to 320 more)
Symptom/function (KDQ physical symptoms, 1-7, high is good outcome)	189 (2 studies) 1 years	VERY LOW[1,2,4] due to risk of bias, inconsistency, indirectness		The mean symptom/function (kdq physical symptoms, 1-7, high is good outcome) in the control groups was 4.8	The mean symptom/function in the intervention groups was 0.50 lower 1.48 lower to 0.48 higher)
Mental wellbeing (KDQ depression, 1-7, high is good outcome)	45 (1 study) 1 years	VERY LOW[1,2,3] due to risk of bias,		The mean mental wellbeing (kdq depression, 1-7, high is good outcome) in the control groups	The mean mental wellbeing (kdq depression, 1-7, high is good outcome), in the intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with HDF (95% CI)
		indirectness, imprecision		was 5.6	groups was 0.2 higher (0.05 to 0.35 higher)
AE (all infections)	819 (2 studies) 2-3 years	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision	RR 1.10 (0.89 to 1.37)	156 per 1000	16 more per 1000 (from 17 less to 58 more)
AE (vascular access related withdrawal from study)	1042 (3 studies) 2 years	VERY LOW[1,2, ,4] due to risk of bias, inconsistency, indirectness,	OR 5.61 (3.07 to 10.23)	29 per 1000	70 more per 1000 (from 50 more to 100 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 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
4 Downgraded by 1 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup analysis
◊ see also subgroup analysis E.5

Table 10: Clinical evidence summary: HD – HD >3x a week vs HD 3x a week, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD 3x a week	Risk difference with HD >3x a week (95% CI)
Mortality, dichotomous, general population	394 (4 studies) 3 years	VERY LOW[1,2,3,4] due to risk of bias, inconsistency, indirectness, imprecision[◊]	Peto Odds ratio 0.83 (0.49 to 1.38)	119 per 1000	30 fewer per 1000 (from 100 fewer to 50 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD 3x a week	Risk difference with HD >3x a week (95% CI)
QoL (SF-36 Mental Composite Score, 0-100, high is good outcome)	317 (3 studies) 1 years	VERY LOW[1,3] due to risk of bias, indirectness		The mean QoL (mental) in the control groups was -0.25 change score	The mean QoL (mental) in the intervention groups was 3.52 higher (3.27 to 3.78 higher)
QoL (SF-36 Physical Composite Score, 0-100, high is good outcome)	318 (3 studies) 1 years	VERY LOW[1,3] due to risk of bias, indirectness		The mean qol (physical) in the control groups was 1.3 change score	The mean qol (physical) in the intervention groups was 2.73 higher (2.52 to 2.95 higher)
QoL (EQ-5D, 0-1.0, high is good outcome)	52 (1 study) 6 months	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision			The mean change in QoL (EQ-5D, 0-1.0, high is good outcome) in the intervention groups was 0.11 higher (0.05 lower to 0.27 higher)
Hospitalisation, rate ratio	383 (3 studies) 1 years	VERY LOW[1,3,4] due to risk of bias, inconsistency, indirectness, imprecision	Rate Ratio 0.96 (0.78 to 1.20)	950 admissions per 1000 approximately	38 fewer per 1000 (from 209 fewer to 190 more)
Symptom/function (SPPB, 0-12, high is good outcome)	248 (2 studies) 1 years	VERY LOW[1,3,4] due to risk of bias, indirectness, imprecision		The mean symptom/function score (SPPB, 0-12, high is good outcome) in the control groups was -0.4 change score	The mean symptom/function score in the intervention groups was 0.14 higher (0.09 to 0.2 higher)
AE (vascular access procedure required)	383 (3 studies) 1 years	VERY LOW[1,3,4] due to risk of bias, indirectness, imprecision	RR 1.42 (1.05 to 1.91)	299 per 1000	126 more per 1000 (from 15 more to 272 more)
AE (bacteraemia)	51 (1 study) 6 months	VERY LOW[1,3,4] due to risk of bias, indirectness, imprecision	RR 1.00 (0.28 to 3.58)	160 per 1000	0 more per 1000 (from 115 fewer to 413 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD 3x a week	Risk difference with HD >3x a week (95% CI)
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 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup analysis 3 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively 4 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs ◊ See also subgroup analysis, section E.5					

Table 11: Clinical evidence summary: HD – HD at home vs HD in centre, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects
				Risk with HD in centre, NRS
Mortality, TTE, general population	3172 (1 study) 4 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 0.58 (0.35 to 0.96)	No control event rate available
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 12: Clinical evidence summary: PD – CAPD compared to APD/CCPD, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with APD/CCPD	Risk difference with CAPD (95% CI)
Mortality, RR, general population	82 (1 study)	VERY LOW[1,2]	RR 0.5 (0.1 to	98 per 1000	49 fewer per 1000 (from 88 fewer to 155 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with APD/CCPD	Risk difference with CAPD (95% CI)
	1.5 years	due to risk of bias, imprecision	2.58)		
Hospitalisation, rate ratio, general population	82 (1 study) 1.5 years	VERY LOW[1,3] due to risk of bias, imprecision	Rate Ratio 1.67 (1.11 to 2.52)	488 per 1000	327 more per 1000 (from 54 more to 742 more)
Symptom scores (physical discomfort, 1-5, high is poor), 6 months	25 (1 study) 6 months	VERY LOW[1,2] due to risk of bias, imprecision		The mean symptom scores (physical discomfort, 1-5, high is poor), 6 months in the control groups was 1.9	The mean symptom scores (physical discomfort, 1-5, high is poor), 6 months in the intervention groups was 0.3 higher (0.61 lower to 1.21 higher)
AE (Exit site infection)	25 (1 study) 6 months	VERY LOW[1,2] due to risk of bias, imprecision	RR 0.92 (0.06 to 13.18)	Study population	
				83 per 1000	7 fewer per 1000 (from 78 fewer to 1000 more)
AE (Peritonitis)	107 (2 studies) 0.5-1.5 years	LOW[1,2] due to risk of bias, imprecision	RR 2.61 (0.73 to 9.27)	Study population	
				66 per 1000	106 more per 1000 (from 18 fewer to 546 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
3 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively

Table 13: Clinical evidence summary: PD – CAPD compared to APD/CCPD, NRS

Outcomes	No of Participants	Quality of the	Relativ	Anticipated absolute effects

	(studies) Follow up	evidence (GRADE)	e effect (95% CI)	Risk with APD/CCPD	Risk difference with CAPD (95% CI)
Mortality, TTE	2890 (1 study) 5 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 1.44 (1.21 to 1.71)	No control event rate available	
QoL (SF-36 Physical Composite Score, 0-100, high is good outcome)	372 (1 study) 1 years	VERY LOW[1,2] due to risk of bias, imprecision			The mean QoL (SF-36 physical, 0-100, high is good outcome) in the intervention groups was 2.2 lower (8.16 lower to 3.76 higher)
QoL (SF-36 Mental Composite Score, 0-100, high is good outcome)	372 (1 study) 1 years	VERY LOW[1,2] due to risk of bias, imprecision			The mean qol (SF-36 mental, 0-100, high is good outcome) in the intervention groups was 1.5 lower (8.16 lower to 5.16 higher)
Modality failure, TTE	3262 (2 studies) 2-5 years	VERY LOW[1,2,3] due to risk of bias, inconsistency, imprecision	HR 1.02 (0.65 to 1.62)	No control event rate available	

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 Downgraded by 1 or 2 increments because the point estimate and the confidence intervals varied widely across studies, unexplained by subgroup analysis

1.4.4.3 Adults >70

Table 14: Clinical evidence summary: RRT vs Conservative Management, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with CM	Risk difference with RRT (95% CI)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with CM	Risk difference with RRT (95% CI)
Mortality in over 75s (RRT = Dialysis/Transplant)	183 (1 study) 0-18 years	VERY LOW1,2 due to risk of bias, imprecision	HR 0.85 (0.57 to 1.27)	No control group available	
Mortality in over 75s (RRT = Dialysis)	129 (1 study) 2 years	VERY LOW1 due to risk of bias	HR 2.94 (1.56 to 5.53)	No control group available	

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 15: Clinical evidence summary: Transplant vs dialysis, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with dialysis	Risk difference with TPx (95% CI)
Mortality, TTE, general population	5163 (1 study) 3 years	LOW[1]	HR 0.59 (0.51 to 0.68)	No control event rate available	

1 Downgraded 2 increments due to risk of bias from non-randomised study design only

Table 16: Clinical evidence summary: HDF compared to HD, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with HDF (95% CI)
Mortality, RR	381	VERY LOW[1,2,3]	RR 0.84	225 per 1000	36 fewer per 1000

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with HDF (95% CI)
	(1 study) 2 years	due to risk of bias, imprecision, indirectness	(0.57 to 1.25)		(from 101 fewer to 52 more)
Hospitalisation (all cause)	381 (1 study) 2 years	VERY LOW[1,2,3] due to risk of bias, imprecision, indirectness	Rate Ratio 0.89 (0.76 to 1.04)	1812 per 1000	199 fewer per 1000 (from 435 fewer to 72 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
3 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively

Table 17: Clinical evidence summary: PD vs HD, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference PD (95% CI)
Mortality, TTE, general population	1041 (1 study) 2.5 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 1.66 (0.93 to 2.96)	No control event rate available	
Mortality, TTE, diabetes mellitus	299800* (2 studies) 2.5 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 1.2 (1.13 to 1.26)	No control event rate available	
Mortality, TTE, no diabetes mellitus	299800* (2 studies) 2.5 years	VERY LOW[1] due to risk of bias	HR 1.06 (1.01 to 1.11)	No control event rate available	
Mortality, RR, diabetes mellitus	400162** (2 studies) 2-3 years	VERY LOW[1,2] due to risk of bias, imprecision	RR 1.12 (0.75 to 1.66)	No control event rate available	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference PD (95% CI)
Mortality, RR, no diabetes mellitus	400162** (2 studies) 2-3 years	VERY LOW[1,2] due to risk of bias, imprecision	RR 1.22 (1.14 to 1.3)	No control event rate available	
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					

** and ** total study size. Size of DM:non-DM subgroup approx. 1:3*

Table 18: Clinical evidence summary: Transplant – pre-emptive vs after up to a year of dialysis, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects
				Risk with TPx after dialysis, NRS
Mortality, TTE, general population	25420 (1 study) 3 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 0.84 (0.74 to 0.95)	No control event rate available
Graft failure, TTE, general population	25420 (1 study) 3 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 0.89 (0.74 to 1.07)	No control event rate available
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.

1.4.4.4 Special Populations – duplicate data from tables above

Note there was no evidence available for the strata of BAME or late starters

1.4.4.4.1 Adults with diabetes mellitus (type 1 or 2)

Table 19: Clinical evidence summary: PD vs HD in adults with diabetes, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference PD (95% CI)
Mortality, TTE, diabetes mellitus	300841* (3 studies) 2.5 years	VERY LOW[1,3] due to risk of bias, imprecision	HR 1.12 (1.06 to 1.19)	No control event rate available	
Mortality, RR, diabetes mellitus	400162** (2 studies) 2-3 years	VERY LOW[1,2,3] due to risk of bias, inconsistency, imprecision	RR 0.47 (0.08 to 2.86)	No control event rate available	

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 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup analysis
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
* and ** total study size (Size of DM subgroup approx. 1/4 of this)

Table 20: Clinical evidence summary: HD – HDF vs HD in people with diabetes, RCT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with HDF (95% CI)
Mortality, TTE, diabetes mellitus population	226 (1 study) 2 years	VERY LOW[1,2,3] due to risk of bias, indirectness, imprecision	HR 0.75 (0.46 to 1.22)	No control event rate available	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with HDF (95% CI)
population	(1 study) 2 years	due to risk of bias, indirectness, imprecision	(0.47 to 1.16)	No control event rate available	

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 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.4.4.4.2 Adults aged >70y with DM (type 1 or 2)

Table 21: Clinical evidence summary: PD vs HD in people aged >70 with diabetes, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with PD (95% CI)
Mortality, TTE, diabetes mellitus	299800* (2 studies) 2.5 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 1.2 (1.13 to 1.26)	No control event rate available	
Mortality, RR, diabetes mellitus	400162** (2 studies) 2-3 years	VERY LOW[1,2] due to risk of bias, imprecision	RR 1.12 (0.75 to 1.66)	No control event rate available	

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
* and ** total study size (Size of DM subgroup approx. 1/4 of this)

1.4.4.4.3 *People with residual kidney function (residual urine output)*

Table 22: Clinical evidence summary: PD vs HD, NRS

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HD	Risk difference with PD (95% CI)
Mortality, TTE, residual urine output	1362 (1 study) 2.5 years	VERY LOW[1,2] due to risk of bias, imprecision	HR 1.15 (0.80 to 1.65)	No control event rate available	

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 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup analysis

1.5 Economic evidence

1.5.1 Included studies

7 health economic studies with relevant comparisons have been included in this review: 1 comparing HD and PD[74]; 3 comparing HDF and HD[235, 276, 354]; 3 including a comparison of HD >3x weekly with HD 3x weekly[41, 204, 249] (where the setting for more frequent HD was sometimes at home). These are summarised in the health economic evidence profiles below (Table 23, Table 24 and Table 25) and the health economic evidence tables in appendix H.

No health economic studies were included comparing transplant and dialysis, conservative management and renal replacement therapy, live-donor transplant and deceased-donor transplant, pre-emptive transplant and non-pre-emptive transplant, home and in-centre HD, APD and CAPD or relating to assisted PD.

None of the included studies were in children.

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

Note that UK RRT intervention costs are included in section 1.5.5 Unit costs.

1.5.2 Excluded studies

49 economic studies relating to this review question were identified but were excluded due to limited applicability, methodological limitations or a combination of both.[4, 32, 38, 47, 64, 77, 80-82, 104, 107, 109, 138, 141, 146, 161, 175, 190, 191, 202, 203, 209, 210, 215, 218, 233, 238, 247, 268, 280-282, 300, 306, 318, 326, 339, 367, 376, 377, 380, 381, 391, 396, 410, 411, 414, 421, 459]

These are listed in appendix I, with reasons for exclusion given.

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

Note that one study included for the frequency comparisons (Beby 2016) also incorporated a comparisons of home vs in-centre HD (of the same frequency) but this comparison has not been presented as it is judged to have very serious limitations. More details are in the health economic evidence table in appendix H.

1.5.3 Summary of studies included in the economic evidence review

Table 23: Health economic evidence profile: PD vs HD

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Chui 2013[74] (Canada)	Partially applicable[(a)]	Potentially serious limitations[(b)]	• Cohort analysis with all cost models adjusted for age, sex, body mass index, race, comorbid conditions, cause of ESRD, and pre-dialysis care. • Comparative costing • Population: Adult patients who initiated long-term dialysis (PD or in-centre HD) for ESRD • Comparators: ○ HD ○ PD ○ HD then switched to PD in first year[(c)] ○ PD then switched to HD in first year[(c)] • Follow-up: 1 and 3 years	**Vs HD 1 year** PD: -£31,097[(d)] **Vs HD 3 years** PD: -£66,404[(d)]	n/a	n/a	**95% CI - 1 year incremental cost vs HD:** PD: -£34,064 to -£28,130 **95% CI - 3 years incremental cost vs HD:** PD: -£45,117 to -£24,523

Abbreviations: CI = confidence interval; HD = haemodialysis; ICER: incremental cost-effectiveness ratio; PD = peritoneal dialysis; QALY: quality-adjusted life years; RCT: randomised controlled trial

(a) 2010 Canadian costs based on resource use from 1999-2006 may not reflect current NHS context. Discounting not applied. Health outcomes not incorporated.

(b) Within-trial analysis (cohort) so does not reflect the full body of evidence in this area (note: no parallel clinical study, costs only). It is unclear whether any transport costs are included.

(c) Not presented here; included in sequencing review.

(d) 2010 Canadian dollars converted to UK pounds.[324] Cost components incorporated: dialysis costs, inpatient costs, medication costs, and physician fees.

Table 24: Health economic evidence profile: HDF vs HD

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Mazairac 2013 (CONTRAST subgroup)[276] (Netherlands)	Partially applicable[a]	Potentially serious limitations[b]	• Markov model based on within-trial analysis of survival, utility and cost data from CONTRAST RCT[140] economic subgroup. • Cost-utility analysis (QALYs) • Population: adults with ESRD undergoing chronic HD ○ 3 age subgroups analysed • Comparators: ○ HD (low-flux) ○ HDF • Time horizon: 5 years	***45-64 years*** £12,775[c] ***<45 years*** £16,867[c] ***≥65 years*** £11,822[c]	***45-64 years*** 0.06 QALYs ***<45 years*** 0.12 QALYs ***≥65 years*** 0.03 QALYs	***45-64 years*** £224,258 per QALY gained ***<45 years*** £140,558 per QALY gained ***≥65 years*** £394,058 per QALY gained	***45-64 years*** Probability Intervention 2 cost-effective (£20K/30K threshold): <10%/<10% ICER in sensitivity analyses: £44,052 to £806,747 per QALY gained. ***<45 years*** Not reported. ***≥65 years*** Not reported.
Levesque 2015 (CONTRAST subgroup)[235] (Canada)	Partially applicable[d]	Potentially serious limitations[e]	• 2 analyses ○ Within-trial analysis from Canadian subset of CONTRAST RCT[140] ○ Markov model based on within-trial analysis data. • Cost-utility analysis (QALYs) • Population: adults with ESRD undergoing chronic HD • Comparators:	***Within-trial analysis (74 months)*** £9327[g] ***Model (lifetime)*** £34,914[g]	***Within-trial analysis (74 months)*** 0.31 QALYs ***Model (lifetime)*** 1.04 QALYs	***Within-trial analysis (74 months)*** £18,275 per QALY gained ***Model (lifetime)*** £30,316 per QALY gained	***Within-trial analysis (74 months)*** Probability cost effective not reported. Removing costs of additional survival time on HDF resulted in a cost saving of £311. ***Model (lifetime)*** Probability HDF cost-effective (£20K/30K threshold): ~40%/~50% ICER in reported

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
			○ HD (low-flux) ○ HDF (high efficiency[f]) • Time horizon: ○ Within-trial analysis: 74 months ○ Model: lifetime				sensitivity analyses: £27,503 to £82,915 per QALY gained.
Ramponi 2016 (Italy) [354]	Partially applicable[h]	Potentially serious limitations[i]	• Markov model – treatment effects based on meta-analysis of RCTs • Cost-utility analysis (QALYs) • Population: adults with ESRD undergoing chronic HD • Comparators: ○ HD (high-flux) ○ HDF • Time horizon: 10 years	***Male, 40 years*** £1,551[j] ***Male, 50 years*** £1,527[j] ***Male, 60 years*** £1,421[j] ***Female, 40 years*** £1,577[j] ***Female, 50 years*** £1,572[j] ***Female, 60 years*** £1,516[j]	***Male, 40 years*** 0.293 QALYs ***Male, 50 years*** 0.237 QALYs ***Male, 60 years*** 0.112 QALYs ***Female, 40 years*** 0.290 QALYs ***Female, 50 years*** 0.248 QALYs ***Female, 60 years*** 0.120 QALYs	***Male, 40 years*** £5,296 per QALY gained ***Male, 50 years*** £6,451 per QALY gained ***Male, 60 years*** £12,628 per QALY gained ***Female, 40 years*** £5,431 per QALY gained ***Female, 50 years*** £6,349 per QALY gained ***Female, 60 years*** £12,655 per QALY gained	***Male, 40 years*** Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%[c] ***Male, 50 years*** Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%[c] ***Male, 60 years*** Probability Intervention 2 cost-effective (£20K/30K threshold): ~60%/~65%[c] ***Female, 40 years*** Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%[c] ***Female, 50 years*** Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%[c] ***Female, 60 years*** Probability Intervention 2 cost-effective (£20K/30K threshold): ~60%/~65%[c] ***Sensitivity analyses*** ICERs increased across when alternative cost

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
							source used (£7,146 to £18,368 across age groups) and when different QOL data used (£17,945/QALY in Male 50 years analysis; other groups not reported).

Abbreviations: HD = haemodialysis; HDF = haemodiafiltration; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial

(a) Resource use from Netherlands, Canada and Norway between 2004 and 2010, and 2009 unit costs may not reflect current NHS context. The cost of productivity losses is included in the intervention costs which is not in line with the NICE reference case, however these costs are relatively small in relation to the total intervention costs in the analysis (a saving of £45 per 3 months with HDF vs HD; overall HDF costs £634 more than HD per 3 months in model); excluding these costs would makes HDF less cost effective. The discount rates used were not in line with the NICE reference case (4% of costs and 1.5% for outcomes, rather than 3.5% for both; a sensitivity analysis was done with 3% for both). QALYs are calculated using the EQ5D Dutch tariff.

(b) Analysis based on subset of a single study (CONTRAST[140]) and so does not reflect full body of available evidence for this area. 5 year time horizon; as survival varies between comparators the impact on QALYs and costs will not be fully captured (sensitivity analysis explores impact of extending to 10 years). Methods for sensitivity analysis where remove costs of additional survival time are unclear. Some sources of funding are from industry however primary funding is not.

(c) 2009 Dutch Euros converted to UK pounds.[324] Cost components incorporated: direct healthcare costs: dialysis and other medical staff, material (water installation, dialysis machines and disposables), vascular access, routine diagnostics of patients and dialysis water quality, meals during dialysis, hospitalisation, medication and overheads. Direct non-healthcare costs: travel expenses. Indirect non-healthcare costs: productivity losses.

(d) Resource use from Canada between 2007 and 2010, and 2013 unit costs may not reflect current NHS context. The discount rate used was not in line with the NICE reference case (3% for costs and outcomes, rather than 3.5%).

(e) Analysis based on subset of a single study (CONTRAST) and so does not reflect full body of available evidence for this area. Funded by Amgen and Fresenius Medical Care.

(f) Defined as online HDF performed with an optimal convection fluid volume (that is the sum of substitution fluid volume and net ultrafiltration).The paper notes that a major limitation of the overall CONTRAST study was the failure to achieve the planned volume of post-dilution substitution fluid (19L instead of the 24L planned by protocol).

(g) 2013 Canadian dollars converted to UK pounds.[324]Cost components incorporated: dialysis and other medical staff, material (water installation, dialysis machines and disposables), vascular access, routine diagnostics of patients and dialysis water quality, meals during dialysis, hospitalization, medication, transport.

(h) UK resource use from before 2011 (exact date not stated) may not reflect current NHS context; Italian cost year not stated (published 2016). Unclear if EQ-5D utilities are based on UK population values.

(i) 10 year time horizon; as survival varies between comparators the impact on QALYs and costs will not be fully captured. Costs other than those relating differences between HDF and HD intervention costs are assumed to be constant but as survival (and therefore life years) varies between HDF and HD this will not be true. Baseline mortality from non-UK clinical trial and so may not best represent general UK HD population. 2 of 10 authors are employees of Fresenius Medical Care; study funding not stated.

(j) 2016 Italian Euros converted to UK pounds.[324] Cost components incorporated: direct healthcare costs that differ between HDF and HD; in base-case analysis the cost difference applied was £1.22 per session (£191 per annum) based on a study which found different line costs (higher with HDF) and saline costs (lower with HDF).

Table 25: Health economic evidence profile: >3x weekly (home or in-centre) vs 3x weekly HD (home or in-centre)

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Klarenbach 2013[204] (Canada)	Partially applicable[a]	Potentially serious limitations[b]	• Markov model using patient level analysis of data from Manns RCT[271] – difference in QOL incorporated, survival assumed to be the same. • Cost-utility analysis (QALYs) • Population: adult patients on conventional HD wishing to commence frequent nocturnal home HD. • Comparators: ○ Conventional HD (3x 4hr sessions per week, in-centre 61%, satellite 14%, home 25%) ○ Frequent home nocturnal (5-6 nights per week) HD (on average 5.7 nights per week for 6-9 hours per session). • Time horizon: lifetime	Saves £3728[c]	0.384 QALYs	Frequent home nocturnal HD dominates (lower costs and higher QALYs)	Probability frequent home nocturnal HD cost-effective (£20K/30K threshold): NR ICERs reported in sensitivity analyses: frequent nocturnal HD dominates to £236,858 per QALY gained.
Liu 2015[249] (UK)	Partially applicable[d]	Potentially serious limitations[e]	• Markov model – difference in QOL and survival incorporated • Cost-utility analysis (QALYs) • Population: adults with ESRD requiring HD	£108,713[f]	0.862 QALYs	£126,106 per QALY gained	Probability high dose in-centre HD cost-effective (£20K/30K threshold): 0%/0%. ICERs reported in sensitivity analyses: £50,598 to £396,614.

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
			• Comparators: ○ In-centre HD x3 sessions weekly ○ In-centre high dose HD x5 sessions weekly • Time horizon: lifetime				Changing setting for high dose HD to home: • Using weekly home PBR tariff (£456): cost saving and higher QALYs • Increasing weekly cost (£575): £17,404 per QALY gained. • Home high dose HD dominates (lower costs and higher QALYs) in-centre high dose HD in both scenarios
Beby 2016 (Netherlands)[41]	Partially applicable[g]	Potentially serious limitations[h]	• Markov model – difference in survival, QOL, hospitalisation and vascular access failure incorporated • Cost-utility analysis (QALYs) • Population: adults with ESRD requiring HD • Comparators in-centre HD: ○ conventional in-centre HD x3 4hr sessions weekly ○ high dose in-centre HD x5 4hr sessions weekly • Comparators home HD: ○ High dose home HD x 5 7hr sessions ○ Home conventional HD	**In-centre**: £95,290[i] **Home:** £4,226[i][j]	**In-centre:** 0.412 QALYs **Home:** 0.361[j]	**In-centre:** £231,028 per QALY gained **Home:** £11,706 per QALY gained[j]	In-centre: Probability high dose cost effective (£20K/30K threshold): 0%/0% Home: Probability high dose cost-effective (£20K/30K threshold): NR ICERs in SA not reported

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
			3x 4hr sessions • Time horizon: 5 years				

Abbreviations: HD = haemodialysis; HDF = haemodiafiltration; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life years; RCT: randomised controlled trial

(a) Resource use from Canada between 2004 and 2006, and 2012 unit costs may not reflect current NHS context. The discount rate used was not in line with the NICE reference case (5% for costs and outcomes, rather than 3.5%). It is unclear whether or not the UK population tariff has been used for EQ5D.

(b) Analysis based on a single study (Manns 2009 RCT[271]) and so does not reflect full body of available evidence for this area (although only study that reported EQ-5D). Hospitalisation costs were excluded although justified on basis that RCT did not show a difference in the risk and duration of hospitalisation by modality and explored in sensitivity analysis. One author is a Baxter employee although not at the time of designing RCT or economic evaluation or conducting the RCT and study funding is not from industry.

(c) 2012 Canadian dollars converted to UK pounds.[324] Cost components incorporated: Dialysis costs, NHD training/setup costs, medication, physician costs. Hospitalisation costs were excluded in base case analysis as RCT did not show a difference in the risk and duration of hospitalisation by modality (explored in SA).

(d) Cost year not stated and costs appear to be from various year from 2009 - 2014, therefore may not reflect current NHS context. Unclear if all EQ5D data is from patients and uses UK tariff; although relative treatment effect data is.

(e) Baseline data for survival on HD is from European registry (20% UK). Relative treatment effects are only partially based on studies included in the clinical review: differences in QOL are based on data from the Mann RCT of frequent home HD vs in-centre HD with an assumption that half the treatment difference is due to the frequency and half due to the home setting (resulting absolute difference in model 0.05); survival difference is based on studies excluded from the clinical review - a HR of 0.76 is applied; hospitalisation differences are based on Chertow 2010 which is included in the clinical review. For the sensitivity analysis where more frequent HD is provided at home Rocco 2011 (included in clinical review) is used for hospitalisations. QOL is based on a home HD baseline with the same relative treatment effect for more frequent HD as in the base case (resulting absolute difference 0.19 between home frequent HD and in centre HD). Costs are based on PBR tariff which may include incentives. In addition for costs of frequent home HD the current PBR tariff for home HD was used in the base-case analysis which may not reflect the cost of frequent home HD. The study is funded by Baxter Healthcare.

(f) Cost components incorporated: In-centre HD costs (using PBR tariff to account for staff costs and consumables per session), dialysis access establishment and maintenance, dialysis service, erythropoietin-stimulating agents, all cause hospitalisations, patient monitoring, transportation, kidney transplantation and maintenance. (In sensitivity analysis where high dose HD is given at home the PBR fixed per week home HD tariff is used this is intended to cover initial training and home modification costs and designed to enable to provider to recover investments over time. it also covers home care visits and machine maintenance.)

(g) Dutch 2015 costs may not reflect current NHS context. The discount rates used were not in line with the NICE reference case (4% of costs and 1.5% for outcomes, rather than 3.5% for both). QALYs are calculated using EQ5D values but it is unclear if the UK population tariff was used in the studies used.

(h) 5-year time horizon may not be sufficient to capture all difference in costs and outcomes given mortality is impacted by treatment. Baseline rates based on Dutch national data may not reflect the UK population. Relative treatment effects are partially based on evidence included in clinical review: mortality benefit used for high dose HD greater than estimate from clinical review; QOL benefit with high dose HD based on study included in clinical review but with assumptions made about whether to attribute benefit to setting or frequency. Difference in vascular access failure rates appear to be based on rates from two different studies (11.00% vs 13.46%) rather than a comparative study. The weekly cost for high dose home HD is lower than conventional home HD and the reason for this is not explained given dialysis is for longer sessions and more often. Study funding is not stated but three of four authors are current or former Baxter employees and Baxter and publication and writing/editorial support was funded by Baxter.

(i) 2015 Dutch Euros converted to UK pounds.[324] Cost components incorporated: Initiation (including house adjustments), dialysis treatment, medication (blood pressure medication, phosphate binders), complications (access failure, hospitalisation), transportation.

(j) Calculated by NGC from reported data.

1.5.4 Health economic model

The committee agreed that new economic analysis of HDF versus HD was the highest economic priority for the guideline due to it being a change in practice that had the potential to have a substantial resource impact for the NHS; while the cost differences might be fairly small per session, most people on HD (around 25,000) are potentially suitable for HDF. It was felt that new cost effectiveness analysis could reduce the uncertainty around the cost effectiveness of HDF in the current NHS setting.

Model methods

A technical report for this analysis including full details of all methods and model inputs is available in a separate PDF 'Health Economic Analysis_HDFvsHD'.

A cost-utility analysis was undertaken to compare HDF and HD. A Markov model was used to estimate lifetime quality-adjusted life years (QALYs) and costs from a current UK NHS and personal social services perspective were considered. Both costs and QALYs were discounted at a rate of 3.5% per annum in line with NICE methodological guidance.[305] An incremental analysis was undertaken.

The comparators selected for the model were:

1. High flux HD 3x per week in-centre
2. HDF 3x per week in-centre

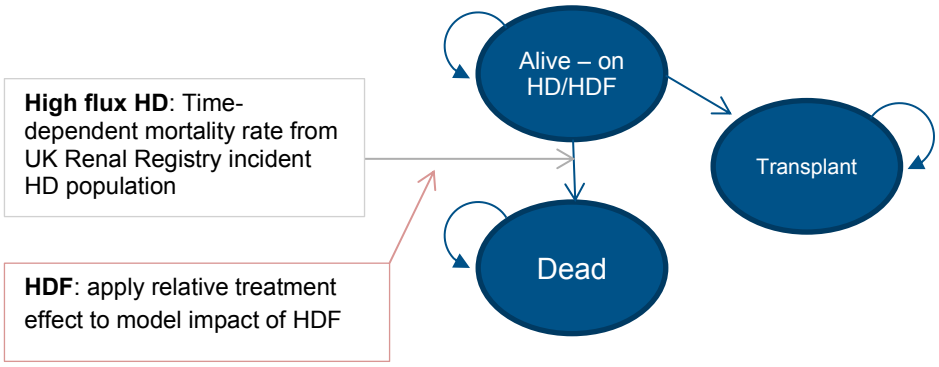
In the clinical review comparisons of HDF with both low flux HD and high flux HD were combined under the heading of HD. However, the committee highlighted that high flux HD is the current standard of care for HD and so this was considered the appropriate comparator for the economic analysis given that the difference in costs between HD and HDF will vary depending on this.

The population considered in the analysis was adults with CKD starting RRT that are naïve to RRT and have chosen dialysis using vascular access. The analysis was limited to adults as the population for children is much smaller (around 100 people), and so a lower priority for modelling, and no clinical evidence for HDF in children was identified.

Following review of the clinical evidence and committee discussion, it was agreed that the key difference in clinical outcomes that needed to be captured in the model was a benefit in terms of mortality with HDF compared to HD. The committee did not consider there to be evidence of other treatment effects. Full details of the evidence can be found in Section 1.4 above and the committee's discussion in Section 1.8 below.

A model was constructed with three health states: alive on HD or HDF, transplant and dead. Figure 1 illustrates the model structure and the possible transitions between health states each cycle. A 1 year cycle length was used. The dead and transplant states are both absorbing states. Time- and treatment-dependent rates define how quickly people in the cohort move from the alive on HD/HDF state to the dead state. Time-dependent rates define how quickly people move from the alive on HD state to the transplant state; it is assumed that transplant numbers are the same on HDF as on HD. Given this costs and outcomes incurred in this state can be excluded (the rationale for this is discussed further below). The state is included however so that the appropriate difference in number of people alive on treatment with HDF and HD is estimated by the model each cycle. People in the model cannot return to dialysis after transplant – this is a simplification of reality but was considered reasonable for modelling purposes. People in the model cannot switch to PD (data showed that a smaller number of people will make this switch and this was unlikely to vary between groups and so the committee agreed this was reasonable to exclude) or between HD and HDF.

Figure 1: Model structure



Summary of key model assumptions:

- Transplant numbers are not affected by the use of HDF and so transplant costs and outcomes can be excluded
- The HDF treatment effect observed in clinical trials can be applied while on treatment throughout the lifetime model
- People cannot switch between HD and HDF in the model
- People cannot switch to PD in the model
- People cannot return to dialysis after transplant in the model

All model inputs are summarised in Table 26 below.

Table 26: Summary of base-case model inputs

Input	Data	Source
Comparators	• High flux HD • HDF	
Population	Adults with CKD starting dialysis that are naïve to RRT	
Perspective	UK NHS & Personal Social Services	NICE reference case
Time horizon	Lifetime	NICE reference case
Discount rate	Costs: 3.5% Outcomes: 3.5%	NICE reference case
Baseline event rates		
Mortality while on HD (annual)	Time-dependent (0.140 to 0.201)	UK Renal Registry novel analysis (years 1-10); assumption (years 11+)
Transplant rate on HD (annual)	Time-dependent (0.017 to 0.060 years 1-10; zero 11 years+)	UK Renal Registry novel analysis (years 1-10); assumption (years 11+)
Relative treatment effects		
Relative difference in mortality with HDF (HR)	0.82 (0.63 to 1.06)	Systematic review of RCTs undertaken as part of guideline development[140, 252, 254, 262, 290, 322, 330, 386, 457]
Quality of life (utilities)		
HRQoL while alive on HD/HDF	0.56 (0.49 – 0.62)	Liem et al 2008[242]

Input	Data	Source
Costs		
Difference in blood line cost with HDF	£2.82 per session / £439.92 per year	Resource used based on manufacturer information, renal technologists and the committee; unit costs based on the NHS supply chain catalogue[315]
Difference in water consumption cost with HDF	£0.04 per session /£6.24 per year	Additional 15 litres per session, expert opinion; average water and sewerage cost of NHS Trusts in England 2016/17[160]
Difference in ESA cost with HDF	-£98.93 per year based on dose reduction of 4.25 U/kg/week	Meta-analysis of dose data from RCTs included in clinical review[262, 322, 386]; UK average weight from HSE 2015[304], BNF epoetin alfa costs[186]
General dialysis-related costs	£32,259 per year	Dialysis (£23,362 – NHS Reference Costs 2016-17[100]), transport (£4058 – 2016-17 data from a London Trust and working group estimate, combined with 2010 patient transport audit[309]), and 15% assumption for other costs (e.g. access related procedures, complications, health care visits, drugs)

Abbreviations: HD = haemodialysis; HDF = haemodiafiltration; ESA = erythropoietin stimulating agent ; HR = hazard ratio; HRQOL = health-related quality of life

The model was built probabilistically to take account of the uncertainty around input parameter point estimates. A probability distribution was defined for each model input parameter. When the model was run, a value for each input was randomly selected simultaneously from its respective probability distribution; mean costs and mean QALYs were calculated using these values. The model was run repeatedly – 5000 times for the base-case analysis and each sensitivity analysis – and results were summarised in terms of mean costs and QALYs, and the percentage of time HDF was the most cost-effective strategy at a threshold of £20,000/£30,000 per QALY gained.

In addition, various deterministic sensitivity analyses were undertaken to test the robustness of model assumptions. In these, one or more inputs were changed and the analysis rerun to evaluate the impact on results and whether conclusions on which intervention should be recommended would change.

In this analysis we present, alongside an analysis using the standard NICE reference case for health care interventions, results where costs incurred in additional years of life not specifically due to differences between the cost of HDF and HD are excluded. This is because the high cost of dialysis may mean that treatments that are effective in sustaining life may not be cost effective even if similar or less costly to deliver due to the additional costs of dialysis in the additional years of life.

Results

Base-case analysis results are presented in Table 27. HDF was associated with higher costs and higher QALYs. In analysis 1, using standard NICE reference case methods, the incremental cost-effectiveness ratio was £61,903 per QALY gained. This would not generally be considered cost-effective using standard NICE decision making criteria and there was

little uncertainty in this conclusion in the probabilistic analysis. In analysis 2, where only intervention cost differences are included (that is, general dialysis-related costs incurred whilst people are alive in the model are excluded), the incremental cost-effectiveness ratio was £4,384 per QALY gained. This would be considered cost-effective using standard NICE decision making criteria and there was little uncertainty in this conclusion in the probabilistic analysis. Note that uncertainty in costs was explored in sensitivity analyses – these are discussed below.

Table 27: Results: base-case analysis (probabilistic analysis)

	Mean lifetime cost per person		Difference (HDF – HD)	*95% LCI*	*95% UCI*
	HD	HDF			
Analysis 1: NICE reference case[a]					
Costs that vary with HDF vs HD	£0	£1,814	£1,814	£1,422	£2,277
Change in dialysis consumables	*£0*	£2,332	£2,332	£1,830	£2,934
Change in ESA use	*£0*	-£518	-£518	-£651	-£405
General dialysis-related costs[b]	£140,525	£168,995	£28,471	-£7,856	£71,394
Total cost	£140,525	£170,809	£30,284	-£6,458	£73,666
Total cost (discounted)	£124,299	£146,435	£22,136	-£4,807	£51,533
Life years	4.36	5.24	0.88	-0.24	2.21
QALYs	2.44	2.94	0.49	-0.14	1.25
QALYs (discounted)	2.16	2.52	0.36	-0.10	0.87
ICER (HDF versus HD)			£61,903	per QALY gained	
% simulations HDF cost-effective (£20K/QALY)			5%		
% simulations HDF cost-effective (£30K/QALY)			4%		
Analysis 2: Intervention cost differences only[c]					
Intervention cost differences only (discounted)	£0	£1,555	£1,555	£1,269	£1,872
ICER (HDF versus HD)			£4,348	per QALY gained	
% simulations HDF cost-effective (£20K/QALY)			87%		
% simulations HDF cost-effective (£30K/QALY)			90%		

Abbreviations: ESA = erythropoietin-stimulating agent; HD = haemodialysis; HDF = haemodiafiltration; LCI = 95% confidence interval lower bound; UCI = 95% confidence interval upper bound; QALY = quality-adjusted life year

(a) Includes costs intervention-related cost differences (bloodlines, water consumption and ESA use) and costs related to the condition of interest and incurred in additional years of life gained as a result of treatment.

(b) These costs vary with HDF and HD because life years vary.

(c) Includes costs intervention-related cost differences (bloodlines, water consumption and ESA use). Costs related to the condition of interest and incurred in additional years of life gained as a result of treatment are excluded.

Overall conclusions were not changed by sensitivity analyses. This included exploration around baseline mortality rate, treatment effects, quality of life weights and intervention costs differences. There were a number of uncertainties in the estimation of differences in costs with HDF compared to HD however the sensitivity analyses exploring the implications of potentially lower and higher costs did not find that conclusions were changed. This included sensitivity analyses to account for the variation in differences in bloodlines between dialysis

machines and the incorporation of potential cost differences due to differences in machine costs. In the base-case analysis a difference in intervention costs of £2.85 per session (£445 per year) was applied. A threshold analysis found that a saving of around £18 per session (-£2,829 per year) with HDF compared to HD was required to reduce the ICER to £20,000 per QALY gained in analysis 1 (NICE reference case where disease-related costs incurred in additional years of life are included) and so for HDF to be considered cost effective. An additional intervention-related cost of around £11 per session (£1,726 per year) with HDF compared to HD would result in the ICER increasing to £20,000 per QALY gained in analysis 2 (intervention cost differences only).

All results and a full discussion of limitations and interpretation of the analysis are included in the full technical report for this analysis available in a separate PDF 'Health Economic Analysis_HDFvsHD'. The committee's discussion and interpretation is summarised in Section 1.8 The committee's discussion of the evidence.

1.5.5 Unit costs

Relevant current UK unit costs were provided to the committee to aid consideration of cost effectiveness for areas where a health economic model was not developed. Key costs are summarised below. Full details of all costs are in Appendix K: Unit costs.

Note that NHS reference costs presented to the committee were generally from 2015/16 reflecting the latest data available at the time of committee meetings. However, the renal dialysis costs were updated to 2016/17 as some of these are used in the cost effectiveness analysis undertaken as part of this guideline.

1.5.5.1 Dialysis costs

1.5.5.1.1 Average annual dialysis costs based on NHS reference cost data

Standard NICE methodology is to use national cost data where available; NHS reference costs are considered a key data source for unit costs. NHS reference cost data is available for renal dialysis and so this was presented to the committee. NHS reference costs are the average unit cost to the NHS of providing defined services to NHS patients in England in a given financial year. They are based on data submitted by all Trusts in England. Note that while NHS reference costs are used to inform the national payment by results tariff the latter incorporates various adjustment and may incorporate financial incentives so they are not the same. For the purposes of assessment of cost effectiveness from an NHS perspective the NHS reference cost is the more appropriate cost as it represents the actual average cost reported by providers.

The committee noted that there have been concerns about the NHS reference costs for renal dialysis and there was therefore uncertainty about their validity. These issues are discussed in subsequent sections and additional analyses were undertaken to explore these issues. The committee took into account uncertainty around the cost of dialysis due to this during decision making (see Section 1.8 for details).

Table 28 below presents estimated annual costs for dialysis based on average unit costs from the NHS reference costs 2016-17. In-centre HD/HDF unit costs are per session, home HD/HDF unit costs are per week and PD unit costs are per day. Weighted average unit costs for each dialysis modality were calculated from all the relevant NHS reference costs categories (details in Appendix K: Unit costs). Weighting was based on activity. These costs were then used to calculate costs per person per year, assuming 3 sessions per week for in-centre HD/HDF and 7 days treatment per week for PD. NHS reference costs exclude transport costs but these have been estimated for inpatient dialysis and included in the table to facilitate comparisons between modalities given this is a substantial additional cost associated with in-centre dialysis. Details about the estimate of transport costs are described in a separate section below – it is noted that national data is not available regarding this and there is uncertainty around this cost. NHS reference cost categories do not distinguish between HD and HDF.

Table 28: Estimated average dialysis costs per person per year based on NHS reference costs 2016/17

	Cost per person per year	Activity (number of sessions)
Adults		
In-centre HD/HDF[(a)] (including transport[(b)])	£23,362 (£27,420)	2,932,931
Home HD/HDF[(c)]	£9,588	160,460
PD[(d)] (APD and CAPD)	£26,857	973,315
APD	*£27,978*	*385,597*
CAPD	*£25,148*	*587,718*

	Cost per person per year	Activity (number of sessions)
Assisted APD	£33,950	113,100
Children		
In-centre HD/HDF[a] (+transport[b])	£61,673 (£65,731)	27,730
Home HD/HDF[c]	£19,985	741
PD[d] (APD and CAPD)	£39,788	24,515
APD	*£37,923*	*12,056*
CAPD	*£41,715*	*12,459*
Assisted APD	£23,613	72

Source: Annual costs calculated based on NHS reference costs 2016/17.[100] Weighted average unit costs for each category were calculated from the NHS reference costs categories (details in Appendix K: Unit costs) and these were used to calculate costs per year. More details about calculation of cost per year are given in the footnotes under the table.

(a) NHS reference costs report in-centre HD/HDF costs per session; this is multiplied by 3 sessions per week and 52 weeks per year to calculate annual costs per person.
(b) Transport costs are excluded from the NHS reference costs and so an estimate has been added to in-centre HD to aid comparisons between modalities. An estimated average transport cost of £4058 is added based on an estimated average journey cost of £33.35 and 78% people not paying for renal transport based on a 2010 survey. See Transport cost section below for more details.
(c) NHS reference costs report home HD/HDF costs per week; annual costs per person are calculated by multiplying by 52 weeks.
(d) NHS reference costs report PD costs per day; these are multiplied by 7 day per week and 52 weeks to calculate annual costs per person.

Costs included and excluded in the NHS reference costs for renal dialysis

Providers cost reference costs on a full absorption basis, which means that all the running costs of providing these services are included within the submission. Each reported unit cost includes: (a) direct costs - relating directly to the delivery of patient care, e.g. medical staffing costs; (b) indirect costs - indirectly related to the delivery of care, but cannot always be specifically identified to individual patients, e.g. catering and linen; and (c) overhead costs - costs of support services that contribute to the effective running of the organisation, and that cannot be easily attributed to patients, e.g. payroll services. Note however that transport costs are excluded from NHS reference costs.

The Reference Costs 2016/17 Collection Guidance for the renal dialysis reference costs also states that:[314]

- Costs should include all the necessary drugs and consumables to deliver the dialysis
- The full range of staffing inputs should be allocated to all dialysis modalities including, but not limited to, medical and nursing staff (including erythropoiesis stimulating agents (ESA) management), pharmacy and medical engineering or technical staff.
- Providers should identify costs related to nutrition and dietetic staff, psychology services and social work where these are delivered at the point of dialysis.
- Costs related to IT infrastructure should be included.
- Costs should also include the revenue costs of buying and maintaining buildings and equipment, allocated appropriately between the different types of dialysis**.**
- The costs of all ESAs and drugs for bone mineral disorders should be included in the dialysis cost (as well as being reported separately where required).
- The cost of the fluids for exchange, plus the operating costs of the machine facilitating the exchange in APD should be included.
- Outpatient activities associated with each dialysis modality should be separately recorded and linked to the outpatient point of delivery e.g. pathology testing or drug prescriptions issued in clinics.

- Patient transport services, which are a significant cost component of HD services, are excluded from reference costs and therefore must be excluded from costs reported for renal dialysis services.

1.5.5.1.2 NHS reference cost quality concerns

The committee noted there had been some concerns about the quality of the NHS reference costs for dialysis and that a renal dialysis expert working group had been dissecting the costing of renal dialysis with the aim of improving data submissions. Concerns highlighted by the committee, members of the working group and/or stakeholders include that costs may be too low, not all relevant costs may be being attributed to dialysis appropriately due to the complex nature of dialysis provision, and that implausible costs are reported at the extremes from some organisations. One example highlighted was that home HD/HDF costs appeared low and were very variable and that a possible explanation for this could be that while the relevant cost unit is per week some Trusts could be reporting per session costs (as is done for in-centre HD/HDF) – this would mean that the average weekly cost based on the NHS reference costs would be too low. It was also noted that PD costs were very variable between organisations and that the cost of PD relative to in-centre HD/HDF based on the current NHS reference costs was noteably different to previous published UK estimates where PD was substantially cheaper than HD.[32]

Conversely, while there will always be some level of issue with data quality from such a data collection the issues noted with regard to renal dialysis are not necessarily greater than for reference costs in general and there are some important advantages of this data:

- Very large dataset – this means that anomalies in individual data submissions are diluted amongst the calculation of the average
- Data from all Trusts in England – all different size and location of Trust are reflected
- Collected and reported annually – costs are up-to-date

Looking at the renal dialysis data specifically the activity levels are particularly high for in-centre HD/HDF in adults which means that cost are more likely to be robust than in areas with low activity levels. The activity levels are particularly low in children reflecting the low number of children that are on dialysis.

Due to the concerns highlighted the NHS reference costs organisational level data was explored and the costs of PD and HD over time in the reference costs were also analysed. These analyses are reported in the subsequent sections.

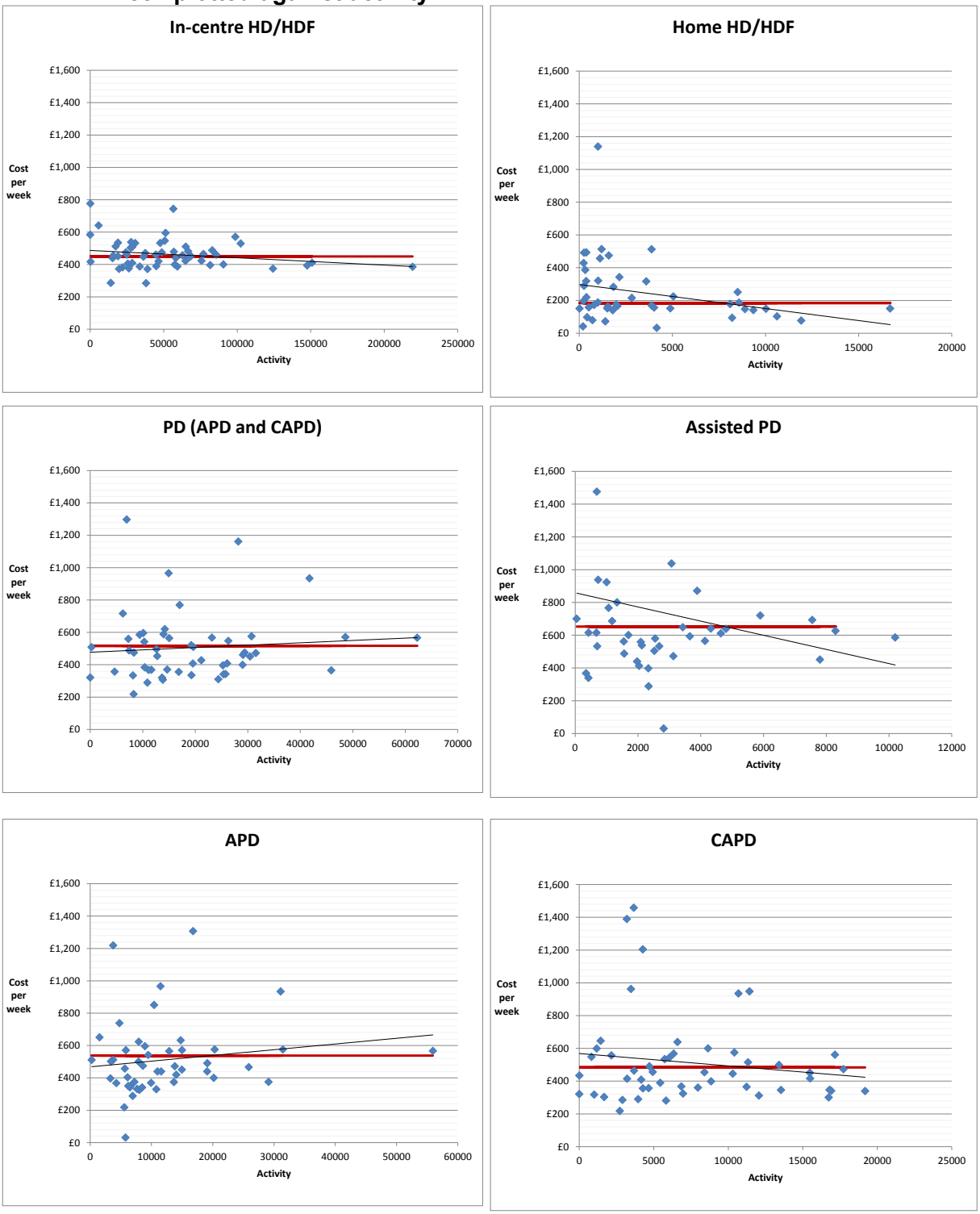
We also explored whether there were other options to obtain alternative estimates of current costs in England however no feasible better options were identified at this time.

1.5.5.1.3 NHS reference cost organisational level data analyses

To address possible concerns regarding the NHS reference costs the organisational data was explored. Figure 2 shows the cost for each dialysis modality plotted against activity level for each organisation. All costs have been converted to per week for comparison using the same methods described previously. Looking at the organisation level data, some potential errors are highlighted where particularly high or low costs are reported. As would be expected to some extent, there is variability between Trusts in reported costs. There was less variation between Trusts for in-centre HD/HDF than other modalities which may be due to the substantially higher activity level for this modality. For most modalities there was a trend between higher activity levels and lower costs although this was not the case for APD. Note that variation between trusts does not necessarily indicate a problem with data reporting; it could indicate genuine variability in costs e.g. due to local factors such as volume or geography.

The organisational level data was also explored in terms of cost differences. Figure 3 shows the cost difference per week with home HD/HDF compared to in-centre HD/HDF by organisation (for those that reported cost for both). 81% of organisations reported lower costs with home HD/HDF compared with in-centre HD/HDF. This assumes that Trusts are correctly submitting home HD/HDF costs per week; however, as described above, one stakeholder highlighted concerns that this may not always be the case. Note that this also excludes transport costs which would increase in-centre costs further. Figure 4 shows the cost difference per week with PD compared to in-centre HD/HDF by organisation (for those that reported cost for both). 54% of organisations reported higher costs with PD compared with in-centre HD/HDF. This does not take account of transport costs which are likely to reduce this considerably.

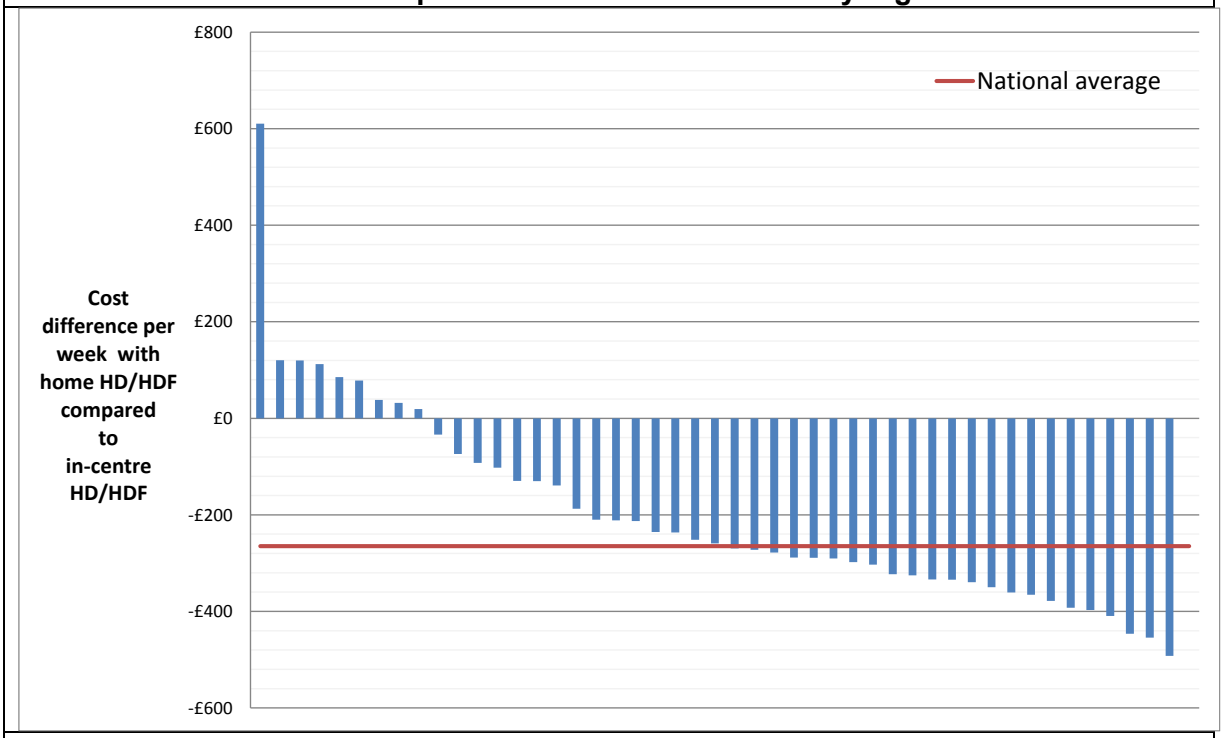
Figure 2: NHS reference costs for dialysis organisational level data (2016/17), cost per week plotted against activity



Source: Costs per week calculated based on NHS reference costs organisational level data 2016/17[100]. In-centre HD/HDF unit costs are per session, home HD/HDF unit costs are per week and PD unit costs are per day; weekly costs have been calculated for comparison by multiplying in-centre HD/HDF unit costs by 3 and PD unit costs by 7.

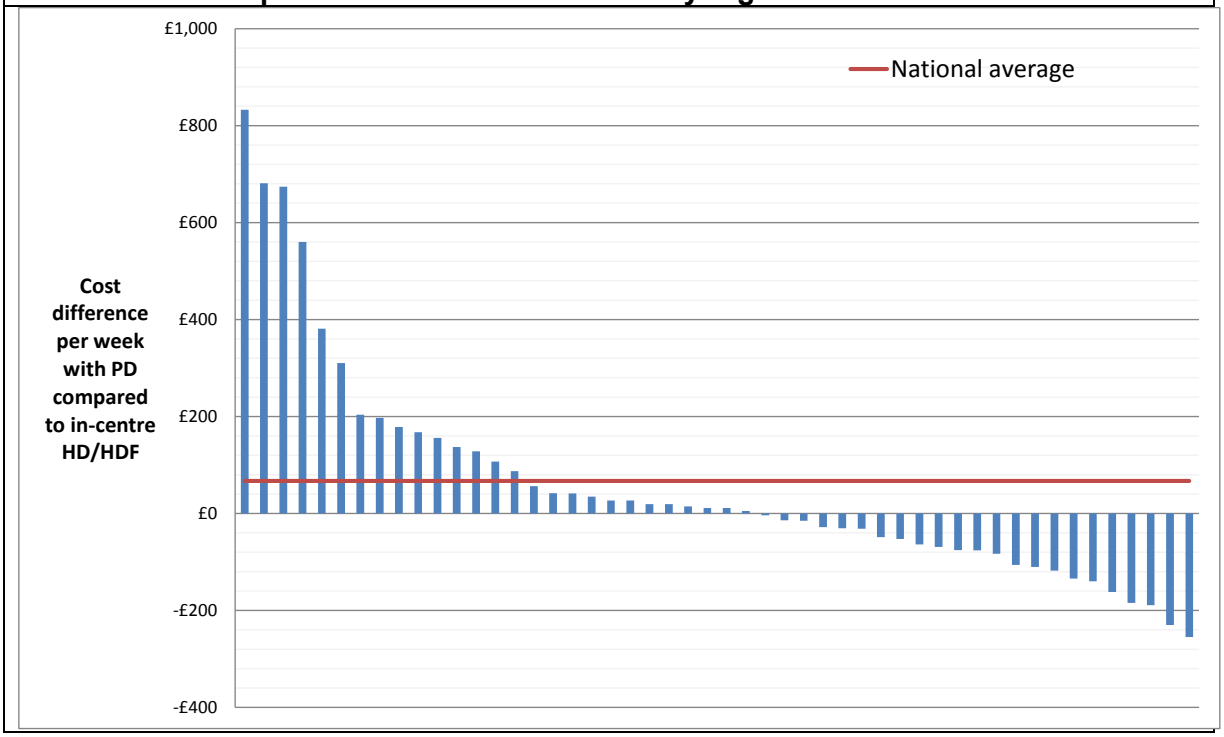
Key: blue diamonds = organisational level data; red line = national average; black line = linear trend line.

Figure 3: NHS reference costs for dialysis (2016/17), difference in cost per week with home HD/HDF compared with in-centre HD/HDF by organisation



Source: Costs per week calculated based on NHS reference costs organisational level data 2016/17[100]. In-centre HD/HDF unit costs are per session and exclude transport, home HD/HDF unit costs are per week; weekly costs have been calculated by multiplying in-centre HD/HDF costs by 3.

Figure 4: NHS reference costs for dialysis (2016/17), difference in cost per week with PD compared with in-centre HD/HDF by organisation



Source: Costs per week calculated based on NHS reference costs organisational level data 2016/17[100]. In-centre HD/HDF unit costs are per session and exclude transport, PD unit costs are per day; weekly costs have been calculated for comparison by multiply in-centre HD/HDF costs by 3 and PD costs by 7.

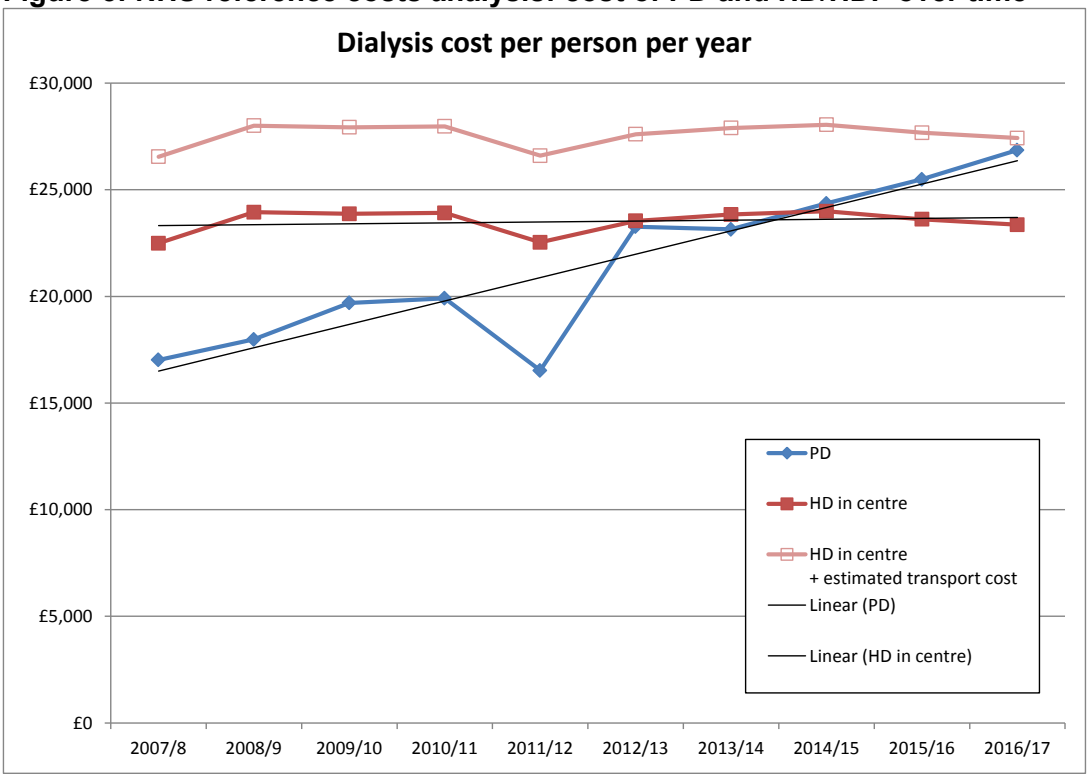
1.5.5.1.4 *Analysis of NHS reference cost data for PD and in-centre HD/HDF over time*

To address concerns about the relative costs of PD and in-centre HD/HDF based on the reference costs, cost over time for PD and in-centre HD/HDF were analysed. NHS reference costs do not include transport costs therefore estimated transport costs were added in for in-centre HD/HDF on the same basis as described above although there is some uncertainty in this estimate as national data is not available.

There has been a general perception based on the international literature that PD costs are lower than in-centre HD but this was not found in the current reference costs. As noted above a previous analysis of UK costs published in 2008 reported substantially lower costs for PD than HD.[32] In this HD costs were £35,023 in a main unit and £32,669 in a satellite unit. PD costs were £21,655 for APD and £15,570 for CAPD.

NHS reference costs for PD at the time of the 2008 paper also showed that these were substantially lower at that time. However, over the intervening period between that study and the current data, whereas in-centre HD/HDF reference costs have changed little, PD reference costs have increased year on year and the average reference costs for PD and HD are now more similar (once transport costs for in-centre HD/HDF have been accounted for).

Figure 5: NHS reference costs analysis: cost of PD and HD/HDF over time



Source: Annual costs calculated based on NHS reference costs.

2010/11 and after: weighted average unit costs for PD and in-centre HD/HDF were calculated from the NHS reference costs categories taking account of activity levels in the same way as detailed in Appendix K: Unit costs. 2009/10 and earlier: NHS reference cost dialysis categories were different and divided into inpatient, day cases, regular attendances and other. Weighted average unit costs for PD and HD/HDF were calculated using all except inpatient.

NHS reference costs report in-centre HD/HDF costs per session; this is multiplied by 3 sessions per week and 52 weeks per year to calculate annual costs per person. NHS reference costs report PD costs per day; these are multiplied by 7 day per week and 52 weeks to calculate annual costs per person.

Transport costs are excluded from the NHS reference costs and so an estimate has been added to in-centre HD/HDF costs to aid comparisons between modalities. An estimated average transport cost of £4058 is added based on an estimated average journey cost of £33.35 and 78% people not paying for renal transport based on a 2010 survey. See transport cost section below for more details.

1.5.5.1.5 Transport costs

Transport costs are not included in the NHS reference costs for dialysis (or in the NHS reference costs separately) but they are an important source of costs to the NHS as people receiving dialysis in-centre will need to come three times a week indefinitely. Data on average transport costs for dialysis patients was sought via committee members from their Trusts. In addition, ad hoc searching was undertaken to look for other relevant data.

Data was only available from one London trust. From this an average cost of a journey was estimated to be £21.70 in 2016/17. This was only for those using patient transport. Some people may use their own method of transportation but have the cost reimbursed.

An alternative estimate of £45 per journey was also suggested by a committee member. This was based on work undertaken by a dialysis transport working group a member of the committee was part of. The group involved the Renal Association and Kidney Care UK and included representation from two individuals with experience of commissioning or providing patient transport services. This estimate is a consensus informed by data from some members of the group. The data related to all patient transport (of which dialysis was estimated to be around 50%).

An average of these two costs (£33.35) has been used to estimate average transport costs and has been used in analyses in the guideline. It is noted this is based on limited data and so is somewhat uncertain.

An Audit from 2010 about dialysis patient transport reported that 78% of people do not pay for transport; that is they either use patient transport services or their transport costs are reimbursed.[309] In order to estimate an average cost per year we assumed that the cost of patient transport for those that have transport costs reimbursed is the same as the average cost using patient transport services and that people have dialysis 3 times a week. This results in an average cost per person per year of £4058 for in-centre dialysis. See also table below:

Table 29: Estimated transport costs for in-centre dialysis

Item	Data	Source
Average cost of journey	£33.35	Average of:[(a)] • £21.70: average cost per renal patient transport journey from a London Trust 2016/17 • £45: estimated average cost of a patient transport journey from a dialysis transport working group
% not paying for transport	78%	2010 audit on patient transport[309]
Sessions per year	156	Assumption based on 3 session per week
Average cost per person on in-centre dialysis, per year	**£4058**	*Using lower estimate only = £2640* *Using higher estimate only = £5476*

(a) In the absence of other data, it is assumed that the cost of a journey where the patient pays and is reimbursed is same as a patient transport journey

Some other estimates were identified and these were generally similar to the calculated value used. Kerr 2012 used a value of £2792 per HD patient in their analysis of the cost of CKD in England.[199] This was based on average transport cost (not specifically renal) and an estimate that NHS-funded transport was provided for 61% of patient journeys in England for hospital and satellite HD (data could not be accessed). Baboolal 2008 reported an estimated transport cost of £2438 and £1905 per year for hospital and satellite HD respectively as part of their dialysis cost analysis.[32] A report from Health Watch Coventry indicated that the average annual cost per patient nationally is £6000 but the source was not clear and it was unclear if this is the average cost in those that have transport paid for by the NHS only or is an average across all patients (as for the other estimates reported here).[85]

1.5.5.1.6 Other costs related to dialysis

There will also be other costs relevant to people on dialysis and these may vary between treatments:

- Access creation
- Inpatient admissions, for example due to an unplanned start on dialysis
- Complications such as infections and access complications
- Outpatient appointments

Details of UK NHS reference costs related access procedures, inpatient admissions and outpatient appointments are included in Appendix K: Unit costs.

1.5.5.2 Transplantation costs

The average cost of kidney transplantation surgery in 2015/2016 NHS reference costs was £15,232 in adults; this did not vary between live and deceased donor surgery. The average cost of live kidney donor surgery was £7,768. The average cost in children was £18,125. However, this is just the cost of the surgery itself will be additional costs related to kidney transplantation before and after surgery. Details of UK NHS reference related to transplant are included in Appendix K: Unit costs.

1.6 Resource impact

The committee has made a recommendation based on this review (see section 1.9) that HDF should be 'considered' over HD. This may result in a substantial resource impact to the NHS in England overall, although this is uncertain as it is not possible to accurately predict how widely HDF will be considered. Currently there is a mix of use of HDF and HD in the UK. The committee noted that where this recommendation changes practice additional costs are likely to be incurred relating to increased consumable costs and water consumption with HDF compared to use of HD although these may be partially offset by reductions in ESA use. There may be additional machine costs where HDF-capable machines are not currently in use; however, as it appears that most centres already have a mixture of HDF-capable and non-HDF capable machines it is considered likely that initial demand for HDF can be accommodated by existing machines and provision can be expanded if demand increases within the usual replacement cycles.

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

1.7 Evidence statements

1.7.1 Clinical evidence statements

Children and young people aged 2 to 18

Pre-emptive transplantation vs transplant after dialysis, NRS

No evidence was identified for quality of life, mortality, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from pre-emptive transplant for graft failure (1 study, very low quality).

Adults aged 18 to 70

Transplant vs dialysis, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from transplant for mortality in the general population (3 studies, low to moderate quality) and in those with a BMI ≥ 30 kg/m^2 (1 study, low quality).

PD vs HD, RCT

No evidence was identified for time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from PD for mortality (1 study, very low quality).

There was a clinically important harm from PD for quality of life (1 study, very low quality).

PD vs HD, NRS

No evidence was identified for quality of life, time to failure, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth and malignancy.

There was a clinically important benefit from PD for mortality in those with diabetes mellitus (2 studies, very low quality).

There were no clinically important benefits from PD for mortality in those without diabetes mellitus (5 studies, very low quality), hospitalisation (1 study, low quality) and adverse events-death from infection (1 study, very low quality).

There was a clinically important harm from PD for mortality in the general population (4 studies, very low quality), mortality in those with diabetes mellitus (time to event data, 3 studies, very low quality) and mortality, residual urine output (1 study, very low quality).

Transplant – pre-emptive vs after dialysis, NRS

No evidence was identified for quality of life, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from pre-emptive transplant for modality failure (2 studies, very low quality).

There was no clinically important benefit from pre-emptive transplant for mortality (1 study, very low quality).

Transplant – living vs deceased donor, NRS

No evidence was identified for quality of life, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from a living donor for mortality (1 study, very low quality) and graft failure (1study, very low quality).

HD – HDF vs HD, RCT

No evidence was identified for time to failure, preferred place of death, cognitive impairment, experience of care, growth and malignancy.

There was a clinically important benefit from HDF for mortality in the general population (9 studies, very low quality), mortality in those with diabetes mellitus (2 studies, very low quality) and mental wellbeing (1 study, very low quality).

There were no clinically important differences for quality of life (4 studies, very low to low quality), hospitalisation (3 studies, very low quality), adverse events (4 studies, very low quality).

There was a clinically important harm from HDF for symptom/function measures (2 studies, very low quality).

HD – HD >3x a week vs HD 3x a week, RCT

No evidence was identified for time to failure, preferred place of death, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth and malignancy.

There was a clinically important benefit of HD>3 times a week for mortality (4 studies, very low quality), quality of life – mental composite score and EQ-5D (4 studies, very low quality).

There were no clinically important benefits of HD>3 times a week for quality of life – physical composite score (3 studies, very low quality), hospitalisation (3 studies, very low quality), symptom/function measures (2 studies, very low quality) and infective adverse events (1 study, very low quality).

There was a clinically important harm of HD >3 times a week for vascular access adverse events (3 studies, very low quality).

HD – HD at home vs HD in centre, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from HD at home for mortality (1 study, very low quality).

PD – CAPD compared to APD/CCPD, RCT

No evidence was identified for quality of life, time to failure, preferred place of death, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth and malignancy.

There was a clinically important benefit from CAPD for mortality (1 study, very low quality).

There was no clinically important difference from CAPD for symptoms (1 study, very low quality) and adverse events (1 study, very low quality).

There was a clinically important harm from CAPD for hospitalisation (1 study, very low quality) and adverse events - peritonitis (2 studies, low quality).

PD – CAPD compared to APD/CCPD, NRS

No evidence was identified for hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There were no clinically important benefits from CAPD for quality of life – mental composite score (1 study, very low quality) and modality failure (2 studies, very low quality).

There was a clinically important harm from CAPD for quality of life – physical composite score (1 study, very low quality) and mortality (1 study, very low quality).

Adults aged over 70

RRT vs Conservative Management

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from RRT in the form of dialysis for mortality in 1 study (very low quality) but a clinically important harm from RRT in the form of dialysis/transplant for mortality in 1 study other study (very low quality).

Transplant vs dialysis, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from transplantation for mortality (1 study, low quality).

HDF vs HD, RCT

No evidence was identified for quality of life, time to failure, preferred place of death, symptom scores/functional measures, psychological distress/mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit for mortality from HDF (1 study, very low quality) and hospitalisation (1 study, very low quality).

PD vs HD, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There were no clinically important benefits from PD for mortality (TTE) in those without diabetes mellitus (2 studies, very low quality).

There was a clinically important harm from PD for mortality in the general population (1 study, very low quality), for mortality in those with diabetes mellitus (4 studies, very low quality) and mortality in those without diabetes mellitus (RR, 2 studies, very low quality).

Transplant – pre-emptive vs after up to a year of dialysis, NRS

No evidence was identified for quality of life, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from pre-emptive for mortality (1 study, very low quality) and graft failure (1 study, very low quality).

Special Populations

Adults aged 18 to 70 with diabetes mellitus (type 1 or 2)

PD vs HD in adults with diabetes, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from PD for mortality (2 studies, very low quality).

There was a clinically important harm from PD for mortality (3 studies, very low quality).

HD – HDF vs HD in people with diabetes, RCT

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from HDF for mortality (2 studies, very low quality).

Adults aged over 70 with diabetes mellitus (type 1 or 2)

PD vs HD in people aged >70 with diabetes, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important harm from PD for mortality (4 studies, very low quality).

People with residual kidney function (residual urine output)

PD vs HD, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from HD for mortality (1 study, very low quality).

People with BMI ≥ 30 kg/m^2 (obese)

Transplant vs dialysis, NRS

No evidence was identified for quality of life, time to failure, hospitalisation, preferred place of death, symptom scores/functional measures, psychological distress/ mental wellbeing, cognitive impairment, experience of care, growth, malignancy and adverse events.

There was a clinically important benefit from transplant for mortality (1 study, low quality).

1.7.2 Health economic evidence statements

PD versus HD

- One comparative cost analysis found that PD was lower cost over 3 years than HD. This analysis was assessed as partially applicable with potentially serious limitations.

HDF versus HD

- One cost–utility analysis found that HDF was not cost effective compared to low flux HD (ICERs: £140,588 to £394,058 per QALY gained depending on age subgroup). HDF was still not cost effective when costs in additional years of life were excluded. This analysis was assessed as partially applicable with potentially serious limitations.
- Another cost–utility analysis found that HDF was not cost effective compared to low flux HD (ICERs: £30,316 per QALY gained). HDF was however cost effective when a shorter

time horizon was used and was cost saving when costs in additional years of life were excluded. This analysis was assessed as partially applicable with potentially serious limitations.

- Another cost–utility analysis found that HDF was cost effective compared to high flux HD (ICER: £34,000 per QALY gained) when only considering intervention cost difference between HDF and HD (that is general dialysis costs in additional years of life were not considered). This analysis was assessed as partially applicable with potentially serious limitations.
- An original cost–utility analysis found that HDF was not cost effective compared to high flux HD (ICER: £61,903 per QALY gained) using the NICE reference case and standard decision making criteria; however this was due to the high cost of dialysis in additional years of life. HDF was cost effective compared to HD when only intervention-related cost differences were considered (that is general dialysis-related costs were excluded) (ICER: £4,348). This analysis was assessed as directly applicable with minor limitations.

HD >3x a week vs HD 3x a week

- Two cost–utility analyses found frequent in-centre HD was not cost effective compared to 3x weekly in-centre HD (ICERs: £126,106 per QALY gained and £231,028 per QALY gained respectively). These analyses were assessed as partially applicable with potentially serious limitations.
- One cost–utility analysis found that frequent home nocturnal HD was cost saving and increased QALYs compared to conventional HD (3x 4hr sessions per week; in-centre 61%, satellite 14%, home 25%). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost–utility analysis found frequent home HD was cost effective compared to 3x weekly home HD (ICER £11,706 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.

1.8 The committee's discussion of the evidence

1.8.1 Interpreting the evidence

1.8.1.1 The outcomes that matter most

Critical outcomes for modality of RRT were mortality, hospitalisations, quality of life and time to failure of RRT, meaning time until that modality of RRT was no longer working or suitable, and a modality switch occurred.

Other important outcomes were measures of mental wellbeing and cognitive impairment, malignancy and adverse events. Growth is considered an important outcome in children. We were also interested in outcomes representing people's experience of care.

The evidence found for each outcome varied between comparisons. In general comparisons in which RCTs were identified (for example the HDF vs HD comparison) reported more of the critical and important outcomes, although quality of life was still reported by relatively few studies. Comparisons in which non-randomised studies were relied on usually only reported mortality.

1.8.1.2 The quality of the evidence

In general, the committee noted a poor evidence base, especially for more established modalities. A significant RCT evidence base was found for two comparisons only.

Modality comparisons

- **Conservative management vs any specific modality**

There were two studies from the UK that were non-randomised, one starting when the decision of dialysis or conservative management was made, and the other from when CKD stage 5 was reached. They were both rated as very high risk of bias for selection bias. Both studies reported only mortality in over 75s, and the results were not consistent with each other. The committee noted that while these studies did adjust for the key confounders in the protocol, for this treatment choice it is likely to be very difficult to fully capture the differences in the populations in baseline even in an adjusted analysis.

- **Transplant vs any other modality of RRT**

There were three studies from two data sources looking at transplant versus dialysis on mortality. Outcomes were graded as moderate to low quality. No other outcomes were reported.

- **HD vs PD**

There was one small RCT with very seriously imprecise evidence across its outcomes. There were a number of large NRS that mostly reported mortality data only. The committee noted that the findings of these trials were inconsistent and not for reasons that could be explained by the underlying populations (for example contrasting findings in studies that used risk ratios and hazard ratios). The committee also noted that there were a number of important outcomes that the studies did not report on. The committee noted their concerns with the quality of the RCT evidence comparing HD and PD.

Transplant submodality comparisons

- **Pre-emptive transplantation vs transplantation after initiation of dialysis**

The committee noted that there was no RCT evidence for this comparison, but there were three NRS with a large sample size that reported graft outcome. However, there was no quality of life or mortality data in two of the studies. The study that had reported mortality was compared pre-emptive transplant with transplant taking place within one year of starting dialysis. The committee agreed that this was likely to underestimate the benefit of pre-emptive transplant, compared to an analysis that contrasted pre-emptive transplant with transplant conducted at any time after starting dialysis.

- **Living donor vs deceased donor**

There was one NRS with data for comparing living and deceased donor outcomes, but since all participants had received dialysis prior to transplant, this was marked down for indirectness, as the participants were not RRT naïve.

Peritoneal dialysis submodality comparisons

- **APD vs CAPD**

There were two randomised and two NRS of APD vs CAPD. The committee noted that APD did not include assisted PD in these studies. All outcomes for RCT and NRS studies were rated as very low quality of evidence except for peritonitis in RCTs, which is still very imprecise. The committee noted that the findings across outcomes were inconsistent in

terms of favouring either APD or CAPD, there was no biologically plausible explanation for this and the committee agreed this likely reflected the low quality of evidence as opposed to any specific effect.

No evidence was identified comparing assisted PD with any other modality of RRT.

Haemodialysis submodality comparisons

- **HDF vs HD**

There were eleven RCTs that compared HDF and HD, as a consequence NRS were not considered. The majority of findings were reported as very low quality, largely due to a combination of indirectness (studies were not typically in people who were RRT naïve), imprecision and risk of bias. The summary statistics for the population in the four largest studies appeared to be a relatively representative sample, with mean age of 63 years, prevalence of diabetes of 27%, and other comorbidities also recorded. The committee noted that the population within the trials considered for HDF vs HD were predominantly previously stable on HD and not RRT naïve, and therefore the findings may not represent the best evidence on how to start new patients. However, the committee's consensus was that if anything, HDF would be expected to be more effective in naïve patients as they would not have been exposed to potential downsides of less "efficient" forms of dialysis.

The committee noted that in one study[322] there was a discrepancy in the drop-out rate due to vascular access issues, with approximately 10% of participants dropping out in the in-centre HDF arm but none in the HD arm. The study was not explicit as to the origin of this differential drop out, however it appeared as if the inclusion criteria (based on a fistula blood flow of >250ml/min) had been applied throughout the course of the trial in the in-centre HDF arm but not in the HD arm. The committee agreed that in their experience, there was no reason to expect fistula blood flow to drop more quickly over time with in-centre HDF compared to HD. The committee noted that the differential dropout had been taken into account in the risk of bias assessment for the specified trial but retained their confidence in the overall assessment of mortality benefit for HDF as the specified trial produced an estimate in line with the overall assessment and was not highly weighted in the analysis. The committee also noted that while there may be some people who are unable to achieve a high enough blood flow through their fistula for HDF, that they would not expect this to be a significant proportion of all those in whom dialysis is otherwise considered appropriate. Furthermore, these people would also be expected to have poorer outcomes on HD.The committee noted that another of the larger studies[262] in the meta-analysis had baseline differences between the HD and HDF arms that could lead to the HD arm experiencing worse outcomes irrespective of the treatment allocation. The HD arm had older participants with more diabetes and less permanent vascular access. These baseline differences were taken into account in the study's risk of bias assessment. However the committee agreed that these differences were generally small and noted that in the multivariable analysis in that study, adjusting for those baseline differences did not lessen the apparent benefit of HDF. The committee agreed it was not appropriate to exclude this study from the analysis.

There was some degree of heterogeneity in the outcome of mortality (I^2 of 45%), therefore. pre-specified subgroup analyses were carried out. None of these subgroup analyses resolved the heterogeneity. The committee noted in particular that splitting the studies based on whether they included high flux or low flux haemodialysis as a comparator did not resolve the heterogeneity. Therefore while the committee agreed based on their experience and knowledge of the underlying mechanisms that the benefit of HDF vs HD is likely to be greater when the HD is low flux, the evidence did not definitively support this hypothesis. The committee noted that the unresolved heterogeneity was notable but neither visually nor statistically very impactful. However on balance, particularly given the potential change in practice from either HDF or HD to HDF only, the committee agreed that it was appropriate to

use a random effects meta-analysis to most conservatively estimate the certainty in the benefit of HDF. Switching to a random effects meta-analysis widened the confidence intervals but neither affected the point estimate lead to an additional downgrade for imprecision (the estimate was already downgraded once).

The evidence taken as a whole benefits from being from RCTs from a variety of providers, and mortality results were felt to be likely representative of a potentially important clinical benefit.

- **HD at home vs HD in centre**

No RCT data was found for this comparison, although there were studies comparing "frequent HD at home vs 3xwk HD in centre", which are considered in the category below. There was one NRS, but the committee did not feel that the adjustment could take into account the different populations of people who dialyse at home vs in centre based just on our key confounders, and with a low number of people at home. Therefore, the committee had very little confidence in the identified evidence.

- **HD >3x wk vs HD 3x wk**

The committee noted that although split in this evidence review, frequency >3x wk often also implies at home, and therefore, this consideration also often involves a home / centre split. However, the committee was able to consider just the issue of in-centre three times a week versus in-centre more than three times a week, as this was what happened in the largest trial. The committee raised concerns over the generalisability of the findings from the RCTs that selected for a relatively well and young population (mean age 52 years), compared to the typical UK RRT population.

There was significant heterogeneity between the four included studies, therefore a pre-specified sub-group analysis of day vs nocturnal frequent HD was carried out, as it was felt that they receive very different amounts of dialysis – nocturnal HD receiving more. Splitting to subgroups did not significantly address heterogeneity. Therefore the committee did not consider that separate recommendations based on these subgroups were appropriate.

Evidence for population strata

Age groups: There was no evidence specifically in under 2 years. For age 2-18 years, there was data only on pre-emptive vs transplant after dialysis. For adults aged 18-70 years, there was evidence for all comparisons except for conservative management vs RRT, which was only available for age 75 years and older.

There was observational level data for over 70 years to compare pre-emptive transplantation, and for over 60 and 65 years there was evidence for comparing HD vs PD. However, the committee were not confident in these results. The results were inconsistent with current clinical consensus and the committee agreed that the quality of evidence, including the impact of likely residual confounding, was not sufficiently high to justify deviating from current practice.

Diabetes: The only outcome reported was mortality. There is evidence stratified by presence of diabetes for the comparisons HD vs PD (adults and people aged > 70 years) and HDF vs HD. The evidence for HD vs PD was from non-randomised studies and was further downgraded for imprecision and/or inconsistency. The evidence for HDF vs HD was also of very low quality despite being from randomised studies. Outcomes were downgraded for risk of bias, imprecision and indirectness.

Black and Minority Ethnic groups: All studies included black and minority ethnic groups, but none reported their outcomes separately.

Unplanned starters: Only one study specified that unplanned starters were included, and none reported their outcomes separately, therefore the committee were not able to make specific recommendations based on the evidence.

BMI >30: There was one NRS study in the comparison of transplant vs dialysis that considered this group and reported mortality only. The committee noted the weakness of the evidence in terms of the non-randomised study design and agreed that the group of people with a BMI >30 that did receive a transplant were likely to be healthier than the general population of all people with a BMI >30 who may need RRT.

Residual Renal Function: There was only one NRS study that had this subgroup, in the comparison of PD vs HD. Mortality was reported and this was graded as very low quality.

1.8.1.3 Benefits and harms

Inter-modality Comparisons

- **Conservative management vs any specific modality**

The committee noted that conservative management is an active treatment option that includes symptom management and monitoring (for example fluid balance, anaemia, calcium and phosphorus) and the management of co-morbidities to improve quality of life. It is not 'no treatment'.

Conservative management is an option in a number of different groups:

i. those that choose not to undergo dialysis,

ii. those who choose to withdraw from dialysis after a period of treatment,

iii. those who are coming to the end of their lives while already on long-term dialysis,

iv. those who have a failing transplant and decide not to return to dialysis.

The committee highlighted that there is a concern that some people are automatically offered RRT when their preference may be to receive conservative management. There is also uncertainty as to whether some people may benefit less than others from RRT or may even experience harm. For example, people who have a short life expectancy and who are very frail may prefer to forego a potential for life extension in order to avoid a demanding dialysis schedule.

Evidence was only identified for the over 75 years population strata. From the evidence identified, it is not clear whether or to what extent RRT reduces mortality in frail, older people. The committee noted that regardless of the evidence available, it is not only length but quality of life that is important to people considering RRT. The committee also agreed that although the evidence was only in those over 75, there may be people in younger age categories for whom the benefit of RRT over conservative management in terms of survival is uncertain. The committee was keen to emphasise that there should not be a hard age cut-off in terms of when conservative management may be appropriate and that any decision would be based on the individual circumstances of each person.

No evidence was identified that reported factors making conservative management a better option for someone who may need RRT. The committee was able to use their experience, to say that poor prognostic factors were likely to include frailty, cognitive decline and other co-existing conditions. In their experience, people with these poor prognostic factors are also more likely to choose conservative management for themselves. Rather than defining

subsets of people to be offered conservative management, the committee felt it would be more helpful to encourage personalisation of care, with individual decisions balanced between the patient, doctor and family where appropriate. It is particularly important in this context to ensure that there is no coercion. Clinicians involved in this decision should be aware of the legal framework for capacity and consent, particularly in children.

- **Transplant vs any other modality of RRT**

Transplant offers a clear advantage in mortality for people currently receiving dialysis, and the committee felt that this was likely to be a true effect. There was no evidence on quality of life or hospitalisation, but it was the committee's opinion based on their experience that both were likely to be improved and reduced respectively by transplantation, given the return to nearer-physiological renal function and decreased treatment burden of transplant versus dialysis in the medium to long term. The committee noted that the risks of transplantation include infection, haemorrhage, thrombosis and rejection. People will have to remain on life-long immunosuppressive therapy. The mortality advantage holds across ages and in people with a raised BMI.

- **HD vs PD**

As described above the evidence for mortality was very low quality and inconsistent between studies. Overall the committee concluded that there was broadly no clinically important difference between HD and PD for mortality. There was very little additional evidence from other outcomes available (only hospitalisations and death due to infection); the committee concluded this also did not suggest a difference between treatments. The committee noted that in practice there will be different potential harms with PD and HD (for example peritonitis and EPS with PD and vascular access infections and complications with HD). The committee did not believe there was sufficient evidence to recommend one modality over the other. They remarked in particular at the evidence for the older adult strata, where there was an apparent advantage to the HD arm, whereas they had expected an advantage to PD. Therefore it was not felt possible to favour one over the other in any subgroup, and it was felt that given the lack of good quality evidence of differences between treatments and the many practical differences between the treatments that impact patients' lives in different ways, it was preferable to allow for patient and clinician choice (see see Other factors the committee took into account). The committee noted that this is in line with current practice.

Looking at outcomes in the group of patients with residual renal function/urine output showed evidence of a small, imprecise, but clinically important, increase of mortality with PD, which was in keeping with the general results, and persuaded the committee that this group did not require separate recommendations.

Transplant submodality comparisons

- **Pre-emptive transplantation vs transplantation after initiation of dialysis**

The committee noted that there was a clinically important benefit of pre-emptive transplantation in terms of time to modality failure for both under 18 years and 18-70 years. There was no clinically important benefit of transplantation in terms of mortality in the 18-70 age group, although the study reporting this outcome compared mortality for pre-emptive transplantation vs transplantation within 1 year of starting dialysis.

The committee's overall view was that the evidence justified promoting pre-emptive transplantation over transplantation after dialysis, when in the context of other considerations, including the likelihood of quality of life benefits and avoidance of complications associated with dialysis.

- **Living donor vs deceased donor**

The evidence base is small, and no absolute effect was available, but it was felt that the relative benefit of live donor transplant on mortality and graft outcome, was likely to represent a plausible clinical benefit in the population.

Peritoneal dialysis submodality comparisons

- **APD vs CAPD**

The RCT evidence shows a benefit from CAPD in mortality, but the committee had very low confidence in this finding, due to the very large confidence intervals, which included both significant benefit and harm, and the opposing direction of some of the other outcomes including hospitalisation. The committee noted the large absolute effect size of the increased risk of peritonitis in the CAPD arm at 106 extra cases per thousand, and it was noted that this was imprecise (from 18 fewer to 546 more), but plausible, and may be one factor in the risk of hospitalisation with CAPD. The committee also noted the contradictory evidence available from non-randomised studies. Overall, they felt the evidence did not favour one form over the other, and that given the practical differences between the options it was important that patients and clinicians were able to choose the one that was most suitable for the individual, and that information such as higher risk of infection in CAPD would be relevant in patient choice.

- **Assisted PD vs conventional PD**

No evidence found to recommend one over the other in the whole population.

Haemodialysis submodality comparisons

- **HDF vs HD**

The committee noted that overall there appeared to be a clinically important benefit of in-centre HDF based on mortality. The committee agreed these data showed a likely benefit, and that this could be increased if people were started on in-centre HDF as soon as they required RRT. The evidence suggested no clinically important benefit for quality of life although the committee were aware of economic evidence showing reduced medication requirements. The committee also noted that the evidence in older adults suggested a benefit of HDF in terms of hospitalisations, while the larger evidence base in adults suggested no clinically important difference between treatments for this outcome. Both comparisons were very low quality evidence but the committee agreed that given the more precise estimates in the adult population, it was not appropriate to put an emphasis on the finding in older adults in terms of decision making.

The committee discussed that the practical difference between conventional HD and HDF was very small for patients, with few identified possible adverse effects, making HDF likely to be as acceptable. The committee considered that many centres already recommend HDF if a patient is likely to be on HD for some time, and felt this should be practiced more broadly if it was shown to be cost effective.

The committee discussed the small difference between in-centre HDF and HD in terms of infections, they noted that the magnitude of the difference did not breach the clinically important boundaries that were pre-agreed. The committee also agreed that there was not an obvious biologically plausible explanation for HDF leading to more infectious events and therefore were comfortable considering this outcome to show no clinically important difference.

The role of convection volume was not an area of focus for this review. However 3 of the larger studies[140, 262, 322] reported greater benefits for HDF compared to HD in segments of their populations that achieved higher convection volumes. The committee noted that these findings were all based on post-hoc subdivisions of the evidence and used different cut-offs to classify their populations (<17.4L vs >17.4L, <18.17L vs 18.18-21.95L vs >21.95L and <23.1L vs 23.1-25.4L vs >25.4L). The committee agreed that based on the evidence it was likely that people who achieved higher convection volumes would get a greater benefit from HDF but also noted that this was not a high quality evidence base, it is not possible to choose a well defined threshold for benefit and that regardless the meta-analysis based on the overall population suggested a clinically important benefit on average. Therefore the committee chose not to make any specific reference to convection volume in the recommendations.

The committee noted that, although not an outcome prioritised for inclusion in the review, a potential additional benefit of HDF over high flux HD may be a reduction in dialysis-related amyloidosis in people on long term dialysis (for example more than 10 years). Although most people will not be on dialysis this long, where it occurs it can cause significant joint problems. It occurs due to accumulation of amyloid proteins in the body and may be improved by HDF as middle molecule clearance is greater.

In-centre HDF was clinically more effective than in-centre HD and was cost effective so the committee agreed, when dialysis via vascular access was in-centre, to recommend HDF rather than haemodialysis. Taking into account the overall strength of the evidence showing a benefit of HDF, the committee agreed it was appropriate to make this recommendation a weak recommendation.

The committee noted that it was possible that HD at home may be done more frequently. The benefits of more frequent HD are not clear but it is possible that if HD is done >3x a week at home, HDF may provide less additional benefit compared with over in centre 3x a week HD. Evidence regarding the frequency of dialysis was inconclusive and there was no evidence assessing the efficacy of HDF at home. The committee was aware that some centres do offer home HDF, although some people opt for transportable dialysis machines (which cannot do HDF currently) and these centres continue to provide home HD. The committee also noted that the additional water required for HDF may make achieving the appropriate quality of water at home challenging. Taking all of this information together, the committee agreed it was appropriate to weakly recommend either HD or HDF at home and to make a research recommendation to compare home HDF with home HD, at different frequencies.

- **HD at home vs HD in centre**

The committee discussed that there was no evidence in this review of any clinically importance differences but noted that there are other considerations in recommending home or in-centre dialysis. Based on their experience, the committee noted that some people gained a benefit to their quality of life and ability to continue with their usual daily activities when performing dialysis at home. However the committee also noted that for some people who are unable to manage their own dialysis at home or who are particularly concerned about potential adverse effects of dialysis, dialysis at home may have harms. The committee noted the intersection with increased frequency, which usually takes place at home, for which there was more evidence.

- **HD >3x wk vs HD 3x wk**

There was considerable overlap between the evidence for more frequent dialysis and dialysis at home, as mentioned above. The committee noted that there was a small but not clinically

important benefit in mortality for the >3x a week haemodialysis. A small but precise, and clinically important, benefit was also seen in quality of life, as measured on the SF-36 physical composite score. However, the committee noted that all of this evidence was in a population who have said they prepared to be potentially randomised to have more frequent dialysis than the general population. Therefore this result may be overly favourable compared with what would be seen in the general population. In terms of potential harms, HD >3x week appeared to increase the risk of vascular access adverse events.

As well as the harms identified in the evidence in terms of the need for repeated access procedures, the committee noted that for some people the increased treatment burden of HD >3x a week would not be justified. Overall the committee did not feel the clinical evidence justified recommending a deviation of clinical practice away from 3x a week for the general population but noted that certain groups may have a clinical need for more frequent dialysis such as people who are pregnant or who have chronic heart failure. The committee highlighted that currently, people who have chosen home haemodialysis may undertake dialysis more frequently as it is easier for them to do so. However the committee did not feel that the evidence was sufficient to make a recommendation on this.

Evidence for population strata

Diabetes: There is evidence stratified by presence of diabetes for the comparisons HD vs PD and HDF vs HD. The committee discussed the evidence for which appears to have a greater benefit for people with diabetes than in the general population, but it was observed that there was actually greater uncertainty in the estimate because of the subgroup size being small. It was not felt that there was a large enough difference here to merit a separate recommendation.

Black and Minority Ethnic groups: No evidence was identified and therefore the committee felt unable to make a recommendation specific to this group.

Unplanned starters: Only one study specified that unplanned starters were included, and none reported their outcomes separately, therefore the committee were not able to make specific recommendations based on the evidence.

BMI >30: Evidence from one NRS showed a clinically important benefit of transplantation (vs dialysis) in people with a BMI >30. The committee noted that some centres will not transplant people with a BMI >30. The committee agreed that the evidence suggested that people with a BMI >30 still gain a benefit from transplantation. However the committee also agreed that an elevated BMI is likely to increase surgical risks and be associated with co-existing conditions which may impact prognosis, particularly at BMI levels >40 and therefore it is appropriate to consider the impact of an elevated BMI in transplant decisions. The committee noted that the study included people with a BMI >30 but did not specify an upper limit in that cohort. The mean BMI of those included was 34.1. Overall the committee agreed that the evidence supported a recommendation not to exclude people from receiving a transplant based on BMI alone. They also noted that people should be encouraged to lose weight and/or have a dietetic referral.

Residual Renal Function: There was only one NRS study that had this subgroup, in the comparison of PD vs HD. The definition of residual renal function (>250ml urine/day at time of starting dialysis) included around 88% of people choosing PD and 81% of people choosing HD. The results did not differ significantly from those seen from other studies overall for PD vs HD.

1.8.2 Cost effectiveness and resource use

Inter-modality comparisons

- **Conservative management vs any specific modality**

No economic evaluations were included relating to this comparison. The cost of delivering conservative management is not well defined but will relate to the package of care required to help provide appropriate support including medical and nursing input and medication, for example to help manage symptoms. The committee highlighted that costs will vary between patients with some requiring little input and others a full package of care. In addition RRT sustains life and so any costs will be incurred for longer than with conservative management. Therefore choosing conservative management instead of RRT is likely to result in a lower cost in the long term.

The committee highlighted that the primarily issue was of people having the choice of conservative management as some people will prefer to forego a potential mortality benefit in order to avoid a demanding dialysis schedule or in some case putting people on dialysis may result in complications. Where people make this choice it is likely to be cost saving to the NHS but the committee highlighted that this should not influence individual patient decisions.

- **Transplant vs any other modality of RRT**

No economic evaluations were included relating to this comparison.

The total cost of a transplant will relate to assessment for suitability for transplant, preparation for transplant, the transplant inpatient episode itself and post-transplant healthcare contacts and medication, including long term immunosuppression. In addition a proportion of transplants will fail and people will require re-transplant or dialysis. Compared to dialysis the committee consider it highly likely that lifetime costs will be lower with transplant. Resource in the year of transplant itself will be fairly high but in subsequent years the costs of follow-up and immunosuppression are likely to be substantially lower than the costs of dialysis. In addition, QALYs were also considered likely to be higher in people with functioning transplants, as the clinical review found that survival was better with a transplant than on dialysis. Evidence was not identified about quality of life although, as described above, in the committee's experience this is also generally improved with a transplant; this would also increase QALYs. The committee considered it likely that transplant is cost effective compared to dialysis and this supports for a recommendation for transplant. This was considered to be in-line with current practice and unlikely to result in a substantial resource impact to the NHS in England.

- **PD vs HD**

The committee discussed current NHS reference cost data for dialysis. They highlighted that there are some concerns regarding the dialysis cost data and work is underway to improve data submissions. However, they agreed it was the best available data at this time, albeit somewhat uncertain, given it represents a very large dataset based on recent data from all Trusts in England. This data suggested dialysis costs excluding transport costs may be higher with PD than HD in adults (in-centre HD average per year based on 3 sessions per week £23,362 / PD average per year based on daily treatment £26,857); however once estimated transport costs are taken into account with in-centre HD costs appear likely to be similar (in-centre HD plus transport estimated to be around £27,000 per year). It is noted that national data was not available to inform the estimate of transport costs and so this cost is somewhat uncertain; this could impact whether PD or HD has higher dialysis costs over all. Estimated dialysis costs for assisted PD were higher (£33,950) and home HD lower (£9,588). The committee discussed that the cost of PD relative to HD based on the current NHS reference costs was notably different to previous published UK estimates where PD was substantially cheaper than HD.[32] However, analysis of the NHS reference costs over time

revealed that whereas the PD reference cost was substantially lower in 2008 when the previous report was published, in the intervening years the costs of PD had risen year on year while HD costs had remained almost unchanged. They agreed that while there are uncertainties regarding the NHS reference cost data, given the clear trend in the analysis they agreed it was likely that the difference in cost between PD and HD had reduced.

NHS reference costs are based on data submitted by all Trusts in England and should include all costs related to provision of dialysis including all related staffing, equipment, high cost drugs such as ESAs, IT infrastructure and overheads. For treatment at home it should also include conversion costs and reimbursement for utilities (e.g. electricity and water). Costs such as access creation, complications (such as access-related issues and infections) and other healthcare contacts such as outpatient appointments and inpatient stays are not included in this and could also vary. NHS reference costs suggested that average PD-access procedure costs may be lower than average HD access procedure costs. Only limited evidence was available in the clinical review regarding complications and did not suggest a difference. The committee commented that complications were likely to be different with PD and HD (for example, peritonitis with PD and vascular access complications with HD) but didn't consider it likely that this would lead to substantial differences in costs between the two options.

One published analysis was included comparing PD and HD. This was a Canadian cost comparison taking into account all direct medical costs over 3 years including dialysis costs, inpatient costs, medication costs, and physician fees. The analysis found than PD had lower costs overall than HD largely attributed to a difference in dialysis costs. Other costs appeared similar although are not reported in detail. This study was judged partially applicable; in particular Canadian costs may not be applicable and the cost savings in dialysis costs with PD in this setting may not be seen in current UK practice based on current NHS reference costs.

The clinical review did not identify any differences in clinical outcomes that might lead to differences in QALYs although no evidence was identified about quality of life.

Latest UK Renal Registry data reported that 83% of dialysis is in-centre HD, 4% home HD and 13% PD.

Overall, the committee concluded that it was uncertain if there were cost or QALY differences between in-centre HD and PD from the evidence identified but that they may be similar. They acknowledged the limitations of the current NHS reference cost data and the uncertainty in costs due to this and the lack of national data regarding the cost of transport for dialysis. The committee also highlighted that these dialysis options are very different practically in many ways and their suitability and acceptability will vary depending on individuals circumstances and preferences (see Other factors the committee took into account for more detail). Therefore the committee felt that patients should have the choice between these treatments, as is current practice. This is not considered likely to result in a substantial resource impact to the NHS in England. Home HD is discussed below.

Transplant Submodality Comparisons

- **Pre-emptive transplantation vs transplantation after initiation of dialysis**

No economic evaluations were included relating to this comparison. As pre-emptive transplant will occur before dialysis has started, it will not be offset by a reduction in dialysis costs for that time period which the committee noted would generally be around 6 months or less. However, costs of starting dialysis may be avoided such as the cost of access creation. In addition, the clinical evidence suggested a benefit of pre-emptive transplantation for modality failure which would be associated with resource use as it would mean either a second transplant procedure or switching to dialysis. The committee considered it likely that

this would offset any additional costs of pre-emptive transplant. While clinical evidence was not directly available to support a QALY difference for pre-emptive transplant the committee felt that this was likely as transplant would be undertaken earlier and so the patient would benefit from improved outcomes earlier and the lower modality failure seen in those transplanted pre-emptively would be likely to impact quality of life in the population. The committee concluded on this basis that pre-emptive transplant was likely to be cost effective. The committee noted that this is current practice and so was considered unlikely to have a substantial resource impact.

- **Living donor vs deceased donor**

No economic evaluations were included relating to this comparison.

The additional cost of living donor transplant compared to deceased donor relates to the assessment of donors (quite often multiple donors will need to be assessed to find a suitable one), preparation of the living donor for surgery, the organ retrieval surgery itself and follow-up of the donor. The costs for the recipient in terms of the transplant surgery itself are similar.

The clinical review found a mortality benefit for living donor over deceased donor transplantation, which would lead to greater QALYs. A reduction in graft failure was also seen that would likely result in cost savings and QALY benefits. There may be some long term negative health effects for the donor although these are generally considered likely to be small compared to the benefit of transplant to the recipient.

The use of living donors will also increase the number of transplants that take place overall and so the committee concluded that a recommendation to include living donor transplant as an option is likely to have cost savings and improved health benefits overall. The committee noted that this was in line with current practice and was unlikely to result in a substantial resource impact to the NHS in England.

Peritoneal dialysis submodality comparisons

- **APD vs CAPD**

No economic evaluations were included relating to this comparison. Current NHS reference costs suggested dialysis costs may be higher with APD than CAPD in adults (APD £27,978 / CAPD £25,148 per year). NHS reference costs are based on data submitted by all Trusts in England and should include all costs related to provision of dialysis. Costs such as access creation, complications (such as access-related issues and infections) and other healthcare contacts such as outpatient appointments and inpatient stays are not included in this and could also vary. The clinical review found some limited evidence suggesting hospitalisation and peritonitis may be higher with CAPD which would be associated with higher costs and this may at least partially offset any intervention cost difference. The committee considered there to be insufficient evidence to suggest a mortality difference between the treatments. No quality of life data was identified. If rates of infection and hospitalisation are lower with APD this may translate to higher QALYs, however the committee highlighted that it may be that the practical differences between APD and CAPD impact individual patients' quality of life more depending on their lifestyle and preferences.

Overall, the committee concluded that despite the potentially higher cost of APD compared to CAPD patients who wished to have PD should have the choice between these treatments, as is current practice, as they are very different practically and their suitability will vary depending on individual circumstances and preferences. These factors are discussed further in the next section.

- **Assisted PD vs conventional PD**

No economic evaluations were included relating to this comparison. Assisted PD involves someone visiting the patients home to help them undertake PD. The committee agreed that it would therefore expect the cost to be higher than conventional PD. Using current NHS reference costs the annual intervention costs of assisted APD in adults was estimated at £33,950 (this is just dialysis costs and does not include access procedures, complications, etc). This is higher than conventional PD (around £7000 higher). It is also higher than home or in-centre HD annual costs based on the NHS reference costs. Although the committee acknowledged the limitations of the current NHS reference cost data and that there is therefore uncertainty as to the estimate of the magnitude of the cost difference. Assisted PD is not that widely used currently and so a recommendation that increases its use may have a substantial resource impact to the NHS. The committee considered it to be of clinical value in some circumstances but no clinical evidence was identified. Given these considerations it was felt that a recommendation could not be made relating to assisted PD.

Haemodialysis Submodality Comparisons

- **HDF vs HD**

Three published economic evaluations were included that compared HDF with HD. Two of these were based on the same RCT (the CONTRAST study) included in the clinical review. This study compared HDF with low flux HD. The two analyses differed with one taking a Dutch perspective and using the overall CONTRAST population and the other using a Canadian perspective and the Canadian subset of the CONTRAST population that the authors described as “all receiving high efficiency HDF” (defined as online HDF performed with an optimal convection fluid volume). Both studies found intervention costs for HDF to be higher than HD due to higher costs for disposables and water treatment, and in one analysis machine costs. Total costs on treatment varied between studies with lower medication costs in the Canadian analysis, offsetting the higher intervention costs; this was not found in the Dutch analysis using the overall CONSTRAST study population. Overall total costs with HDF were higher in both analyses but for different reasons: in the Dutch analysis costs on HDF were higher and there was a small increase in survival where additional costs would be accrued; in the Canadian analysis costs on HDF were lower and so higher total costs is presumably due to costs accrued during the considerably greater survival. The committee highlighted that the comparator in the CONTRAST study was low flux HD and that high flux HD was widely used in current practice. The cost difference between high flux HD and HDF would be smaller because the cost of filters and water treatment is more similar. The committee also discussed the relatively high cost difference in medication between the two arms in the Canadian study – the committee could not see how this would happen in modern UK practice. It was noted in the Canadian study that HDF is cost-effective at 74 months but not over the lifetime. Lifetime is the preferred time horizon to fully account for QALY and cost differences when mortality is impacted. However, it was also noted that HDF would be dominant in this analysis if only intervention-related cost differences were considered. Costs incurred during additional survival present a challenge for interpretation in this therapy area due to the high costs of dialysis – the cost of dialysis would result in a cost per QALY higher than generally considered cost-effective (£20,000 per QALY gained). This means that a treatment that is more clinically effective and cheaper to deliver could come out as not cost-effective due to high costs during additional years of survival. This is an important consideration when interpreting the evidence. In the Dutch analysis, even when these costs were excluded HDF was not cost-effective. The committee also noted the funding from Fresenius in the Canadian study. A third economic evaluation compared HDF with high flux HDF using a decision model. Cost differences in terms of delivering HDF compared to HD were included in the analysis (general dialysis-related costs incurred in additional years of life were not included). It found that HDF was more expensive with higher QALYs and was cost effective. However, there was concern as to whether the costs of HDF used in the analysis

reflected current costs and all relevant costs and methods were not fully in line with NICE reference case methods.

After reviewing the published evidence, the committee considered there to be uncertainty about the cost effectiveness of HDF versus HD in the NHS setting and prioritised this area for new analysis as part of the development of the guideline given that the clinical evidence supported use of HDF but there may be additional costs and this would potentially be a substantial change in practice for the NHS. A decision model was constructed to compare HDF with high flux HD. Current UK costs of HDF were explored in detail. HDF was found likely to have higher intervention costs in terms of bloodlines and water consumption, although a reduction in ESA dose may offset this partially. Overall HDF had higher lifetime costs due to higher costs of delivering HDF compared to HD but also due to general-dialysis costs incurred in the additional years of life conferred by use of HDF. HDF was found to have higher QALYs. HDF was not cost effective using NICE reference case methods with an ICER of around £60,000 per QALY gained however this was due to the high cost of dialysis in additional years of life with HDF. When these costs were excluded the ICER reduced to around £4000 (cost differences with HDF over HD were included for the full lifetime). There is no specific methodological guidance regarding this from NICE however the problem high cost existing treatments creates in analyses such as this has been acknowledged as a methodological issue[90, 419] The committee discussed the interpretation of these results and concluded that given that dialysis is an accepted treatment despite its high cost it did not make sense to deny treatment due to costs incurred because of it and therefore felt it was more appropriate to consider the ICER where these costs were excluded (that is the analysis of intervention-related cost differences only, where general dialysis costs in additional years of life are excluded). On this basis they concluded that HDF was likely to be cost effective. This approach has been taken before, for example in NICE guideline CG157 Chronic kidney disease (stage 4 or 5): management of hyperphosphataemia.[308] There were a number of uncertainties in the estimation of differences in costs with HDF compared to HD however sensitivity analyses explored the implications of potentially lower and higher costs and this did not impact conclusions. The base-case analysis did not incorporate any cost differences due to machine costs because many current machines can do both HDF and high flux HD. However, sensitivity analyses where additional costs were included to account for potential additional machine costs did not change conclusions. A number of other sensitivity analyses were also undertaken and these did not did change conclusions. The clinical evidence found that relative treatment effects did not vary greatly in different subgroups, where evidence was available. In sensitivity analyses baseline mortality risk did not change conclusions regarding cost effectiveness and so the committee considered it reasonable to conclude that conclusions were generalizable across different subpopulations.

The committee discussed whether conclusions regarding the cost effectiveness of HDF could be extrapolated to the home setting. As discussed in the clinical evidence section above, HD at home may be done more frequently. The benefits of more frequent HD are unknown but it may be that if HD is done more than 3 times a week at home, HDF may provide less additional benefit compared with in-centre 3 times a week HD. Evidence regarding the frequency of dialysis was inconclusive and there was no evidence assessing the efficacy of HDF at home. In general the committee considered cost differences of delivering HDF compared to HD in-centre in the model (bloodlines, water consumption and ESA dose) likely to be similar at home and that there would not be any additional differences in resource use required. If HDF-capable machines suitable for home use are higher cost than those currently used there may be additional costs related to this but this was unclear due to a lack of national cost data. However, generally dialysis costs are lower at home and so costs occurred during additional years of life may be lower. Overall, HDF at home was considered likely to be cost effective when compared to home HD at the same frequency, however it was noted that none of the clinical evidence for HDF versus HD was in the home setting and there were other considerations relating to home HDF as described in the discussion of the clinical evidence above. Taking all these factors into consideration the committee concluded it was appropriate for a choice between HDF and HD to be considered in the home setting.

The committee also discussed whether conclusions could be extrapolated to children. The number of children on dialysis is much lower than adults with only around 100 people recorded as on HD in the UK Renal Registry latest report (this will include both HD and HDF). None of the RCTs comparing HDF with HD were in children. The committee considered that in general costs differences between delivering HDF and HD in children were likely to be similar to in adults although general dialysis costs are higher based on NHS reference cost data. On this basis HDF was considered likely to be cost effective when considering intervention-related cost difference only and so the committee concluded it was reasonable to extrapolate this evidence to children when making recommendations.

The committee discussed that recommending HDF may be a significant change in practice for the NHS that could have a substantial resource impact due to the additional costs associated with HDF over HD and the large numbers of people who have dialysis via vascular access. It was noted however that data obtained towards the later stages of development suggested that HDF may now be more widely used in the NHS than originally thought. An email survey of members of the Association of Renal Technologists found that amongst those that replied (9 centres, 972 machines) 68% of machines in-centre were HDF capable currently (ranging from 30% to 100%). These are not used for HDF all of the time. This is only a limited selection of renal units and so it is unknown if this is representative for the whole country. Some committee members thought that the number would be lower overall. There may be additional costs for machines where HDF-capable machines are not currently used. However, most centres appear to already have some HDF-capable machines and the committee agreed that it is likely that these will be able to accommodate any initial increased demand for HDF in-centre and provision can be expanded as demand increases within the usual replacement cycles. The committee noted that at home HDF may be less widely used than in-centre currently although they were aware that some centres do currently offer it. This however is a much smaller population (latest UK Renal Registry data reported that 4% of people use dialysis via vascular access at home) and the recommendation is for a choice between HDF and HD and so HDF uptake at home may be lower than in-centre. Given the uncertainties in the clinical data described above and the potential for a substantial resource impact to the NHS in England the committee agreed to recommend that HDF be considered over HD in centre.

- **HD at home vs HD in centre**

The committee noted that home HD is likely to have higher initial costs than in-centre HD due to the need for home modifications, purchase of a machine per person and training time in order for the person to be able to carry out HD at home but staff costs will be lower with home HD and transport costs will also be avoided. The committee discussed current NHS reference cost data for dialysis. They highlighted that there are some concerns regarding the dialysis cost data and work is underway to improve data submissions. However, they agreed it was the best available data at this time, albeit somewhat uncertain, given it represents a very large dataset based on recent data from all Trusts in England. Average annual costs calculated based on UK NHS reference costs suggested that overall dialysis costs may be lower with home HD than in-centre-HD in adults (in-centre HD average per year based on 3 sessions per week £23,362 not including transport costs / home HD average per year £9,588; unit cost is per week for home HD so no assumption regarding number of session has been made (the committee noted that some people will be having more than 3 sessions per week at home). NHS reference costs are based on data submitted by all Trusts in England and should include all costs related to provision of dialysis including all related staffing, equipment, high cost drugs such as ESAs, IT infrastructure and overheads. For treatment at home it should include also include conversion costs and reimbursement for utilities (e.g. electricity and water). The committee noted that activity in home dialysis is much lower than in-centre dialysis which may mean the costs are less reliable, that home dialysis costs appeared more variable by organisation than the in-centre costs and there also appeared to be a stronger relationship between activity level and average cost per patient. It

was also suggested by a stakeholder that home costs appeared low and were very variable and that a possible explanation for this could be that while the relevant cost unit is per week that some Trusts could be reporting per session costs (as is done for in-centre HD) – this would mean that the average weekly cost based on the NHS reference costs would be too low. The committee acknowledged the limitations of the current NHS reference cost data and that there is therefore uncertainty as to the estimate of the magnitude of the cost difference, however they agreed it is likely that costs with home HD would be lower. The NHS reference costs exclude transport costs and so these were estimated separately for in-centre dialysis so that these could be taken into account when comparing costs between modalities. Costs such as access creation, complications (such as access-related issues and infections) and other healthcare contacts such as outpatient appointments and inpatient stays are not included in this and could also vary although there was no evidence in the clinical review to inform this.

No economic evaluations were included that compared home versus in-centre HD where frequency of dialysis was the same. Note that some economic analyses were included in the frequency review where both frequency and setting varied – these are discussed in the next section.

The clinical review identified very little evidence for home versus in-centre HD (where frequency did not also vary) and it did not suggest differences in clinical outcomes that might lead to differences in QALYs between home and in-centre HD. The committee however noted that in their experience some people preferred being at home as it avoided frequent trips to hospital and allowed them to better carry on with their usual activities.

Latest UK Renal Registry data reported that 83% of dialysis is in-centre HD and 4% home HD (the rest is PD). Current good practice is to offer a choice between home and in-centre HD.

Overall, the committee concluded that it was unclear if there were QALY differences between in-centre and home HD from the evidence identified but it seemed that costs may be lower with home HD based on national UK dialysis cost data, although it was noted that there is uncertainty in current UK dialysis cost data. The committee also highlighted that these dialysis options are very different practically in many way and their suitability and acceptability will vary depending on individual's circumstances and preferences (see Other factors the committee took into account for more detail). Therefore the committee felt that patients should have the choice between these treatments, as is current practice. This is not considered likely to result in a substantial resource impact to the NHS in England.

- **HD >3x wk vs HD 3x wk**

More frequent dialysis is likely to be higher cost to deliver although it was noted that potentially sessions may be shorter if more frequent, which may impact costs. The clinical review found it to be associated with more frequent vascular access issues which will also be associated with an increase in costs. The additional costs of more frequent dialysis are likely to be lower for those dialysing at home than in-centre as the machine will be already available at home and no staff are involved so it will just be the additional cost of consumables.

Three economic evaluations presenting four analyses were included relating to frequency of dialysis. Two analyses found frequent in-centre HD was not cost effective compared to 3x weekly in-centre HD. One study found that frequent home nocturnal HD was cost saving and increased QALYs compared to conventional HD (3x 4hr sessions per week; in-centre 61%, satellite 14%, home 25%), although this conclusion was sensitive to some key sensitivity analyses, including the setting of HD 3x weekly. One analysis found frequent home HD was cost effective compared to 3x weekly home HD (ICER ~£12,000 per QALY gained) although there were a number of limitations including the weekly unit cost of more frequent dialysis

applied in the model being higher that that applied for 3x weekly home dialysis despite longer and more frequent sessions and this was not explained. Analyses were based on studies included in the clinical review and so the concerns regarding the quality of this evidence outlined in previous discussion about the clinical evidence will also affect the interpretation of these analyses. In addition, there were also assumptions involved in using the limited available evidence. Taken together the committee considered there to be uncertainty in the evidence about cost effectiveness of more frequent dialysis.

Overall given the potential for additional costs of more frequent dialysis and the uncertainty in the net clinical benefits the committee did not make a recommendation regarding frequency of dialysis.

1.8.3 Other factors the committee took into account

The committee felt that patient choice is essential and that it is important that any decisions regarding the choice of renal replacement therapy or conservative management are made through shared decision making. Enabling open and direct communication throughout the decision-making process and allowing time for questions both within the consultation and at future meetings are key. These discussions will be initiated in advance of a deterioration in the person's health. The person's preferences should be recorded in their medical notes. The committee highlighted the need to adhere to the Mental Capacity Act (2005) during discussions. The committee were aware of other existing NICE guidance on tailoring healthcare services for each patient and enabling patients to actively participate in their care in CG138 Patient experience in adult NHS services: Improving the experience of care for people using adult NHS (CG138)

The modalities are so different in their delivery of RRT that they involve undertaking very different lifestyle changes and adjustments. Factors that need to be considered include the ability to travel for in-centre haemodialysis, the ability to self-care or have someone at home to help, the capacity to store equipment and duration and frequency of dialysis sessions. It is important that the health professional understands what is important to a person so that they can support the person when making decisions about their care. Choosing the best option for the person's individual circumstances and personal preferences will enhance quality of life. If an option is not suitable or represents practical difficulties then the reason for this should be discussed with the person. See recommendations on information and support.

The committee noted that some people participate in shared haemodialysis care.

The committee were aware of the ongoing trial 'Prepare for Kidney Care Trial' that aims to investigate how older people with kidney disease make the right decision for themselves when their renal function is very low.

Switching modalities

The committee considered it important for people to regularly be given the opportunity to consider switching treatment modalities. People may begin their RRT with a certain modality based on acute need or lifestyle factors that no longer pertain later in their treatment pathway. They may also experience complications on their initially chosen modality of RRT and an alternative may be more clinically suitable. The committee agreed that currently patients are often not offered regular opportunities to discuss the option of switching treatment modality or discontinuing RRT however it was concluded that it was likely that this could be absorbed into current patient reviews and so would not result in a difference in resource use. It may be that more regular discussion will lead to an increase in switching or discontinuing. This may result in changes in resource use, for example: increased switching from HD to PD or PD to HD could increase access procedure costs and training costs; increased discontinuation from RRT would decrease RRT costs. It is uncertain if there would

be a difference in resource use overall. However, the aim of switching is to benefit the patient in terms of quality of life or clinical outcomes and potentially these benefits may be seen over a long time period given that the need for renal replacement therapy is life-long and so the committee felt that this strategy was likely to be cost effective. The committee concluded it was unlikely that there would be a substantial resource impact overall.

Intermodality comparisons

Although evidence suggests that transplantation should be first-line treatment for many, the availability of a donor kidney is the main determinant of treatment modality for these people. Therefore they may be offered treatment that is both clinically and economically less beneficial. Currently choice is usually made between the patient and clinician during the pre-dialysis assessment. Therefore choice may be more difficult to offer to unplanned starters within current structures, meaning they tend to begin on HD by default. It was discussed that this initial decision for HD should not deter shared decision-making, which could occur while the patient received RRT.

Previously clinical practice was to use PD less in older age groups but the committee noted that this no longer applies and the choice is guided more by functional ability. Lay members noted that for older people there may be a greater requirement for assistance with PD, and the availability of help was identified as an area where there is variation in clinical practice.

Transplant submodality comparisons

- **Pre-emptive transplantation vs transplantation after initiation of dialysis**

The committee noted that current clinical practice was to transplant at the point at which one would estimate that the person was six months away from requiring dialysis and that in essence this translated to transplanting at an eGFR of ~14ml/min. In addition to the evidence identified the committee noted that pre-emptive transplant reduces the risk of cardiovascular disease and complication of dialysis.

The committee noted that outside of the outcomes identified in the review, recommendations to transplant earlier in the treatment pathway would have implications for the limited resource of deceased donor pools, potentially causing a reduction in kidneys available to people already on dialysis. Matching algorithms are beyond the scope of this guideline, but obviously have a role in balancing the competing needs of individuals, and have a role in promoting equity.

Some people may participate in a kidney sharing scheme for example if they are antibody incompatible with the living donor related or known to them.

- **Living donor vs Deceased donor**

Since a living donation can often be performed pre-emptively, this has the potential to have a benefit slightly better than reported in the studies (where transplant post-dialysis is considered). However, the committee was aware that decisions regarding living donation involved consideration of the risks and benefits to the donor as well as the recipient. Early identification of a potential live donor to enable work up for pre-emptive transplantation should be encouraged. The committee discussed that the risk of complication is very low and it often had important emotional benefits – especially for parents donating to children. It was felt to be important that decisions were made without coercion, and with the knowledge of the modest average improvement in outcomes of living compared with deceased donation.

A pre-emptive transplant should be discussed in a fully informed discussion of the potential benefit and risks of all of the treatments including why some may not be an option for the individual. The guideline committee noted that some units may list for transplantation even when a living donor may also be an option.

The committee highlighted that living donors are assessed separately from the potential recipient. In particular the donor is subject to the Human Tissue Authority Independent Assessment Process.

Peritoneal Dialysis Submodality Comparisons

- **Assisted PD vs Conventional PD**

For people who cannot receive HD, but are not able to manage PD themselves, this may be the only option, and should continue to be offered in these cases. However, given the lack of evidence on assisted PD and its expense (over conventional PD) means it cannot be recommended more widely.

Haemodialysis Submodality Comparisons

- **HD at home vs HD in centre**

In general, patients suitable for home haemodialysis will be those who:

- have the ability and motivation to learn to carry out the process and the commitment to maintain treatment
- are stable on dialysis
- are free of complications and significant concomitant disease that would render home haemodialysis unsuitable or unsafe
- have good functioning vascular access
- have a carer who has (or carers who have) also made an informed decision to assist with the haemodialysis unless the individual is able to manage on his or her own
- have suitable space and facilities or an area that could be adapted within their home environment

The lay members talked about the different factors that would influence their decision – including space at home, wellness, rurality (distance to receive care e.g., in-centre dialysis may be a factor), and confidence in being able to carry out dialysis themselves or the presence of someone who could assist them. It may be that there needs to be more information given in order to facilitate patient choice. The committee noted that the opportunity of dialysing at home may also allow for people who have difficulty accessing in centre/satellite services to continue to access HD.

A recommendation to encourage patient choice on location of dialysis would be in concert with other guidance, and would not represent a large change in policy.

- **HD >3x wk vs HD 3x wk**

The committee noted that current clinical practice is typically three times a week, and considered this to be the minimum required for established RRT. However, it was also recognised that people who already dialyse at home, often take advantage of the opportunity to perform dialysis more often, and the committee supported this on an individual patient basis.

Considerations for population strata

Age groups:

The committee noted that based on their experience some elderly people find HD more intrusive than PD.

Infants, children and young people

Conservative management will generally (although not always) be less appropriate for younger, healthier people. Conservative management is rarely an option for children and should only be considered within appropriate legal frameworks. The committee were aware of NICE's guideline on end of life care for children and young people with life-limiting conditions (NG61)

The committee agreed that the remaining recommendations were applicable to infants children and young people (but see below).

Infants < 2 yrs:

The committee agreed that HD may be difficult to achieve in very young children due to difficulties with vascular access and extracorporeal blood volume. Furthermore access to lines, circuits and equipment for new born and infants may be limited. PD was therefore recommended for this group

Older adults

The committee were aware that there is a current research trail (PREPARE-ME) comparing dialysis with conservative management in this group.

Black and ethnic minority groups:

The committee were aware of registry data that reported poorer outcomes in people from BAME groups. However, in the absence of any evidence showing that any one modality was more effective for these groups than others available, they were unable to make any specific recommendations.

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Appendices

Appendix A: Review protocols

Table 30: Review protocol: Modalities of RRT

Field	Content
Review questions	What is the clinical and cost effectiveness of different modalities of renal replacement therapies and conservative management for established renal failure? Are there factors which suggest that certain forms of renal replacement therapy may be more appropriate for certain groups of people? Are there groups of people in which conservative management is more appropriate than RRT?
Type of review question	Intervention
Objective of the review	Comparing the clinical and cost effectiveness of various modalities of RRT and determining if certain populations should opt for certain modalities
Eligibility criteria – population / disease / condition / issue / domain	People requiring RRT for CKD, who were previously RRT naïve. Studies will be included where the majority of the population was RRT naïve. Studies will be downgraded for indirectness if >25% of the population was not RRT naïve. Stratified by: • Age (<2, 2 to <18, 18 to <70, ≥70) • DM vs no DM • BAME vs non-BAME • Unplanned starters vs planned starters • People with a BMI ≥30 vs BMI <30 • Residual renal function vs no residual renal function
Eligibility criteria – interventions	Haemodialysis (HD) – including home or in centre, 3 days a week or more frequently, haemodialysis or haemodiafiltration Peritoneal dialysis (PD) – including CAPD, assisted PD or APD/CCPD Transplant (TPx) – including live donor or deceased, pre-emptive or reactive Conservative management (CM)
Eligibility criteria – comparator(s) / control or reference (gold) standard	Each of the 4 main modalities (HD, PD, TPx, CM) will be compared with each other. Each of the submodalities will be pooled within the larger modalities intermodality comparisons, the submodalities will be used as subgroups to investigate any heterogeneity. Studies comparing individual submodalities within the same modality (e.g. haemodialysis vs haemodiafiltration) will be extracted and presented separately. Transplant will also be compared to dialysis (HD and/or PD) Conservative management will also be compared to any RRT (HD and/or PD and/or TPX)
Outcomes and prioritisation	Critical Patient, family/carer health-related quality of life (continuous) Mortality (dichotomous and time to event)

	Time to failure of RRT form (time to event) Hospitalisation (rates or continuous) Important Preferred place of death (dichotomous) Symptom scores and functional measures (continuous) Psychological distress and mental wellbeing (continuous) Cognitive impairment (dichotomous) Patient, family and carer experience of care (continuous) Growth (continuous) Malignancy (dichotomous) Adverse events Infections (dichotomous) Vascular access issues (dichotomous) Dialysis access issues (dichotomous) Acute transplant rejection episodes (dichotomous) Strategy: When outcomes are reported at multiple timepoints, the later timepoints will be prioritised. Mortality and hospitalisation must be reported after at least 6 months of the intervention under investigation. All other outcomes must be reported after at least 1 month of the intervention under investigation. For the outcomes of quality of life, symptom scores/functional measures, psychological distress/mental wellbeing and experience of care – any validated measure will be accepted. Absolute MIDs of 30 per 1000 will be used for mortality and modality failure. Absolute MIDs of 100 per 1000 will be used for all other outcomes dichotomous outcomes. Where relative MIDs are required (if absolute effects are unavailable), 0.90 to 1.11 will be used for mortality and modality failure. The default relative MIDs of 0.8 to 1.25 will be used for all other dichotomous outcomes. Default continuous MIDs of 0.5x SD will be used for all continuous outcomes, except where published, validated MIDs exist.
Eligibility criteria – study design	RCTs will be prioritised. If insufficient evidence is found for any specified comparisons non-randomised studies will be considered but only if outcomes are adjusted for the following key confounders: • Age • Health at baseline • Co-morbidities • Ethnicity
Other inclusion exclusion criteria	Any studies where the RRT is being delivered for acute kidney injury, not in the context of chronic kidney disease, will be excluded. Any studies where the RRT is being delivered in a level 2 or 3 care setting, will be excluded.
Proposed sensitivity / subgroup analysis, or meta-regression	Aged ≥80 vs aged <80 (included as a stratum for conservative management vs RRT) T1DM vs T2DM Submodalities (for intermodality comparisons) Nocturnal vs diurnal HD High flux HD vs low flux HD
Selection process –	A sample of at least 10% of the abstract lists were double-sifted by a

duplicate screening / selection / analysis	senior research fellow and discrepancies rectified, with committee input where consensus could not be reached, 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 Quality of life search used Medline and Embase and searched all years Language: Restrict to English only Supplementary search techniques: backward citation searching Key papers: Not known
Identify if an update	Not an update
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10019
Highlight if amendment to previous protocol	Not an amendment
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendices of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Dr Jan Dudley in line with section 3 of Developing NICE

	guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 31: 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 D.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.[307] 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 32: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 11 December 2017	Exclusions Observational studies
Embase (OVID)	1974 – 11 December 2017	Exclusions Observational studies

3. 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

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
	17 not 20

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 and quality of life studies

B.2.1 Health economic search terms

Table 33: 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

B.2.2 Quality of life search terms

Table 34: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	1946 – 11 December 2017	Exclusions Quality of life studies
Embase	1974 – 11 December 2017	Exclusions Quality of life studies

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.	(euroqol* or eq5d* or eq 5*).ti,ab.
31.	29 and 30

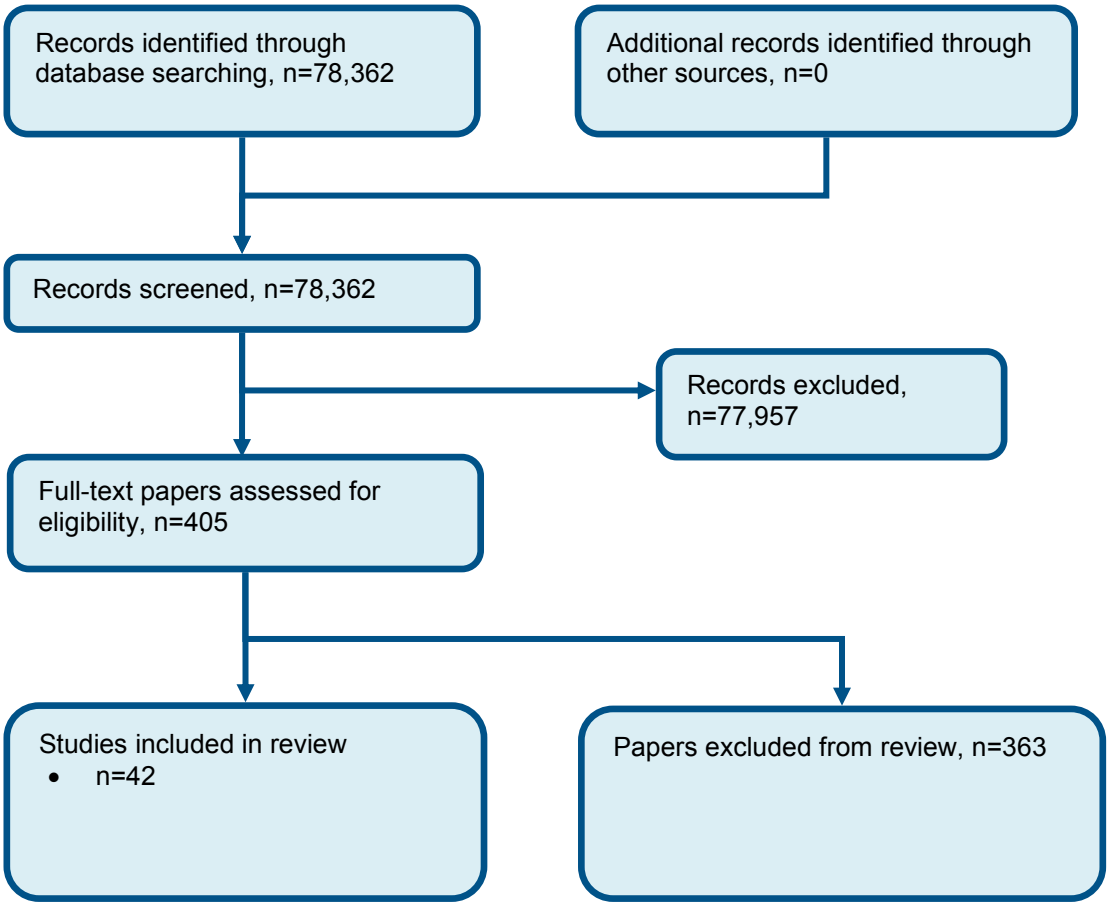
Embase (Ovid) search terms

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.	(euroqol* or eq5d* or eq 5*).ti,ab.
29.	27 and 38

Appendix C: Clinical evidence selection

Figure 6: Flow chart of clinical study selection for the review of RRT modalities



Appendix D: Clinical evidence tables

For Abbott, Glanton and Merion, see “USRDS”

Study	Amaral 2016[15]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=7527)
Countries and setting	Conducted in USA; Setting: USA
Line of therapy	1st line
Duration of study	Follow up (post intervention): Median 5.2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	<18, from USRDS, entered Medicare between 2000 and 2012
Exclusion criteria	Previous renal transplant, multiorgan transplant
Recruitment/selection of patients	All incident patients from USRDS meeting inclusion criteria
Age, gender and ethnicity	Age - Mean (SD): 10.8 (5.3. Gender (M:F): 59:41. Ethnicity: 50% white, 20% hispanic, 20% black

Further population details	
Indirectness of population	No indirectness
Interventions	(n=1668) Intervention 1: Transplant - Pre-emptive. Transplant with no history of dialysis. Duration Median follow-up 5.2 years. Concurrent medication/care: Usual care (n=5859) Intervention 2: Transplant - Not pre-emptive. Transplant after dialysis. Duration Median follow-up 5.2 years . Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PRE-EMPTIVE versus NOT PRE-EMPTIVE Protocol outcome 1: Time to failure of RRT form - Actual outcome for General population: Graft failure at Median follow-up 5.2 years; Group 1: n=1668 ; Group 2: n=5859; HR 0.75; Lower CI 0.64 to Upper CI 0.91 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	ANZDATA (dialysis) trial: Johnson 2009[183]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=21935)
Countries and setting	Conducted in Australia, New Zealand; Setting: All centres in Australia or New Zealand
Line of therapy	1st line
Duration of study	Intervention time: Up to 10 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	18 years or older, starting dialysis for CKD between 1995 and 2005 in a centre in Australia or New Zealand
Exclusion criteria	Nil recorded
Recruitment/selection of patients	ANZDATA registry data 1995-2005
Age, gender and ethnicity	Age - Mean (SD): PD 62.7(51.0-71.3), HD 60.4(47.8-70.8). Gender (M:F): 41:59. Ethnicity: White 74%
Further population details	1. Age: Not applicable (Ave 61). 2. BMI: Not applicable 3. DM: Not applicable (Prev 38%). 4. Ethnicity: Not applicable (White 74%).
Extra comments	Paper reports significant difference between PD and HD in age (HD younger), gender (HD less women), late referral (HD more), smoking (HD more), DM (PD more) and residence (HD less likely new zealand). Pt characteristics (PD/HD): BMI - underweight 4/5%, obese 20/24% Late referral - 17/28% Current smoker - 12/14% IHD - 41/40% DM - 40/37%

	Dialysis features: Started 1995-97 23/20%, started 1998-2000 27/27%, started 2001-03 31/31%, 2004-2005 18/21%. Centre in NZ 26/15%. Centre size <340pt 20/28%, size >740 29/28%
Indirectness of population	No indirectness: Inclusion criteria mean most pts will be RRT naive
Interventions	(n=15916) Intervention 1: Haemodialysis - HD (generic). Received haemodialysis as first dialysis therapy. Duration Up to 10y (mean 2.4y). Concurrent medication/care: Not controlled, observational study Comments: Proportion switching to PD was 21.1% at 6 months, 24.7% at 2 years, and 26.9% at 6 years; proportion receiving transplant 14%; recovery 0.29%, lost to FU 0.1% (n=6020) Intervention 2: Peritoneal dialysis - PD (generic). Received peritoneal dialysis as first modality of dialysis. Around 15.7% received automated PD. Duration Up to 10y (ave 3.2y). Concurrent medication/care: Not controlled, observational study Comments: Switched to HD 8.5% at six months, 27.9% at 2y, 63.6% at 6y; received transplant 10%; recovered 0.04%; lost to FU 0.1%
Funding	Principal author funded by industry (Johnson is a consultant for Baxter, and has received funds from Fresenius. Bannister is a consultant for Baxter. McDonald has received speak honoraria and travel grants from AMGEN, Fresenius, Solvay, Genzyme and Jansen-Cilag)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC)

Protocol outcome 1: AEs - infections
- Actual outcome for General population: Death from infection (after 6 months) at 6 months - 2 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Imbalance at baseline, care not standardised between groups, not clear how dealt with switching; Indirectness of outcome: Serious indirectness, Comments: Adjusted HR for overall deaths (not censored for time of occurrence) not available. There were also values for before 6m, and between 2y and 6y, and more than 6 years - which are statistically different from this result; Baseline details: Multiple indicators of imbalance, inc age, ethnicity, DM status and late referral; Key confounders: age, ethnicity, comorbidities, health at baseline (late referral used as proxy); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ;

	Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	ANZDATA registry trial: Milton 2008[293]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=2603)
Countries and setting	Conducted in Australia, New Zealand; Setting: As recorded in ANZDATA, a registry of residents in Aus and NZ who receive chronic renal replacement therapy
Line of therapy	1st line
Duration of study	Follow up (post intervention): Up to 10 years post-transplant
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients in Australia or New Zealand who received a first kidney transplant from a live donor
Exclusion criteria	Not defined
Recruitment/selection of patients	April 1991 - December 2005
Age, gender and ethnicity	Age - Mean (SD): 35y (34-36) PreT, 38y (37-38) Non-PreT. Gender (M:F): Not stated. Ethnicity: Non-indigenous 94%, Aboriginal/Torres Strait Islander 2%, Maori/Islander 4%
Further population details	1. Age: Not applicable (Ave 36). 2. BMI: Not applicable (Ave 24). 3. DM: Not applicable (Ave type1 4%, type2 5%). 4. Ethnicity: Not applicable (94% non-indigenous).
Extra comments	Demographics in the two groups are said to vary, and particularly for age (PreT younger), GFR (PreT higher), ethnicity (PreT less indigenous), heart disease (PreT less), hypertension (PreT less) and smoking (PreT less). There were no statistically significant differences in donor characteristics. Demographics between the two

	groups (PreT v Non): Age 35v38, GFR at RRT 13.1v9.9, Non-indigenous 97v93%, Hx IHD 3v7%, DM type1 3v4%, DM type2 2v5%, HTN 91v95%, BMI 23.7v23.9, current smoker 5v10%, late referral 3v18%
Indirectness of population	Serious indirectness: The distinction between pre-emptive and not has been made by the presence or absence of preceding dialysis, therefore most are not naive to RRT. Those in non-PreT started RRT an average of 1.6 years prior to transplant
Interventions	(n=578) Intervention 1: Transplant - Pre-emptive. Received a first kidney transplant without a prior period of dialysis from a living donor (related or unrelated). Duration Up to 10 years. Concurrent medication/care: Not controlled (observational study) (n=2025) Intervention 2: Transplant - Not pre-emptive. Received a first kidney transplant from a living donor (related or unrelated) after starting dialysis. Duration Up to 10 years. Concurrent medication/care: Not controlled (observational study)
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PRE-EMPTIVE versus NOT PRE-EMPTIVE

Protocol outcome 1: Time to failure of RRT form
- Actual outcome for General population: Risk of graft failure at Up to 10 years; Group 1: n=578 ; Group 2: n=2025; HR 0.8; Lower CI 0.64 to Upper CI 0.99; Test statistic: p=0.036
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Younger and healthier at baseline, confounders addressed with Cox multivariate analysis, background treatment not controlled and may be different; Indirectness of outcome: No indirectness, Comments: Corrected as reported; Baseline details: Younger, healthier; Key confounders: Age, ethnicity, comorbidity, health at commencement (variable "late referral" used as proxy); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Balasubramanian 2011[36]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=372)
Countries and setting	Conducted in United Kingdom; Setting: Single centre (Barts and The London Hospital)
Line of therapy	1st line
Duration of study	Intervention time: Ave 2.2y
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients starting peritoneal dialysis
Exclusion criteria	Define
Recruitment/selection of patients	Pts starting PD June 2003 to June 2006 had data reviewed January 2003 to January 2008
Age, gender and ethnicity	Age - Mean (SD): APD 51.2(14.5) v CAPD 57.6(15.3). Gender (M:F): 62:38. Ethnicity: White 44%, Afro-Caribbean 17%, Indian SC 33%, Other 6%
Further population details	1. Age: Not applicable (ave 55). 2. BMI: Not stated / Unclear 3. DM: Not applicable (Prev 40%). 4. Ethnicity: Not applicable (White 44%, Indian sub-Continent 33%).
Extra comments	. Prev diabetes 40%, Independent for dialysis 75%, eGFR at start 6.9, Hb at start 9.5
Indirectness of population	No indirectness: Incident dialysis pts, so most will be RRT naive

Interventions	(n=194) Intervention 1: Peritoneal dialysis - APD/CCPD. APD preferred method of dialysis. Duration Ave 2.2y (up to 4.5y). Concurrent medication/care: The same pre-dialysis team saw all patients, they received pre-PD training, and were seen at three months and at one year routinely (n=178) Intervention 2: Peritoneal dialysis - CAPD. CAPD preferred modality of dialysis. Duration Ave 2.18y (max 4.5y). Concurrent medication/care: The same pre-dialysis team saw all patients, they received pre-PD training, and were seen at three months and at one year routinely
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: APD/CCPD versus CAPD Protocol outcome 1: Quality of life - Actual outcome for General population: SF36 mental composite score at 1 year; MD; -1.5 (p-value: 0.66) pt SF36 MCS 0-100 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear what statistical methods used and whether appropriate; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Key confounders: age, ethnicity, comorbidity score, Karnofsky score (for health at baseline); Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: SF36 physical composite score at 1 year; MD; -2.2 (p-value: 0.47) pt SF36 PCS 0-100 Top=High is good outcome; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear what statistical methods used and whether appropriate; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Key confounders: age, ethnicity, comorbidity score, Karnofsky score (for health at baseline); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to failure of RRT form - Actual outcome for General population: Failure of technique at Ave 2.2y; HR; 0.751 (SE (of coefficient): 0.182)); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Very high, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear what statistical methods used and whether appropriate; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, comorbidity score, Karnofsky score (for health at baseline); Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource

	use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	BRAZPD II trial: Beduschi gde 2015[43]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=2890)
Countries and setting	Conducted in Brazil; Setting: Centres recruited into the study
Line of therapy	1st line
Duration of study	Intervention time: Up to 7 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Attending dialysis centre, received at least 90 days' PD which was exclusively APD or CAPD (not mixture of both)
Exclusion criteria	Less than 90 days' treatment
Recruitment/selection of patients	December 2004 to January 2011, 9,905 pts identified, 4198 did not receive 90 days of PD, 1308 received more than one modality
Age, gender and ethnicity	Age - Mean (SD): 59. Gender (M:F): 55:45. Ethnicity: white 50%
Further population details	1. Age: Not applicable (ave 59y). 2. BMI: Not applicable (Ave BMI 25). 3. DM: Not applicable (Prev 43%). 4. Ethnicity: Not applicable (White 50%).
Extra comments	Etiology: HTN 18%, DM 36%, G'nephritis 9%, unknown 18% BMI >25Kg/m2 41% IHD 21%, DM 43%, HTN 77%

Indirectness of population	Serious indirectness: 36% had a history of prior haemodialysis
Interventions	(n=1334) Intervention 1: Peritoneal dialysis - APD/CCPD. Received APD. Duration Up to 7 years. Concurrent medication/care: No detail given Comments: - paper does not say how decision on modality was reached (n=1556) Intervention 2: Peritoneal dialysis - CAPD. Received CAPD. Duration Up to 7 years. Concurrent medication/care: Not detailed Comments: paper does not say how decision on modality is reached
Funding	Study funded by industry (Baxter healthcare)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CAPD versus APD/CCPD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Overall mortality at Up to 7 years; Group 1: Observed events 245 ; Group 2: Observed events 305; HR 1.44; Lower CI 1.21 to Upper CI 1.71
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Indication of allocation unstated, standard of care not stated; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Group 1 Number missing: , Reason: possible that no loss as registry-type study; Group 2 Number missing:

Protocol outcome 2: Time to failure of RRT form
- Actual outcome for General population: Technique failure at Up to 7 years; HR 0.83; Lower CI 0.69 to Upper CI 1.02
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Indication of allocation unstated, standard of care not stated; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Group 1 Number missing: , Reason: possible that no loss as registry-type study; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection

episodes

Study	Bro 1999[53]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=34)
Countries and setting	Conducted in Denmark; Setting: Three Danish CAPD units
Line of therapy	1st line
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 18 or over, at least 1 month CAPD treatment judged to be adequate (creatinine clearance at least 50L/wk/1.73m3), recent peritoneal equilibration test showing high or high-average peritoneal transport characteristics and judged to be able to learn the APD technique
Exclusion criteria	Pregnancy, lactation, mental retardation or dementia, psychiatric illness, inability to speak Danish, major medical or surgical event in the last 3 months or malignancy
Recruitment/selection of patients	Total population of units 118. 34 met criteria and agreed to take part. 25 completed protocol
Age, gender and ethnicity	Age - Mean (SD): 50 (5) amongst completers. Gender (M:F): 16:9 (amongst completers). Ethnicity: Not stated
Further population details	1. Age: Not applicable (ave 52). 2. BMI: Not stated / Unclear 3. DM: Not applicable 4. Ethnicity: Not stated / Unclear
Extra comments	. Baseline characteristics for completers: Primary kidney disease (n for CAPD/ n for APD) Diabetes 3/4, HTN 1/1 glomerulonephritis 5/3 other 4/4

	Time on PD (months) 13, previous transplant 2/2, in work 1/4 Comorbidity HTN 8/7, IHD 1/2, DM 1/0* (* this appears to be incorrect, but is what is written in the paper)
Indirectness of population	Serious indirectness: Not RRT naive. Required to be stable on CAPD
Interventions	(n=17) Intervention 1: Peritoneal dialysis - APD/CCPD. Automated peritoneal dialysis. Trained by skilled PD nurse. Prescription changed for APD process based on pre-study PET, and would usually consist of nightly intermittent PD, with an added bag in the morning and an additional manual exchange in the afternoon if necessary. Duration 6 months. Concurrent medication/care: Seen monthly. Dialysis adequacy tested every 3 months (PET). Biochemical data monitored Comments: 5 patients dropped out (1 transplant, 1 request, 2 disliked APD, 1 other) (n=17) Intervention 2: Peritoneal dialysis - CAPD. Continued with previous regimen. Prescription altered during trial if necessary to maintain adequacy. Duration 6 months. Concurrent medication/care: Seen monthly. Dialysis adequacy tested every 3 months (PET). Biochemical data monitored Comments: 4 pts dropped out (1 transplant 2 decision to start HD 1 other)
Funding	Other (Danish Society of Nephrology Research Foundation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: APD/CCPD versus CAPD

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: Physical discomfort at 6 months; Group 1: mean 1.9 pt (SD 1); n=12, Group 2: mean 2.2 pt (SD 1.3); n=13; Treatment-Specific Questionnaire 1-5 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - More in APD group working, discomfort at baseline not given, unvalidated scale; Indirectness of outcome: No indirectness, Comments: One dimension of 11-item/5-dimension treatment-specific questionnaire. Appears to be author's own scale with no published validation; Baseline details: Age 54/50, female 5/4, HTN 1/1, DM 3/4, time on CAPD 15/12, yrs education 10/13, working 1/4; Group 1 Number missing: 5, Reason: dropped out; Group 2 Number missing: 4, Reason: dropped out

Protocol outcome 3: AEs - infections
- Actual outcome for General population: Peritonitis at 6 months; Group 1: 1/12, Group 2: 2/13
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - More in APD group working (not felt to be large threat, hence not downgraded twice); Indirectness of outcome: No indirectness ; Baseline details: Age 54/50, female 5/4, HTN 1/1, DM 3/4, time on CAPD 15/12, yrs

education 10/13, working 1/4; Group 1 Number missing: 5, Reason: dropped out; Group 2 Number missing: 4, Reason: dropped out - Actual outcome for General population: Exit-site infection at 6 months; Group 1: 1/12, Group 2: 1/13 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - More in APD group working (not felt to be large threat, hence not downgraded twice); Indirectness of outcome: No indirectness ; Baseline details: Age 54/50, female 5/4, HTN 1/1, DM 3/4, time on CAPD 15/12, yrs education 10/13, working 1/4; Group 1 Number missing: 5, Reason: dropped out; Group 2 Number missing: 4, Reason: dropped out	
Protocol outcomes not reported by the study	Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Chandna 2011[65]
Study type	Non randomised study
Number of studies (number of participants)	183 >75s (n=844)
Countries and setting	Conducted in United Kingdom; Setting: Nephrology clinic, Lister hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: Up to 18 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Planned starters: Late starters unlikely to be captured in this database
Subgroup analysis within study	Not applicable: Over 75s analysed separately, made up 78% of incident conservative management, and 11% of incident dialysis
Inclusion criteria	Attended nephrology clinics with chronic progressive kidney disease who registered an eGFR10-15ml/min/1.73m² (MDRD-4 equation) with all subsequent eGFR measurements <15.
Exclusion criteria	Patients presenting for the first time in advanced stage 5 CKD (eGFR<10)
Recruitment/selection of patients	Retrospective ascertainment through hospital database 1990-2008
Age, gender and ethnicity	Age - Mean (SD): age at stage 5 CKD: 60(15) overall. Gender (M:F): 65:35 (overall) 64:36 (>75s). Ethnicity: Non-white 14% (overall) 6.5% (>75s)
Further population details	1. Age: >80 (results given for >75s). 2. BMI: Not stated / Unclear 3. DM: Not applicable (51% of all pts have diabetes, 28% in over 75s). 4. Ethnicity: Not applicable (non-white 16% overall, 7% in >75s).
Extra comments	No age restriction, but >75s analysed in more detail. Characteristics of >75 cohort: Comorbidity high 39%, diabetes 28%

Indirectness of population	No indirectness: All RRT naive
Interventions	(n=689) Intervention 1: Haemodialysis - HD (generic). Following progression into stage 5 CKD they commenced haemodialysis or peritoneal dialysis, or received kidney transplant, or had intervention suggesting preparation for dialysis (such as creation of A-V fistula) but died before dialysis commenced. Duration Up to 18 years. Concurrent medication/care: Uncontrolled (n=155) Intervention 2: Conservative management. Did not receive RRT during the progression of their kidney disease (or prepared for dialysis and die before it could commence). Duration Up to 18 years. Concurrent medication/care: Patients opting for conservative management were offered ongoing support by the MDT in liaison with community, primary care and hospice services. Full medical treatment continued, which included the use of erythropoietin as appropriate to treat or prevent anaemia
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RRT (GENERIC) versus CONSERVATIVE MANAGEMENT

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for Planned starters: Mortality in over 75s at up to 18y; Group 1: n=106 ; Group 2: n=77; HR 0.85; Lower CI 0.569 to Upper CI 1.271; Test statistic: p=0.428
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference at baseline, unclear comparability of care, unclear if subgroup a priori but unlikely to compromise results; Indirectness of outcome: No indirectness ; Baseline details: Differed in age (68v82); Key confounders: age, diabetes, comorbidity score, ethnicity; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	CONvective TRAnsport STudy (CONTRAST) trial: Grooteman 2012[140] (Den Hoedt 2014[97], Den Hoedt 2015[98], Mazairac 2013[276])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=714)
Countries and setting	Conducted in Canada, Netherlands, Norway; Setting: Multi-centre trial recruited 597 in the Netherlands, 102 in Canada, 15 in Norway
Line of therapy	1st line
Duration of study	Intervention time: Study stopped early due to results Dec 2010. Follow-up range 0.4-6.6 years, median 2.9 years, mean 3.0 years.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults, treated by low-flux HD 2 or 3 times a week for at least two months, able to understand the study procedures and willing to provide written consent
Exclusion criteria	Age <18y, treatment with HDF or high-flux HD in the preceding 6 months, severe incompliance, life expectancy <3m due to non-renal disease, participation in other clinical intervention trials evaluating cardiovascular outcomes
Recruitment/selection of patients	June 2004 - December 2009
Age, gender and ethnicity	Age - Mean (SD): HDF 64.1(14.0) HD 64.0(13.4). Gender (M:F): 270:444. Ethnicity: Caucasian 84%, Afro-Caribbean 8%, Asian 6%, Other 2%
Further population details	1. Age: Not applicable (ave age 64). 2. BMI: Not applicable (ave BMI 25). 3. DM: Not applicable (DM in 24%).

	4. Ethnicity: Not applicable (84% Caucasian).
Extra comments	Baseline characteristics: Years on dialysis 2.9; vascular access AVF 80%, graft 14%, catheter 6%; 3xwk 94%; blood flow 300ml/min; residual renal function 52%. Clinical factors: CV disease 44%, diabetes 24%, Hb 11.9g/dl, BMI 25kg/m2, Albumin 40g/L Prescribed med: B-blockers 52%, ACE-ARB 49%, statin 50%
Indirectness of population	Serious indirectness: Not naive to RRT. Protocol requires 2 months stability on low-flux HD prior to commencement (6 months if new patient)
Interventions	(n=358) Intervention 1: Haemodialysis - HDF. Online HDF. Treated with a target post-dilution dose of 6 l/h (~100 ml/min) and a high-flux synthetic dialyser (UF-coefficient > 20 ml/mmHg/h). Blood flow will be set at >300 ml/min, if possible, in order to achieve a substitution volume of 100 ml/min. If the blood flow is less than 300 ml/min, the post-dilution volume will be decreased accordingly (filtration and post-dilution <25–33% of blood flow). If necessary, the dose of LMWH will be increased and given in two separate doses. Treatment times will be fixed according to the prescription in the stabilisation period and adjusted only when spKt/V urea is < 1.2 / treatment. Duration Ave 3y (total 1085 person-yr). Concurrent medication/care: Metabolic control will be performed according to the guidelines of the Quality of Care Committee of the Dutch Federation of Nephrology. Anti-hypertensive medication, lipid lowering therapy, platelet aggregation inhibitors and medication to treat renal anaemia and renal osteodystrophy will also be prescribed according to these guidelines, and, if not available, according to usual care. Comments: 121 stopped HDF, mainly due to transplant (n=356) Intervention 2: Haemodialysis - HD (generic). Low-flux haemodialysis. Low-flux synthetic dialysers (UF-coefficient < 20 ml/mmHg/h). Blood flow will be maintained at 250–400 ml/min. Anticoagulation is performed with low molecular weight heparin (LMWH) before HD. Patients on coumarins receive 50% of the LMWH dose. Treatment times will be adapted to a target dialysis spKt/V urea of ≥ 1.2 per treatment. Duration Ave 3y (total 1085 person-yrs). Concurrent medication/care: Metabolic control will be performed according to the guidelines of the Quality of Care Committee of the Dutch Federation of Nephrology. Anti-hypertensive medication, lipid lowering therapy, platelet aggregation inhibitors and medication to treat renal anaemia and renal osteodystrophy will also be prescribed according to these guidelines, and, if not available, according to usual care. Comments: 118 stopped, mainly due to transplant
Funding	Other (Dutch Kidney Foundation and Fresenius Medical Care, Netherlands, and Gambro Lundia AB, Sweden. Additional support was received from the Dr. E.E. Twiss Fund, Roche Netherlands, the International Society

	of Nephrology/Baxter Extramural Grant Program, and the Netherlands Organization for Health Research and Development.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD Protocol outcome 1: Quality of life - Actual outcome for General population: EQ5D at Ave 3y; Group 1: mean 0.74 (SD 0.19); n=205, Group 2: mean 0.73 (SD 0.38); n=204 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Mortality at >/= 6 months - Actual outcome for General population: All-Cause Mortality at Ave 3y; Group 1: Observed events 131 n=358 ; Group 2: Observed events 137 n=356; HR 0.95; Lower CI 0.75 to Upper CI 1.2 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: All-Cause Mortality at Ave 3y; Group 1: 131/358, Group 2: 138/356 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: AEs - infections - Actual outcome for General population: All infections at Ave 3y; Group 1: 118/358, Group 2: 106/356 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Etiology not included in baseline measures, adjudication by blind committee; Indirectness of outcome: No indirectness ; Baseline details: Age 64.1/64.0, female 40v35%, BAME 15v17%, CV disease 84v83%, DM 26v22%, SBP 147v148, AVF 78v81%, catheter 6v7%, 2xwk 7v5%, vintage 2.8v3.0, eGFR 2.1v2.0; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant

rejection episodes

Study	De Fijter 1994[92]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=97)
Countries and setting	Conducted in Netherlands; Setting: Single university hospital
Line of therapy	1st line
Duration of study	Intervention time: Up to 30 months (723 patient-months)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable:
Inclusion criteria	Patients referred to peritoneal dialysis for end-stage renal failure
Exclusion criteria	Absolute contraindications to peritoneal dialysis
Recruitment/selection of patients	From January 1988 - August 1991, all previously untreated patients considered, 97 randomised (50 CAPD and 47 APD), 82 started allocated intervention (41 CAPD and 41 APD)
Age, gender and ethnicity	Age - Median (range): 55 (18-86). Gender (M:F): 52:45. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 55, 42% over 60y). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	Stratified by age and sex. Primary renal disease (CAPD/APD)%: glomerulonephritis 16/23, interstitial nephritis 10/17, diabetes 16/17. nephrosclerosis 30/15, PKD 6/11, other 14/15, unknown 8/2
Indirectness of population	No indirectness

Interventions	(n=41) Intervention 1: Peritoneal dialysis - CAPD. Continuous ambulatory peritoneal dialysis with a Y-connector. Pts used the Y set without disinfectant and performed three to five daily 2-L exchanges. Duration 6-30 months. Concurrent medication/care: Standardised training for home peritoneal dialysis (on an outpatient basis) usually began within two weeks after the insertion of the peritoneal catheter. Median 8.5 days training (range 3 to 26 days) Comments: By the end of the follow-up, 11 pts still receiving. Reason for stopping: death 2, recovery 1, transplant 13, method failure 14 (n=41) Intervention 2: Peritoneal dialysis - APD/CCPD. Continuous cyclic peritoneal dialysis, using an automated cycler (PAC-X) that provided four or five nocturnal cycles and one diurnal cycle (2-L volume per cycle). Duration 6-30 months. Concurrent medication/care: Standardised training for home peritoneal dialysis (on an outpatient basis) usually began within two weeks after the insertion of the peritoneal catheter. Median 8.5 days training (range 3 to 26 days) Comments: At the end of follow-up, 16 were still using CCPD. Reasons for dropout: death 4, renal transplant 13, method failure 8
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CAPD versus APD/CCPD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death at during follow-up (6-30 months, 1411 pt months in total); Group 1: 2/41, Group 2: 4/41
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail on randomisation, limited baseline details (no ethnicity or comorbidities), background care not described, high dropout due to transplantation; Indirectness of outcome: No indirectness ; Baseline details: Female 27/25, median age 55.5/54, %>60y 42/42.5, median duration CKD tx 17.5/19.5, caused by diabetes 8/8; Group 1 Number missing: 14, Reason: 1 recovery, 13 transplant; Group 2 Number missing: 13, Reason: 13 transplant

Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations at during follow-up (6-30 months, 1411 pt months in total); rate ratio: 1.67 hospital admissions per patient per year);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail on randomisation, limited baseline details (no ethnicity or comorbidities), background care not described, high dropout due to transplantation; Indirectness of outcome: No indirectness ; Baseline details: Female 27/25, median age 55.5/54, %>60y 42/42.5, median duration CKD tx 17.5/19.5, caused by diabetes 8/8; Group 1 Number missing: 16, Reason: 2

death, 1 recovery, 13 transplant; Group 2 Number missing: 17, Reason: 4 death, 13 transplant Protocol outcome 4: AEs - infections - Actual outcome for General population: Method failure due to peritonitis at during follow-up (6-30 months, 1411 pt months in total); Group 1: 6/23, Group 2: 2/24; Comments: Number analysed calculated from patients randomised x (actual patient-months)/(potential patient-months if all randomised completed 30 months) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail on randomisation, limited baseline details (no ethnicity or comorbidities), background care not described, high dropout due to transplantation; Indirectness of outcome: No indirectness ; Baseline details: Female 27/25, median age 55.5/54, %>60y 42/42.5, median duration CKD tx 17.5/19.5, caused by diabetes 8/8; Group 1 Number missing: 16, Reason: 2 death, 1 recovery, 13 transplant; Group 2 Number missing: 17, Reason: 4 death, 13 transplant	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Estudio de Supervivencia de Hemodiafiltración On-Line (ESHOL) trial: Maduell 2013[262]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=906)
Countries and setting	Conducted in Spain; Setting: All haemodialysis units of Catalonia, either in hospital or out-hospital units
Line of therapy	1st line
Duration of study	Intervention time: Ave 1.9y (Median{IQR} 2.1 {0.86-3.00}y)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients older than 18 years with end-stage renal disease receiving thrice-weekly standard haemodialysis for more than 3 months
Exclusion criteria	Exclusion criteria consisted of active systemic diseases, liver cirrhosis, malignancies, immunosuppressor treatment, infradialysis dose (Kt/V <1.3), unipuncture dialysis and temporal nontunnelized catheter
Recruitment/selection of patients	May 2007 - September 2008. 939 identified in 27 centres. Exclusions: 18 did not meet the inclusion criteria, 5 refused to provide informed consent and 10 for logistical reasons
Age, gender and ethnicity	Age - Mean (SD): 65(14). Gender (M:F): 606:300. Ethnicity: Not stated
Further population details	1. Age: Not applicable (ave 65). 2. BMI: Not stated / Unclear 3. DM: Not applicable (Prev 25%). 4. Ethnicity: Not stated / Unclear
Extra comments	Baseline characteristics: %diabetes 24.9, Charlson comorb 6.6(2.3), time on dialysis 48.8(64) months

	Dialysis: AVF 85.8%, Catheter 10.5%, high flux 93.7%, Kt/V 1.66(0.36)
Indirectness of population	Serious indirectness: Not RRT naive, recruited people on conventional HD
Interventions	(n=456) Intervention 1: Haemodialysis - HDF. Online haemodiafiltration with post dilution, receiving a minimum of 18 litres/session replacement volume. Other aspects of HD prescription kept the same, all 3 x wk. Utilised synthetic high-flux dialyser with ultrapure dialysis fluids, the composition of which was specified in the protocol. Duration Ave 1.9y. Concurrent medication/care: Every 3 months the doses of erythropoiesis-stimulating agents, iron supplements, antihypertensive drugs and phosphate binders will be recorded Comments: 265 completed protocol, discontinuation most commonly for transplant (101/191) (n=450) Intervention 2: Haemodialysis - HD (generic). Haemodialysis to continue as previously (92% high flux, 8% low flux) using ultrapure dialysis fluid, composition specified, 3 x wk. Duration Ave 1.9y. Concurrent medication/care: Every 3 months the doses of erythropoiesis-stimulating agents, iron supplements, antihypertensive drugs and phosphate binders will be recorded Comments: 286 completed protocol, most common reason for discontinuation was transplant (79/164)
Funding	Other (Partly supported by grants from Fresenius Medical Care and Gambro Healthcare)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death at Ave 1.9y;
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete (less of a problem for HR); Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study
- Actual outcome for General population: Death at Ave 1.9y; Group 1: 85/265, Group 2: 122/286
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete; Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study
- Actual outcome for People and children with diabetes: Death at Ave 1.9y; Group 1: n=104 ; Group 2: n=122; HR 0.75; Lower CI 0.46 to Upper CI 1.21; Test statistic: p-value interaction between diabetes status and survival = 0.776

Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete (less of a problem for HR), appears to be post-hoc sg analysis; Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months - Actual outcome for General population: All-cause hospitalisation (count) at Ave 1.9y; RR; Rate ratio 0.78 (95%CI 0.67 to 0.9) (p-value: 0.001) ; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Difference in vascular access at baseline, up to 40% did not complete; Indirectness of outcome: No indirectness ; Baseline details: More use of fistula v. catheter in HDF group. Age 66v65, male 64v70, DM 27v23, CCI 7v6, using catheter 13.1v7.5; Group 1 Number missing: 191, Reason: discontinued study; Group 2 Number missing: 164, Reason: discontinued study	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	Frequent Hemodialysis Network (Daily) trial: F. H. N. Trial Group 2010[110] (Chertow 2016[70], Hall 2012[145], Kurella Tamura 2013[220], Suri 2013[408], Unruh 2013[426])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=245)
Countries and setting	Conducted in USA; Setting: 11 university-based and 54 community-based haemodialysis facilities
Line of therapy	1st line
Duration of study	Intervention + follow up: 12m intervention, with selected outcomes in sub-set after follow-up of 3y
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with renal disease requiring chronic renal replacement therapy, aged >12 years (elsewhere says 18 or over), achieved mean eKt/V ≥ 1.0 for last two baseline HD sessions, weight ≥ 30kg
Exclusion criteria	Unable or unwilling to follow the study protocol, or not consenting. Requiring HD > 3xwk (not just occasional HDF), unable to attend for HD 6xwk, or history of poor compliance. Pregnant or expecting to become so. Expecting to move such that would be unable to attend any participating HD centre. Problems with heparin, or use of any experimental drugs that may interact with treatment. Expectation that there would be kidney recovery or transplant in the next 14 months. Life expectancy < 6 month or disorder that might limit ability to complete the 12 month trial [examples listed]. Unable to undergo MRI [examples listed]. Inability to communicate verbally in English or Spanish. Vascular access is a non-tunnelled catheter.
Recruitment/selection of patients	January 2006 - March 2009, 378 identified, 133 excluded for: 6xwk not feasible (38), residual renal function (27), no MRI (18), adherence judged unlikely (13), other (37)
Age, gender and ethnicity	Age - Mean (SD): Int 49(14) Control 52(14), Gender (M:F): 38:62, Ethnicity: % Black 44, White 38, Native 9,

	Asian 6, other/mixed 10
Further population details	1. Age: Not applicable (Ave 50y. Unclear minimum age). 2. BMI: Not applicable (Ave 27.5). 3. DM: Not applicable (41% had DM 1/2). 4. Ethnicity: Not applicable (Over 50% non-white).
Extra comments	Baseline characteristics: BMI 27.5, serum creatinine 10.5(0.3), Kt/Vurea equilibrated 1.43(0.25). Etiology%: Diabetes 35, Glomerulonephritis 19, HTN 21, PKD 4. Time on dialysis: <2y 16%, >5y 45%. Comorbidities%: HTN 90, DM 41, HF 20, prev MI 10.
Indirectness of population	Serious indirectness: Not RRT naive, needed to have been on haemodialysis at time of enrolment
Interventions	(n=125) Intervention 1: Haemodialysis - HD >3x a week. Haemodialysis six times a week in a centre. The target equilibrated Kt/Vn was 0.9, with the length of the session between 1.5 and 2.75 hours. Duration 12 months. Concurrent medication/care: Prescriptions for dialysis were determined centrally and were transmitted to each clinical centre. Non-dialysis treatment that forms the minimum expected for both arms detailed in full protocol Comments: 77.7% participants attended >80% sessions (n=120) Intervention 2: Haemodialysis - HD 3x a week. Haemodialysis three times a week in-centre continued their usual dialysis prescriptions, which included a minimum target equilibrated Kt/Vurea of 1.1 and a session length of 2.5 to 4.0 hours. Duration 12 months. Concurrent medication/care: Prescriptions for dialysis were determined centrally and were transmitted to each clinical centre. Non-dialysis treatment that forms the minimum expected for both arms detailed in full protocol Comments: 94.9% participants attended >80% of sessions
Funding	Other (National Institute of Diabetes and Digestive and Kidney Diseases and National Institute of Health Research Foundation (contributors the NIH Foundation in support of the FHN trials included Amgen, inc; Baxter, inc; and Dialysis Clinics, Inc))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD >3X A WEEK versus HD 3X A WEEK

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical composite score at 12m; Group 1: mean 3.4 pt (SD 0.8); n=100, Group 2: mean 0.4 pt (SD 0.8); n=90; SF-36 PHC 0-100 Top=High is good outcome; Comments: Adjusted mean differences
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. Subjective.; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 21, Reason: Death (5), transplant (11), did not complete (5); Group 2 Number missing: 27, Reason: Death (9) transplant (13) did not complete (5)
- Actual outcome for General population: SF-36 mental health composite at 12m; Group 1: mean 3.7 pt (SD 0.9); n=100, Group 2: mean 0.2 pt (SD 1); n=89; SF-36 MHC 0-100 Top=High is good outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. Subjective.; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 21, Reason: Death (5), transplant (11), did not complete (5); Group 2 Number missing: 27, Reason: Death (9) transplant (13) did not complete (5)

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: Short physical performance score at 12m; Group 1: mean -0.2 pt (SD 0.19); n=96, Group 2: mean -0.4 pt (SD 0.21); n=81; Short Physical Performance Battery (SPPB) 0-12 Top=High is good outcome; Comments: Involves gait speed, sit to stand x5, and standing balance
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 21, Reason: Death (5), transplant (11), did not complete (5); Group 2 Number missing: 27, Reason: Death (9) transplant (13) did not complete (5)

Protocol outcome 3: Mortality at >/= 6 months
- Actual outcome for General population: Death at 3y; Group 1: 20/122, Group 2: 34/118; Comments: Breakdown by time: during trial 5v10, 1-2y 5v6, 2y+ 10v18
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness ; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%).
6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 2, Reason: ltfu; Group 2 Number missing: 3, Reason: ltfu

Protocol outcome 4: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations (count) at 12m; Rate ratio: 1.09);
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover

- Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness ; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%). 6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 1, Reason: lost to follow up; Group 2 Number missing: 1, Reason: lost to follow up Protocol outcome 7: AEs - vascular access issues - Actual outcome for General population: Underwent vascular access procedure at 12m; Group 1: 47/125, Group 2: 29/120; Comments: No of events: 65 vs 95 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Selection bias: Intervention group longer with ESRD, have less renal function and more likely to have fistula. ; Indirectness of outcome: No indirectness ; Baseline details: SPPB at baseline 8.2v8.6. Age 52/49, diabetes 50/50, black 53/49, ESRDy 3.4/3.9 (+15%), weight 78.5/81, urine<50ml/d 60v72 (+20%), fistula 71/82 (+15%). 6x group longer with ESRD, have less renal function and more likely to have fistula.; Group 1 Number missing: 1, Reason: lost to follow up; Group 2 Number missing: 1, Reason: lost to follow up	
Protocol outcomes not reported by the study	Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Preferred location of death ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	Frequent Hemodialysis Network Nocturnal trial: Rocco 2011[365] (Rocco 2015[364])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=87)
Countries and setting	Conducted in USA; Setting: University and community haemodialysis centres
Line of therapy	1st line
Duration of study	Intervention + follow up: 12 month intervention, with survival also followed over three years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	ESRD requiring chronic RRT. Age ≥ 18. Achieved mean eKt/V ≥ 1.0 for last two baseline HD sessions. Willing to perform dialysis at home.
Exclusion criteria	Unable or unwilling to carry out protocol, or give informed consent, or train to carry out HD at home. Requires >3 x wk HD or currently on daily or nocturnal HD. Expected to move to an area with no trial centres. Currently in hospital. Contraindication to Heparin, currently on any investigational drugs that could interfere, or less than three months since returned to HD due to rejected transplant. Scheduled to receive transplant within 12 months, life expectancy less than six months, or medical condition that could interfere with completing the 12 month protocol. Inability to communicate verbally in English or Spanish. Current access is temporary non-tunneled catheter.
Recruitment/selection of patients	March 2006 - May 2009. Originally aiming to recruit 250 participants, struggled to recruit, and recruitment stopped early. 118 pts identified, 31 excluded.
Age, gender and ethnicity	Age - Mean (SD): 52.8 (13.6). Gender (M:F): 30:57. Ethnicity: Black 26%, White 55%, Native 5%, Asian 14%

Further population details	1. Age: Not applicable (ave 53). 2. BMI: Not applicable (ave 29). 3. DM: Not applicable (prev 45). 4. Ethnicity: Not applicable (White 55).
Extra comments	Baseline characteristics: BMI 29, ESRD vintage <2y 55%, anuric 28%, equilibrated Kt/V 1.38, dialysis access through fistula 47%. Etiology: diabetes 35%, glomerulonephritis 36%, HTN 8%, PKD 22%. Comorbidities: HTN 90%, DM 43%, prev MI 10%, HF 14%
Indirectness of population	Serious indirectness: Not RRT naive, as have all been receiving 3xwk HD
Interventions	(n=45) Intervention 1: Haemodialysis - HD >3x a week. 6 nights per week at home dialysis following dialysis prescriptions subject to a stdKt/Urea of ≥4.0 and a treatment time of ≥6h . Duration 12m. Concurrent medication/care: All study participants were dialyzed using single-use high-flux dialyzers. A committee on standards of care, blinded to intervention, periodically reviewed and reported to clinical centres results of prespecified measures (phosphate, haemoglobin, bicarbonate, normalized protein nitrogen appearance, and blood pressure relative to achieved target post-dialysis weight) that were outside of values recommended in published guidelines. Comments: 72.7% participants dialysed at least 4.8 time per week (80% concordance) (n=42) Intervention 2: Haemodialysis - HD 3x a week. 3 days per week haemodialysis in home or at centre (depending on when recruited into study) target eKt/V ≥ 1.1/session, time ≤ 2.75h. Duration 12m. Concurrent medication/care: All study participants were dialyzed using single-use high-flux dialyzers. A committee on standards of care, blinded to intervention, periodically reviewed and reported to clinical centres results of prespecified measures (phosphate, haemoglobin, bicarbonate, normalized protein nitrogen appearance, and blood pressure relative to achieved target post-dialysis weight) that were outside of values recommended in published guidelines. Comments: 98% attended at least 2.4 treatments a week
Funding	Other (Supported by national Institute for Diabetes and Digestive and Kidney Diseases. Received some industry funding via donations to the NIH Research Foundation (Amgen, Baxter, Dialysis Clinics and Fresenius Medical Center) and through funding of authors (DaVita, Satellite Healthcare, Baxter, Eli Lilly, Amgen, Cormedix, Keryx, Nephrogenex, Merck, Sigma Tau and DCI))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD NOCTURNAL >3X WK versus HD 3X A WEEK

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical health composite at 12m; Group 1: mean 2.7 pt (SD 1.4); n=39, Group 2: mean 2.1 pt (SD 1.5); n=38; SF-36 PHC 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died
- Actual outcome for General population: SF-36 mental health composite at 12m; Group 1: mean 3 pt (SD 1.6); n=38, Group 2: mean -0.7 pt (SD 1.6); n=39; SF-36 MHC 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: Short Physical Performance Battery at 12m; Group 1: mean -0.92 pt (SD 0.44); n=34, Group 2: mean -0.41 pt (SD 0.43); n=37; SPPB score 0-12 Top=High is good outcome
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness, Comments: Adjusted as reported; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died

Protocol outcome 3: Mortality at >/= 6 months
- Actual outcome for General population: Deaths at 3y; Group 1: 14/45, Group 2: 5/42
Risk of bias: All domain - ; Indirectness of outcome: No indirectness

Protocol outcome 4: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations (count) at 12m; rate ratio: 1.34);
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37;

Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died Protocol outcome 7: AEs - vascular access issues - Actual outcome for General population: Vascular access procedures at 12m; Group 1: 23/45, Group 2: 15/42; Comments: Numbers of events 43v30 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: Age 54v52, Female% 33v36, Black% 26v27, BMI 38v30, aetiology similar, ESRD vintage<2y% 71v61, diabetes% 43v42, anuric% 26v27, fistula% 47v41. Baseline PHC 38v37; Group 1 Number missing: 6, Reason: 3 transplanted, 1 not filled in, 2 died; Group 2 Number missing: 4, Reason: 2 transplanted, 1 not filled in, 1 died	
Protocol outcomes not reported by the study	Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Preferred location of death ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Grams 2013[139]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=120,753)
Countries and setting	Conducted in USA; Setting: Public and private insurance, with data from the Organ Procurement and Transplantation Network
Line of therapy	1st line
Duration of study	Follow up (post intervention): 3 years (average)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population: Adults
Subgroup analysis within study	Not applicable
Inclusion criteria	First-time kidney-only adult deceased donor kidney transplant recipients
Exclusion criteria	Live-donor recipients
Recruitment/selection of patients	Transplant recipients from January 1, 1995 to May 31, 2011 were identified through the scientific registry of Transplant Recipients (SRTR) n=121,853
Age, gender and ethnicity	Age - Mean (SD): pre 52.7(12.5), early 50.6(13.2), late 50.9(13.0). Gender (M:F): Given as % of males/females receiving pre-emptive, early and late: 8.3/10.2, 12.0/11.6, 79.7/78.3. Ethnicity: % of the Caucasian, African American and Other ethnicities in each treatment category given but not numbers overall, i.e. 13% of Caucasians received pre, 16% received early and 70% received late; for AAs 5%, 7% and 89%; for others 5%, 9% and 86%.

Further population details	1. Age: Not applicable (Adults). 2. BMI: Not applicable (Ave BMI 27 kg/m2). 3. DM: Not applicable (Mixed). 4. Ethnicity: Not applicable (Mixed).
Extra comments	Not described in this study. Factors associated with pre-emptive transplant were zero-antigen mismatch, older recipient age, female sex, hepatitis C infection, private insurance (OR 3.2), and negatively associated with African American ethnicity (OR 0.44). Multivariable model adjusts for Recipient factors (age, sex, ethnicity, impaired functional status, reactive antibody >40%, hepatitis C virus, previous non-kidney transplant, private insurance, aetiology of kidney disease) and Transplant factors (transplant year, expanded criteria donor, non-heart-beating donor, HLA zero-mismatch, donor age, cold ischaemia time, centre)
Indirectness of population	No indirectness
Interventions	(n=10992) Intervention 1: Transplant - Pre-emptive. Transplant not preceded by dialysis. Duration up to 15 years. Concurrent medication/care: Not controlled (n=14428) Intervention 2: Transplant - Not pre-emptive. "Early" deceased donor transplant, within one year from starting dialysis. Duration Up to 15 years. Concurrent medication/care: Not controlled (n=96433) Intervention 3: Transplant - Not pre-emptive. Deceased donor transplant after more than one year on dialysis. Duration Up to 15 years. Concurrent medication/care: Not controlled Comments: Not extracted as evidence presented only in terms of statistical significance
Funding	Academic or government funding (This work was funded by the National Kidney Foundation of Maryland, National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases Grant and National Institutes of Health Grants cofunded by the American Federation of Aging Research)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY TRANSPLANT versus PRE-EMPTIVE

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death, recipient under 65y at up to 15y;
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness. Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent

	associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: Death, recipient 65y or older at up to 15y; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness, Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for General population: Graft loss, recipient 65y or older at up to 15y; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No definition of graft loss given. Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness, Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to failure of RRT form - Actual outcome for General population: Graft loss, recipient under 65y at up to 15y; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - High, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No definition of graft loss given. Between-centre variance means background care may not have been the same.; Indirectness of outcome: No indirectness, Comments: Hazard ratio from multivariate model; Baseline details: Multiple independent associations demonstrated. Model takes these into account (except blood type); Key confounders: age, ethnicity, comorbidities and health pre-transplant; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Jaar 2005[172]
Study type	Non randomised study
Number of studies (number of participants)	(n=)
Countries and setting	Conducted in USA; Setting: 81 dialysis clinics in 19 US states
Line of therapy	1st line
Duration of study	--:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	>17, starting dialysis in 1995-1998 in 81 participating dialysis clinics, oversampled for peritoneal dialysis
Exclusion criteria	None specified
Recruitment/selection of patients	None further specified
Age, gender and ethnicity	Age - Mean (SD): ~55 (14.9). Gender (M:F): Define. Ethnicity:
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	No indirectness
Interventions	(n=1041) Intervention 1: Haemodialysis - HD (generic). Generic HD, no further details provided, 5% switched type of dialysis. Duration Mean follow-up 2.4 years . Concurrent medication/care: Usual care (n=609) Intervention 2: Peritoneal dialysis - PD (generic). Generic HD, no further details provided but included

	CAPD and CCPD, 25% switched type of dialysis. Duration Mean follow-up 2.4 years . Concurrent medication/care: Usual care
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: <65 subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 1.67; Lower CI 1.01 to Upper CI 2.75
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: >65 subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 1.66; Lower CI 0.93 to Upper CI 2.97
Risk of bias: All domain - ; Indirectness of outcome: No indirectness
- Actual outcome for People and children without diabetes: No DM subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 2.78; Lower CI 1.36 to Upper CI 5.68
Risk of bias: All domain - ; Indirectness of outcome: No indirectness
- Actual outcome for People and children with diabetes: DM subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=274 ; Group 2: n=767; HR 1.23; Lower CI 0.79 to Upper CI 1.94
Risk of bias: All domain - ; Indirectness of outcome: No indirectness
- Actual outcome for General population: residual urine output subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=860 ; Group 2: n=502; HR 1.15; Lower CI 0.8 to Upper CI 1.64; Test statistic: P.interaction (residual urine output) x (PDvHD) >0.2
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Concern over baseline comparability and consistency of care; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, coexistent disease score, albumin level; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: no residual urine output subgroup, mortality at Mean follow-up 2.4 years; Group 1: n=181 ; Group 2: n=107; HR 3.78; Lower CI 1.33 to Upper CI 10.7
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Concern over baseline comparability and consistency of care; Indirectness of outcome: No indirectness ; Key confounders: age, ethnicity, coexistent disease score, albumin level; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Jain 2009[173]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=755)
Countries and setting	Conducted in United Kingdom; Setting: Four NHS units in West Midlands of UK
Line of therapy	1st line
Duration of study	Intervention + follow up: mean 4.6y
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population:
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults starting dialysis at one of four centres
Exclusion criteria	Previous transplant, died or recovered in first 90 days of dialysis
Recruitment/selection of patients	Consecutive pts from 1996 until the centre had fulfilled its allocated study slots (between 1998 and 2000)
Age, gender and ethnicity	Age - Median (range): 62 (16-86). Gender (M:F): 1.7:1. Ethnicity: White 85%, Black 3%, SE Asian 11%
Further population details	1. Age: Not applicable (18-86y). 2. BMI: Not stated / Unclear 3. DM: Not applicable (25% had DM). 4. Ethnicity: Not applicable (RR given for survival in Blacks and SE Asian, but not in interaction with treatment).
Extra comments	. Proportion starting dialysis on temporary access 39% Comorbidity score 0 - 43%, 1-2 - 48%, >2 - 9%
Indirectness of population	No indirectness: All pt naive at start of study, although those who get transplants later will have received dialysis

Interventions	(n=598) Intervention 1: Haemodialysis - HD (generic). Undifferentiated dialysis for >90 days, with no transplantation before follow-up finished. Duration mean 4.6y +/- 3.1y. Concurrent medication/care: Uncontrolled Comments: Ratio HD:PD overall 2.6:1 (n=157) Intervention 2: Transplant - Transplant (generic). Received dialysis for at least 90 days, and went on to receive a kidney transplant. Duration mean 4.6y +/- 3.1y. Concurrent medication/care: Uncontrolled
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIALYSIS (GENERIC) versus TRANSPLANT (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Death (adjusted) at 4.6y; RR; 0.20 (95%CI 0.11 to 0.34); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Differences at baseline, no comparability of care; Indirectness of outcome: No indirectness ; Baseline details: Differences reached stat sig for age, ethnicity, presence of diabetes, glomerulonephritis; Key confounders: age, individual comorbidity, comorbidity score, ethnicity; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Kantartzi 2013[192]
Study type	RCT (Patient randomised; Crossover: Adequate, according to protocol)
Number of studies (number of participants)	1 (n=24)
Countries and setting	Conducted in Greece; Setting: Appears to be performed at one university hospital
Line of therapy	1st line
Duration of study	Intervention time: Four blocks of treatment, of three months each
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Anuric pts, receiving HD through AVF or graft
Exclusion criteria	Nil listed
Recruitment/selection of patients	Unclear
Age, gender and ethnicity	Age - Mean (SD): 62(13)y. Gender (M:F): 19:5. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 62). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	Etiology CKD: diabetes 2 (although only 1 currently has DM), glomerulonephritis 5, HTN 6, pylenephritis 4, unknown 7. Average time on dialysis 31(23) months
Indirectness of population	Serious indirectness: Not RRT naive, existing HD pt

Interventions	(n=24) Intervention 1: Haemodialysis - HDF. Haemodiafiltration, postdilutional, one block being online HDF and one block using prepared bags (results combined), with blood flow 250-350ml/min, diasylate flow rate 500-700ml/min and substitution fluid 3.75-5litres/h, with prescription using Daugirdas formula to calculate Kt/V. Duration 3 months. Concurrent medication/care: Protocol alternates 3 months HDF with 3 months HD for 12 months total, with order randomised. Other treatment not specified (n=24) Intervention 2: Haemodialysis - HD (generic). Low-flux haemodialysis with blood flow 250-350ml/min and diasylate flow rate 500-700ml/min, with prescription using Daugirdas formula to calculate Kt/V. Duration 3 months. Concurrent medication/care: Protocol alternates 3 months HDF with 3 months HD for 12 months total, with order randomised. Other treatment not specified
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 Physical Health Composite at 3 months; Mean; HDF 40.7 (30.2-62.8), HD 36.1 (26.7-45.7) - statistics based on 44 independent ratings, which may be inappropriate (p-value: 0.029) pt 0-100 SF-36 Top=High is good outcome;
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - High, Other 2 - Low, Other 3 - Low, Comments - Unblind, no statement re comparability of care, no detail re where pt come from or how selected; Indirectness of outcome: No indirectness ; Baseline details: Age: 62/62, years on dialysis 2.5/3.7, female 2/3, DM 0/1; Group 1 Number missing: 1, Reason: unstated; Group 2 Number missing: 1, Reason: unstated

Protocol outcomes not reported by the study	Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Katopodis 2009[196]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=18)
Countries and setting	Conducted in Greece; Setting: One haemodialysis unit in university hospital
Line of therapy	1st line
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	People and children without diabetes
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults, stable 6 months on HD through an AVF/AV graft with minimal (<5%) recirculation. All had residual diuresis <100ml
Exclusion criteria	Diabetes, uncured malignancy, active inflammation, liver or severe heart failure (NYHA IV), malnutrition and medications affecting urea metabolism
Recruitment/selection of patients	All eligible pts informed
Age, gender and ethnicity	Age - Mean (SD): 53.6(15.1) int, 60.1(10.1) control. Gender (M:F): 12:6. Ethnicity: Not stated
Further population details	1. Age: Not applicable 2. BMI: Not stated / Unclear 3. DM: Not applicable (All non-diabetic). 4. Ethnicity: Not stated / Unclear
Extra comments	Body weight (kg): 69.7(9.1) int, 70.1(9.1) control. Etiology: Glomerulonephritis 11, HTN 2, other 5

Indirectness of population	Serious indirectness: Not RRT naive, required to have been stable on HD for six months prior to entry
Interventions	(n=8) Intervention 1: Haemodialysis - HD >3x a week. HD every other day (eod), with equal intervals of 44 hours between sessions, with other aspects of the dialysis prescription being carried over from their conventional dialysis, and amended as needed every three months. Duration 12 months. Concurrent medication/care: Protocol given for blood pressure, Hb and PTH management Comments: All pts completed (n=8) Intervention 2: Haemodialysis - HD 3x a week. HD on a conventional schedule, with 2 x 44h and 1 x 72h intervals between sessions. Dialysis prescriptions remained unchanged on entry, and were reviewed every three months for necessary changes. Duration 12 months. Concurrent medication/care: Protocol given for blood pressure, Hb and PTH management Comments: All pts completed
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD >3X A WEEK versus HD 3X A WEEK

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for People and children without diabetes: Death at 12 months; Group 1: 0/8, Group 2: 0/8
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Inadequate randomisation (alphabetic-alternate) and limited baseline stats; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Korevaar 2003[211]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=38)
Countries and setting	Conducted in Netherlands; Setting: 38 Dutch dialysis centres
Line of therapy	1st line
Duration of study	Intervention + follow up: Median 2.5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	>18, dialysis as first form of RRT, no medical/social/logistic objections against HD or PD
Exclusion criteria	Nil else
Recruitment/selection of patients	Nil specified
Age, gender and ethnicity	Age - Range of means: 55-62. Gender (M:F): 22:16. Ethnicity:
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	No indirectness
Interventions	(n=18) Intervention 1: Haemodialysis - HD (generic). HD, nil else specified, of 18 randomised to HD: 1 started with PD, 5 received a kidney transplant, 1 changed to PD after starting with HD . Duration Median follow-up 2.5 years . Concurrent medication/care: Usual care

	(n=20) Intervention 2: Peritoneal dialysis - PD (generic). PD generic, majority CAPD, of 20 randomised to PD: 3 started with HD instead of PD, 3 received a kidney transplant during follow-up and 4 changes to HD after receiving PD . Duration Median follow-up 2.5 years. Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC) Protocol outcome 1: Quality of life - Actual outcome for General population: EuroQol VAS mean over 2 years (0-100, higher is better) at 2 years; Group 1: mean 59.2 (SD 11.8); n=18, Group 2: mean 54.4 (SD 21.9); n=20 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Mortality at >/= 6 months - Actual outcome for General population: Mortality, time to event (up to 5 year follow-up) at Median follow-up 2.5 years; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Lafrance 2012[224]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=1820)
Countries and setting	Conducted in Canada
Line of therapy	1st line
Duration of study	Intervention time:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	None
Exclusion criteria	Less than 90 days dialysis. Kidney transplant
Age, gender and ethnicity	Age - Mean (SD): HD 58.5 (16.4) PD 58.8 (15.5). Gender (M:F): 41% female. Ethnicity: > 86% white
Further population details	
Extra comments	Patients on long term dialysis between Jan 2001 and Dec 2007
Indirectness of population	No indirectness
Interventions	(n=910) Intervention 1: Haemodialysis - HD (generic). Home and in-centre combined. Duration At least 90 days. Concurrent medication/care: No details

	(n=910) Intervention 2: Peritoneal dialysis - PD (generic). No details. Duration At least 90 days. Concurrent medication/care: No details
Funding	Academic or government funding (Fonds de la recherche en sante du Quebec)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC) Protocol outcome 1: Hospitalisation - length of stay at >/= 6 months - Actual outcome for General population: Length of stay at Median 2 yrs; ; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Age HD 58.5 PD 58.8; Key confounders: Age, ethnicity, baseline health, comorbidities; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Locatelli 1996[254]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=105)
Countries and setting	Conducted in Italy; Setting: Part of multi-centre trial, in a stratum of 30 centres
Line of therapy	1st line
Duration of study	Intervention time: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 18-70y, 'very stable' clinical condition - including on RRT for at least two months - with regular thrice weekly haemodialysis
Exclusion criteria	Malignant disease (ascertained or suspected), MI within 12 months, stroke or TIA in last 6 months or severe heart failure (NYHA III-IV)
Recruitment/selection of patients	May 1991 - November 1992
Age, gender and ethnicity	Age - Mean (SD): 52.7(12.9) HDF, 54.8(12.6) HD. Gender (M:F): 71:29. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 54y). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	. Prev. diabetic nephropathy 2.0% HDF, 5.5% HD
Indirectness of population	No indirectness

Interventions	(n=50) Intervention 1: Haemodialysis - HDF. High-flux polysulfone hemodiafiltration (8 to 12 litre/session in post-dilution). The dialysate was to be carefully handled to ensure its high quality and prevent pyrogen. Session time and blood flow being scheduled in order to obtain a Kt/V of at least 1 and an ultrafiltration rate < 2% body wt/hr, adjusted according to the actual value obtained from the domain map. Duration 24 months. Concurrent medication/care: All other treatments to be continued. If treatment was deemed inadequate, physician was free to adjust as necessary Comments: Drop-outs: 12 technical, 3 inadequacy, 8 transplant (n=105) Intervention 2: Haemodialysis - HD (generic). Mix of high-flux and low-flux polysulfone haemodialysis (8 to 12 litre/session in post-dilution). Session time and blood flow being scheduled in order to obtain a Kt/V of at least 1, adjusted according to the actual value obtained from the domain map. Duration 24 months. Concurrent medication/care: All other treatments to be continued. If treatment was deemed inadequate, physician was free to adjust as necessary Comments: Dropouts: 26 technical, 4 acute clinical, 3 fistula-related, 6 inadequacy, 10 transplant
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Deaths at 24 months;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HD has more men and diabetics, high numbers not completing; Indirectness of outcome: No indirectness ; Baseline details: HD has more men and diabetics; Group 1 Number missing: 23, Reason: up to 23; Group 2 Number missing: 49, Reason: up to 49

Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: Hospitalisations at 24 months; rate ratio: 1.5);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HD has more men and diabetics, high numbers not completing; Indirectness of outcome: No indirectness ; Baseline details: HD has more men and diabetics; Group 1 Number missing: 23, Reason: up to 23; Group 2 Number missing: 49, Reason: up to 49

Protocol outcome 3: AEs - vascular access issues
- Actual outcome for General population: Fistula-related reason for withdrawal from study at 24 months; Group 1: 0/50, Group 2: 3/105

Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HD has more men and diabetics, high numbers not completing; Indirectness of outcome: No indirectness ; Baseline details: HD has more men and diabetics; Group 1 Number missing: 23, Reason: up to 23; Group 2 Number missing: 49, Reason: up to 49	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	**Locatelli 2010[252]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=146)
Countries and setting	Conducted in Italy; Setting: Italian dialysis centres
Line of therapy	1st line
Duration of study	Intervention time: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	At the time of randomization, patients must have been on thrice weekly HD for at least 6 months. Other inclusion criteria will be: age between 18 and 80 years, body weight not higher than 90 kg, and stable clinical

	conditions.
Exclusion criteria	Patients with clinically relevant infections, malignancies, active systemic diseases, active hepatitis or cirrhosis, unstable diabetes, diuresis >200ml/24 h or a malfunction of vascular access with a blood flow rate <300ml/min will be excluded from the study. Follow-up monitoring and data registration Patients will be asked to sign a detailed informed consent. All relevant anamnestic and clinical data will be recorded. Particular attention will be paid to nutritional and cardiovascular parameters and to general co-morbid conditions. Registration of all data will be performed by one or two nephrologists and one or two nurses, appointed as study monitors in each collaborative centre. Laboratory parameters The pre-dialysis levels of the following parameters will be registered monthly: haemoglobin, leukocytes, platelets, serum electrolytes (sodium, potassium, bicarbonate, calcium, phosphorus), BUN, creatinine, total protein and albumin. BUN, sodium, potassium, bicarbonate, calcium, phosphorus and total proteins will also be evaluated at the end of session. The following parameters will be determined every 3 months: iron, ferritin and transferrin. Cholesterol, triglyg
Age, gender and ethnicity	Age - Median (IQR): 67.4 (58.1 to 73.3). Gender (M:F): 84 male, 62 female. Ethnicity:
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	Very serious indirectness: All on RRT previously
Interventions	(n=70) Intervention 1: Haemodialysis - HD (generic). HD was performed with a low-flux membrane and with a dialysate flow rate of 500 ml/min. . Duration 24 months. Concurrent medication/care: HD, HF, and HDF machines all were provided by a dialysis fluid UF system for the production of ultrapure dialysate and sterile nonpyrogen substitution fluid, checked at monthly intervals. Dialysate/infusate conductivity, dialysate/infusate calcium and bicarbonate concentrations and the dialysate/infusate temperatures, food ingestion habits during the study, and the use of

	antihypertensive drugs before the dialysis session were kept constant according to the centre's policy, to follow everyday clinical practice as much as possible. Blood flow was between 300 and 400 ml/min, and the treatment time was between 3.0 and 4.5 hours for each session. Dialysate/infusate compositions were sodium 133 to 152 mEq/L, potassium 1 to 3 mEq/L, calcium 2.5 to 4.0 mEq/L, acetate 4 mEq/L, bicarbonate 26 to 38mEq/L, and glucose 1 g/L. . Indirectness: No indirectness (n=40) Intervention 2: Haemodialysis - HDF. HDF was performed with a synthetic high-flux membrane with an infusate/blood flow ratio of 0.6 and a dialysate plus infusate rate of 700 ml/min. . Duration 24 months . Concurrent medication/care: HD, HF, and HDF machines all were provided by a dialysis fluid UF system for the production of ultrapure dialysate and sterile nonpyrogen substitution fluid, checked at monthly intervals. Dialysate/infusate conductivity, dialysate/infusate calcium and bicarbonate concentrations and the dialysate/infusate temperatures, food ingestion habits during the study, and the use of antihypertensive drugs before the dialysis session were kept constant according to the centre's policy, to follow everyday clinical practice as much as possible. Blood flow was between 300 and 400 ml/min, and the treatment time was between 3.0 and 4.5 hours for each session. Dialysate/infusate compositions were sodium 133 to 152 mEq/L, potassium 1 to 3 mEq/L, calcium 2.5 to 4.0 mEq/L, acetate 4 mEq/L, bicarbonate 26 to 38mEq/L, and glucose 1 g/L. . Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus HDF

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Mortality at 24 months at 24 months; Group 1: 8/66, Group 2: 2/39
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in diabetes and dialysis technique before study; 87.1% on HD in HD group, 77.5% on HD before study
17.1% diabetic in HD group, 27.5% diabetic HDF group; Group 1 Number missing: 4, Reason: Dropped out during 3 month adaptation period; Group 2 Number missing: 1, Reason: Dropped out during 3 month adaptation period

Protocol outcome 2: AEs - infections at Define
- Actual outcome for General population: Infection at 24 months at 24 months; Group 1: 1/66, Group 2: 0/39
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in diabetes and dialysis technique before study;

87.1% on HD in HD group, 77.5% on HD before study 17.1% diabetic in HD group, 27.5% diabetic HDF group; Group 1 Number missing: 4, Reason: Dropped out during 3 month adaptation period; Group 2 Number missing: 1, Reason: Dropped out during 3 month adaptation period Protocol outcome 3: AEs - vascular access issues at Define - Actual outcome for General population: Thrombosis or vascular access infection at 24 months at 24 months; Group 1: 2/66, Group 2: 0/39 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in diabetes and dialysis technique before study; 87.1% on HD in HD group, 77.5% on HD before study 17.1% diabetic in HD group, 27.5% diabetic HDF group; Group 1 Number missing: 4, Reason: Dropped out during 3 month adaptation period; Group 2 Number missing: 1, Reason: Dropped out during 3 month adaptation period	
Protocol outcomes not reported by the study	Quality of life at Define; Symptom scores/functional measures at Define; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form at Define; Psychological distress and mental wellbeing at Define; Preferred location of death at Define; Cognitive impairment at Define; Patient/family/carer experience of care at Define; Growth at Define; Malignancy at Define; AEs - dialysis access issues at Define; AEs - acute transplant rejection episodes at Define

Study (subsidiary papers)	Manns 2009[271] (Culleton 2007[87], Klarenbach 2013[204])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=52)
Countries and setting	Conducted in Canada; Setting: 10 dialysis centres at two universities in Alberta, Canada.
Line of therapy	1st line
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 18y or older, receiving conventional haemodialysis three times weekly, interested and willing to train for and commence nocturnal haemodialysis
Exclusion criteria	Lacked physical or mental capacity to train to carry out procedure independently
Recruitment/selection of patients	Recruitment started August 2004 and study completed in December 2006, six months after the enrolment of the last participant
Age, gender and ethnicity	Age - Mean (SD): int 55.1(12.4) control 53.1(13.4). Gender (M:F): 32:20. Ethnicity: 86% Caucasian
Further population details	1. Age: Not applicable (Adults, ave 54y). 2. BMI: Not applicable (Mixed, ave 25). 3. DM: Not applicable (41% diabetic). 4. Ethnicity: Not applicable (86% white race).
Extra comments	Baseline characteristics for int/control: White race% 69/56, BMI 26/24, year on dialysis 5.5/4.8, prior transplant% 27/36, already home/self-care HD% 31/48, AVF% 58/56, comorbid diabetes% 38/44, serum albumin 3.7/3.6, ferritin 427/493 , aetiology of CKD: diabetic 30%, Gnephritis 25%, urologic 12%, PKD 8%,

	vascular 8%. medication use: aspirin 40%, ACE/ARB 60%, CaCB 45%, Bblocker 37%, phosphate binder 72%.
Indirectness of population	Serious indirectness: Not RRT naive, moving from their existing modality to a related sub-modality
Interventions	(n=27) Intervention 1: Haemodialysis - HD at home >3x a week. Nocturnal home haemodialysis, for or six times per week. Trained in-centre 4 to 5 times per week, for 2 to 6 weeks, with direct nursing supervision and monitoring of biochemical parameters. Upon completion of training, nocturnal haemodialysis was performed at home by the patient, without remote monitoring, 5 to 6 nights per week for a minimum of 6 hours per night. Dialysis was performed using Bellco Formula (Mississauga, Ontario, Canada) machines using polysulfone synthetic membranes. Bloodflow rates up to 250 mL/min were prescribed and dialysate flow rates of 300mL/min were used in all patients. Water was purified using reverse osmosis and ultrapure dialysate was not used. Dialysate calcium was 5.0 to 7.0 mg/dL(1.25-1.75 mmol/L) and phosphate was added to the dialysate bath as needed to prevent hypophosphatemia. Duration 6 months. Concurrent medication/care: Blood pressure was managed by haemodialysis physicians according to a published algorithm targeting a goal post-dialysis blood pressure of less than 130/80 mm Hg. Anaemia management was carried out according to a standardized nursing-led anaemia protocol with a target haemoglobin of 11.0 to 12.5 g/dL using intravenously administered erythropoietic-stimulating proteins and iron supplements as necessary. Mineral metabolism was managed to achieve local treatment goals of 8.0 to 10.2mg/dL (2.00-2.55 mmol/L) for serum calcium, less than 5.6 mg/dL (1.80 mmol/L)for serum phosphate, and 150 to 300 pg/mL (150-300 ng/L) for intact parathyroid hormone. Comments: 26 received intervention, 3 discontinued before six months (n=25) Intervention 2: Haemodialysis - HD 3x a week. Usual haemodialysis: Patients continued their prerandomization dialysis modality with thrice-weekly haemodialysis and a dialysis prescription to target a single-pool Kt/V (normalized clearance by time product, a derived quantity related to treatment-related changes in urea concentrations) of greater than 1.2. Dialysate calcium was adjusted between 4.0 and 7.0 mg/dL (1.00-1.75 mmol/L)depending on the serum calcium level. Duration 6 months. Concurrent medication/care: Blood pressure was managed by haemodialysis physicians according to a published algorithm targeting a goal postdialysis blood pressure of less than 130/80 mm Hg. Anaemia management was carried out according to a standardised nursing-led anaemia protocol with a target haemoglobin of 11.0 to 12.5 g/dL using intravenously administered erythropoietic-stimulating proteins and iron supplements as necessary. Mineral metabolism was managed to achieve local treatment goals of 8.0 to 10.2mg/dL (2.00-2.55 mmol/L) for serum calcium, less than 5.6 mg/dL (1.80 mmol/L) for serum phosphate, and 150 to 300 pg/mL (150-300 ng/L) for intact parathyroid hormone. Comments: 25 received intervention, 2 discontinued before six months

Funding	Other (Funded entirely by the Kidney Foundation of Canada)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NOCTURNAL HD versus HD 3X A WEEK

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical composite score at 6 months; MD; 1.24 (95%CI -3.59 to 6.07) (p-value: 0.61) pt SF-36 physical composite score mean difference of change score Top=High is good outcome, Comments: Using difference in quality of life (nocturnal haemodialysis-conventional haemodialysis) comparing pre-randomisation and 6 months after start;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: SF-36 mental composite score at 6 months; MD; 0.71 (95%CI -5.85 to 7.26) (p-value: 0.61) pt SF-36 mental composite score mean difference in change score Top=High is good outcome, Comments: Using difference in quality of life (nocturnal haemodialysis-conventional haemodialysis) comparing pre-randomisation and 6 months after start.;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: EQ5D at 6 months; Group 1: mean 0.6 (SD 0.28); n=27, Group 2: mean 0.6 (SD 0.29); n=25
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Symptom scores/functional measures
- Actual outcome for General population: KDQOL symptom score at 6 months; MD; -1.04 (95%CI -8.31 to 6.23) (p-value: 0.77) pt KDQOL symptom score mean difference in change score Top=High is good outcome, Comments: Using difference in quality of life (nocturnal haemodialysis-conventional haemodialysis) comparing pre-randomisation and 6 months after start;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Hospitalisation - length of stay at >/= 6 months
- Actual outcome for General population: Death at 6 months; Group 1: 1/26, Group 2: 0/25
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal). No mention of baseline rate of hospitalisations; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 6: AEs - infections - Actual outcome for General population: Bacteraemia at 6 months; Group 1: 4/26, Group 2: 4/25; Comments: No events: nHD 5 vs cHD 4 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal). No mention of baseline rate of hospitalisations; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: AEs - vascular access issues - Actual outcome for General population: Insertion or replacement of tunneled dialysis catheter at 6 months; Group 1: 7/26, Group 2: 5/25; Comments: Numbers of events: nHD 7 vs cHD 7 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Baseline details: More men, more in-centre experience in intervention group (both marginal). No mention of baseline rate of hospitalisations; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Hospitalisation or other healthcare resource use at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Growth ; Malignancy ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	McDonald 2009[278]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=25287)
Countries and setting	Conducted in Australia, New Zealand; Setting: Australia and New Zealand
Line of therapy	1st line
Duration of study	Follow up (post intervention): Maximum follow-up 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients commencing dialysis from 1991 to 2005 in Australia and New Zealand
Exclusion criteria	Survived less than 90 days from commencement of dialysis
Recruitment/selection of patients	Retrospective cohort analysis from ANZDATA
Age, gender and ethnicity	Age - Median (IQR): 60 (48 to 70). Gender (M:F): 55:45. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=14733) Intervention 1: Haemodialysis - HD (generic). Including hospital, satellite and home based. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care

	(n=10554) Intervention 2: Peritoneal dialysis - PD (generic). Including CAPD and APD . Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care
Funding	Principal author funded by industry
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality, HR, general population, median age ~60 at From 1 year onwards, median duration of follow-up ~2.5 years; Group 1: n=10554 ; Group 2: n=14733; HR 1.35; Lower CI 1.27 to Upper CI 1.42 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Mehrotra 2011[284]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=252961)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up: Median follow-up ~2.5years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients from US renal data system 1996-2004, recorded as on dialysis modality as specified 90 days after service date, continuous treatment for 60 days
Exclusion criteria	-
Recruitment/selection of patients	Retrospective cohort analysis
Age, gender and ethnicity	Age - Other: >18, results stratified by age. Gender (M:F): Define. Ethnicity:
Further population details	
Extra comments	Latest of 3 3 year cohorts extracted to avoid overlap with other publications
Indirectness of population	No indirectness

Interventions	(n=233082) Intervention 1: Haemodialysis - HD in centre. In centre HD only. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care (n=19879) Intervention 2: Peritoneal dialysis - PD (generic). CAPD or APD but not other forms of PD. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care
Funding	Study funded by industry
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD IN CENTRE Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for People and children without diabetes: Mortality, HR, 18-64, with at least one comorbidity and no DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Mortality, HR, 65 and older, with at least one comorbidity and DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children without diabetes: Mortality, HR, 65 and older, with at least one comorbidity and no DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Mortality, HR, 18-64, with at least one comorbidity and DM at Median follow-up 2.5 years; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Mesaros-Devcic 2013[290]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=85)
Countries and setting	Conducted in Croatia; Setting: Three dialysis centres in Croatia
Line of therapy	1st line
Duration of study	Intervention time: 36 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Unclear: A number of subgroup comparisons presented in paper, only overall analysed here
Inclusion criteria	Aged over 18, with established renal failure, on chronic program at HD centre for at least three months
Exclusion criteria	Blood flow <250ml/min in more than 30% treatments in the three months before enrolment
Recruitment/selection of patients	Selected by centres for the trial
Age, gender and ethnicity	Age - Mean (SD): HDF 58(11), HD 62(12). Gender (M:F): 50:35. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Does present results separately for older than 65y vs not). 2. BMI: Not applicable 3. DM: Not applicable (Does present results separately for diabetic nephropathy vs not, but not by current DM status). 4. Ethnicity: Not applicable
Extra comments	Pt Characteristics: vascular access via AVF 87%, catheter 13%, time on dialysis 90 months, SBP 140mmHg, on antiHTN 72%, Hb 108g/L Etiology: G.nephritis 32%, diabetes 12%, N.sclerosis 8%, P.nephritis 7%, PKD 5%, unknown 5%

Indirectness of population	Serious indirectness: Not RRT naive, chosen on basis had at least 3 months on HD
Interventions	(n=42) Intervention 1: Haemodialysis - HDF. Online haemodiafiltration performed in the postdilution mode, with the filtration rates were adjusted to be between 25 and 30% of the achieved blood flow rate and substitution volume was targeted to be above 19 L per session. The electrolyte composition of the infusate was the same as the composition of the dialysis fluid. The intended HD treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min, as registered in a single haemodialysis treatments. The dialysate flow rate was kept at 500mL/min in both groups. The same high-flux dialyser was used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 36 months. Concurrent medication/care: In keeping with good practice guidelines Comments: Unclear how many completed protocol (n=43) Intervention 2: Haemodialysis - HD (generic). Low flux haemodialysis referred to as "standard dialysis". The intended HD treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min, as registered in a single haemodialysis treatments. The dialysate flow rate was kept at 500mL/min in both groups. The same high-flux dialyser was used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 36 months. Concurrent medication/care: In keeping with good clinical practice guidelines
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Death at 36 months; Group 1: 5/42, Group 2: 14/43 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No detail re randomisation, missing data not mentioned (high in other studies); Indirectness of outcome: No indirectness ; Baseline details: Female 17v18, age 62v58, time on RRT 85v100; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress

	and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Morena 2017[296]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=381)
Countries and setting	Conducted in France; Setting: Dialysis facilities
Line of therapy	1st line
Duration of study	Intervention + follow up: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged ≥65 years, with no significant diuresis and/or residual kidney function, on HFHD for ≥3 months, and considered stabilised, with 3-times-weekly HD sessions and haemoglobin within 9-13g/dl.
Exclusion criteria	Patients with severe malnutrition, unstable clinical condition, unipuncture or failed vascular access flow, or known problems of coagulation.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): 76.2 (4.9). Gender (M:F): 229/152. Ethnicity: Not reported
Further population details	1. Age: 2. BMI: 3. DM: 4. Ethnicity:
Indirectness of population	No indirectness
Interventions	(n=190) Intervention 1: Haemodialysis - HDF. Online hemodiafiltration (OLHDF) 3 time a week, 3 to 4 hours per sessions, with blood flow of 350 to 400 ml/min and a dialysate flow of 500 to 600 ml/min. Duration 24

	months. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=191) Intervention 2: Haemodialysis - HD 3x a week. High-flux haemodialysis (HFHD) 3 time a week, 3 to 4 hours per sessions, with blood flow of 350 to 400 ml/min and a dialysate flow of 500 to 600 ml/min. Duration 24 months. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Academic or government funding (Supported by a grant from the French Ministry of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OLHDF versus HFHD Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Deaths at 24 months; Group 1: 36/190, Group 2: 43/191 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: 47; Group 2 Number missing: 58 Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months - Actual outcome for General population: Hospitalisation at 24 months; Group 1: 309/190, Group 2: 346/191 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: 47; Group 2 Number missing: 58	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Murtagh 2007[301]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=129)
Countries and setting	Conducted in United Kingdom; Setting: Four major renal units in South Thames Region
Line of therapy	1st line
Duration of study	Intervention time: 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: 75-79y 28%, 80-84y 46%, 85-89y 23%, >89y 4%
Stratum	Planned starters: "Late starters" would not be captured, as different pathway
Subgroup analysis within study	Not applicable
Inclusion criteria	Age >75 receiving routine pre-dialysis care - that is, under the care of dedicated multidisciplinary team for people expected to need renal replacement therapy in the next 18 months, who had chosen to prepare for dialysis or receive conservative care
Exclusion criteria	"Late starters" would not be captured, as different pathway, and those with incurable solid organ cancers were excluded
Recruitment/selection of patients	September 2003 to August 2004
Age, gender and ethnicity	Age - Range: . Gender (M:F): 85:44. Ethnicity: White 83%, black 11%, Asian 5%, other 1%
Further population details	1. Age: >80 (Age >75). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear (total comorbidity score given). 4. Ethnicity: Not applicable (83% white).
Extra comments	Analysis of prognosis by comorbidity performed. Proportion dialysis/conservative. Age <80y: 46/16%, 80-84y: 44/47%, >85y: 10/37%

	Etiology: uncertain 23/35%, GN 4/3%, diabetes 25/23%, renovascular 16%. Comorbidity (Davies) score 0: 15/13%, 1: 65/69%, 2: 19/18%
Indirectness of population	No indirectness
Interventions	(n=52) Intervention 1: Haemodialysis - HD (generic). After assessment and support, chose to start dialysis when indicated (HD or PD), whether or not started during the time of study. Duration 2 years. Concurrent medication/care: Multidisciplinary pre-dialysis care (n=77) Intervention 2: Conservative management. After assessment and support, chose not to receive dialysis. Duration 2 years. Concurrent medication/care: Multi-disciplinary pre-dialysis care
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIALYSIS versus CONSERVATIVE MANAGEMENT

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for Planned starters: Mortality in age >75 at 2 years; Group 1: Observed events 14 ; Group 2: Observed events 40; HR 2.94; Lower CI 1.56 to Upper CI 5.53; Test statistic: p=0.001
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Only 6 events per covariate, comparability of care unclear; Indirectness of outcome: No indirectness, Comments: Adjusted, as reported; Baseline details: Difference seen in age (not comorbidity, ethnicity, aetiology or comorbidity score); Key confounders: age (not significant in multivariate model), ethnicity (not significant in univariate model), comorbidity (only vascular disease significant in multivariate model), aetiology (not significant in univariate model); Group 1 Number missing: , Reason: believable for registry trial; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Park 2013[330]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=26)
Countries and setting	Conducted in South Korea; Setting: Single university hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: 24 months, with selected 7 year follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	End-stage renal disease, receiving regular chronic haemodialysis at least three months, three times a week, using high flux
Exclusion criteria	Any of the following medical events: MI, CVA, surgical procedure in last 2 months, CHF >NYHA2 or valvular or congenital heart defect, AF, pacemaker, COPD, severe hepatic disease, malignant neoplasm, or other physical or mental problems that limit normal daily activities
Recruitment/selection of patients	2005-6 from HD outpatients
Age, gender and ethnicity	Age - Mean (SD): HD 59.8(6.5) HDF 55.7(18.5). Gender (M:F): 11:15. Ethnicity: Not stated
Further population details	
Extra comments	. Baseline characteristics: HD duration 36 months, cause diabetic 65%, cause HTN 19%, comorbid diabetes 65%, comorbid HTN 54%, ave SBP 145mmHg

Indirectness of population	Serious indirectness: Not naive to RRT - all receiving HD prior to randomisation
Interventions	(n=20) Intervention 1: Haemodialysis - HDF. Online haemodiafiltration with postdilution, 4h, 3 x week with bicarbonate dialysis fluid and heparin as an anticoagulant. Used the AK200 ULTRA S with nonreprocessed polyamide membrane. Blood flow was maintained at 250ml/minute, dialysate flow was 600ml/minute, and the temperature of the dialysate was approximately 36 degrees. Duration 24 months. Concurrent medication/care: Not stated Comments: 11 completed trial, with 3 of drop-outs switching to HD (n=20) Intervention 2: Haemodialysis - HD (generic). conventional HD (4-hour sessions, three times a week, high-flux). Duration 24 months. Concurrent medication/care: Not stated Comments: 15 completed trial, with one drop-out switching to HDF
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Death at 24 months; Group 1: 1/20, Group 2: 1/20 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unclear randomisation/concealment, no statement re comparability of care, unclear whether those who left study were followed for mortality; Indirectness of outcome: No indirectness ; Group 1 Number missing: , Reason: unclear ? 4 that transferred hospital; Group 2 Number missing: , Reason: unclear ? 2 that transferred hospital	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Schiffl 2007[386]
Study type	RCT (Patient randomised; Crossover: Adequate according to protocol)
Number of studies (number of participants)	1 (n=76)
Countries and setting	Conducted in Germany; Setting: Unclear
Line of therapy	1st line
Duration of study	Intervention time: Two blocks of two years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Clinically stable, CKD on 3 x wk conventional HD for at least 6 months and a permanent vascular access capable of a blood flow of at least 250ml/min
Exclusion criteria	Malignancy, severe comorbidity (e.g. heart failure NYHA III-IV) or infectious disease
Recruitment/selection of patients	Unclear
Age, gender and ethnicity	Age - Mean (range): 62 (32-78). Gender (M:F): 42:34. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 62). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	At entry, pts had completed between 9 and 280 months of HD, mean 25. Etiology: glomerulonephritis (22) HTN (18) diabetes (22) PKD (8) chronic tubulointerstitial (7) unknown (6)
Indirectness of population	Serious indirectness: Not RRT naive, required to have been on HD for six months prior to entry

Interventions	(n=76) Intervention 1: Haemodialysis - HDF. Online HDF utilising high-flux polysulfone dialysers performed thrice per week for 4 to 5 hours, blood flow rates ranged from 250-350ml/min, with dialysis flow rate 500ml/min and substitution fluid at 4.5litres/hour, with prescription adapted to the individual and reviewed intermittently. Study involves 24 months on HDF and 24 months on HF-HD in random order. Duration 24 months. Concurrent medication/care: Protocol for management of other aspects of CKD (n=76) Intervention 2: Haemodialysis - HD (generic). High-flux conventional haemodialysis utilising high-flux polysulfone dialysers performed thrice per week for 4 to 5 hours, blood flow rates ranged from 250-350ml/min, with dialysis flow rate 500ml/min, and prescription adapted to the individual and reviewed intermittently. Study involves 24 months on HDF and 24 months on HF-HD in random order. Duration 24 months. Concurrent medication/care: Protocol for managing other aspects of CKD
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD Protocol outcome 2: Symptom scores/functional measures - Actual outcome for General population: Physical symptoms at 24 months; Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Unblinded and query selective reporting (only dimension of QoL measure that is reported well enough to analyse); Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2 Protocol outcome 3: Mortality at >/= 6 months - Actual outcome for General population: Death at 24 months; Group 1: 3/73, Group 2: 3/72 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 2	
Protocol outcomes not reported by the study	Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Snyder 2002[402]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=22776)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	First started therapy between 1995 and 1998 and had been on the same dialysis modality for at least 60 days on day 90 of therapy
Exclusion criteria	Not reported
Age, gender and ethnicity	Age - Other: 80% between 30 and 64 yrs. Gender (M:F): 48%. Ethnicity:
Further population details	
Extra comments	Patients who had been on PD or HD prior to transplantation
Indirectness of population	No indirectness
Interventions	(n=22776) Intervention 1: Transplant - Living donor. Not reported. Duration Not relevant. Concurrent medication/care: Not reported

	(n=22776) Intervention 2: Transplant - Deceased donor. Not reported. Duration Not applicable. Concurrent medication/care: Not reported
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LIVING DONOR versus DECEASED DONOR Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality at Up to 5 yrs; RR; 0.71 (95%CI 0.6 to 0.83) (p<0.05) ; Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: Unclear number of confounders and events; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to failure of RRT form - Actual outcome for General population: Graft failure at Up to 5 yrs; RR; 0.88 (95%CI 0.79 to 0.98) (p<0.05) ; Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: Unclear number of confounders and events; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Stefansson 2012[407]
Study type	RCT (Patient randomised; Crossover: None)
Number of studies (number of participants)	1 (n=20)
Countries and setting	Conducted in Sweden; Setting: Single HD unit in a university hospital
Line of therapy	1st line
Duration of study	Intervention time: 2 months in each treatment
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults aged >18 years, in a clinically stable condition, receiving HD or HDF for last three months
Exclusion criteria	Acute inflammation, infection or cardiovascular disease
Recruitment/selection of patients	Recruited twenty, then another five to replace dropouts
Age, gender and ethnicity	Age - Mean (SD): 60.6(13.6). Gender (M:F): 14:6. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 61y). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	Scant baseline information given. Etiology of kidney disease - diabetic (7), glomerulonephritis (4), nephrosclerosis (4), PCKD (2) and chronic interstitial nephritis (3)
Indirectness of population	Serious indirectness: Not naive to RRT. All had received HD or HDF for at least 3 months.

Interventions	(n=20) Intervention 1: Haemodialysis - HDF. Haemodiafiltration, on-line post-dilution, with replacement volume standardised to 25-30% total blood treated. All treatments were carried out on AK 200 ULTRA dialysis machines (Gambro, Lund, Sweden) and with BL 200B blood tubing. Polyamide dialysis membranes were used in all treatments. All treatments were patient-blinded; the dialysis machine was concealed behind a screen, making it impossible for the patient to identify which treatment was given. Anticoagulation was performed with tinzaparin sodium (Innohep , Leo Pharma, Bellerup, Denmark). For each patient, the dialysis prescription was kept constant throughout the study (total dialysis time, dialysate flow = 500 ml/min, dialysate temperature and dialysate composition) and the blood flow was kept as stable as possible. Duration 60 days. Concurrent medication/care: Individual ESA and iron prescription as indicated (n=20) Intervention 2: Haemodialysis - HD (generic). Conventional low-flux haemodialysis. All treatments were carried out on AK 200 ULTRA dialysis machines (Gambro, Lund, Sweden) and with BL 200B blood tubing. Polyamide dialysis membranes were used in all treatments. All treatments were patient-blinded; the dialysis machine was concealed behind a screen, making it impossible for the patient to identify which treatment was given. Anticoagulation was performed with tinzaparin sodium (Innohep , Leo Pharma, Bellerup, Denmark). For each patient, the dialysis prescription was kept constant throughout the study (total dialysis time, dialysate flow = 500 ml/min, dialysate temperature and dialysate composition) and the blood flow was kept as stable as possible. Duration 60 days. Concurrent medication/care: ESA and iron prescriptions as indicated
Funding	Other (The Swedish Medical Research Council 9898, the Inga-Britt and Arne Lundberg Research Foundation, the John and Brit Wennerström Research Foundation, the Medical Association of Gothenburg, and the Sahlgrenska University Hospital Grant LUA/ALF)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD

Protocol outcome 1: Quality of life
- Actual outcome for General population: SF-36 physical composite score at 60 days; Group 1: mean 46 pt (SD 17); n=20, Group 2: mean 47 pt (SD 14); n=20; SF-36 PCS 0-100 Top=High is good outcome
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - 5 people dropped out and were replaced, unclear how chosen, unclear randomisation, little baseline data, no washout period but uncertain would be carry-over at 60 days; Indirectness of outcome: No indirectness ; Baseline details: Crossover, and scant detail; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for General population: SF-36 mental composite score at 60 days; Group 1: mean 63 pt (SD 10); n=20, Group 2: mean 65 pt (SD 11); n=20; SF-36 MCS 0-100 Top=High is good outcome Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - 5 people dropped out and were replaced, unclear how chosen, unclear randomisation, little baseline data, no washout period but uncertain would be carry-over at 60 days; Indirectness of outcome: No indirectness ; Baseline details: Crossover, and scant detail; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Symptom scores/functional measures ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Termorshuizen 2003[416]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=1222)
Countries and setting	Conducted in Netherlands; Setting: Netherlands
Line of therapy	1st line
Duration of study	Intervention + follow up: Median follow-up ~2.5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Post-hoc subgroup analysis
Inclusion criteria	>18 years of age, begin chronic dialysis as first form of RRT, survived first 3 months of dialysis, modality classified at 3 months
Exclusion criteria	Nil else
Recruitment/selection of patients	From NECOSAD
Age, gender and ethnicity	Age - Range: 52-62. Gender (M:F): 60:40. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=742) Intervention 1: Haemodialysis - HD (generic). Nil else specified. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care

	(n=480) Intervention 2: Peritoneal dialysis - PD (generic). Nil else specified. Duration Median follow-up ~2.5 years. Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for People and children without diabetes: Death, RR, <60, no DM, ITT censoring at 3 to 24 month follow-up; RR; 0.77 (95%CI 0.34 to 1.73, Comments: n = 488); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Death, RR, <60, with DM, ITT censoring at 3 to 24 month follow-up; RR; 6.35 (95%CI 1.42 to 28.36, Comments: n = 108); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children without diabetes: Death, RR, >60, no DM, ITT censoring at 3 to 24 month follow-up; RR; 1.03 (95%CI 0.62 to 1.72, Comments: n = 479); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for People and children with diabetes: Death, RR, >60, with DM, ITT censoring at 3 to 24 month follow-up; RR; 1.28 (95%CI 0.65 to 2.52); Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Turkish HDF study trial: Ok 2013[322]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=782)
Countries and setting	Conducted in Turkey; Setting: 10 HD centres operated by Fresenius Medical Care in south and southeast Turkey
Line of therapy	1st line
Duration of study	Intervention time: Ave 23 months (1-39 months)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Recruitment/selection of patients	January 2007 - March 2008 (extended due to initial slow recruitment) 899 identified, 117 did not meet inc/exc
Age, gender and ethnicity	Age - Mean (SD): 56.5(13.9). Gender (M:F): Define. Ethnicity: Not stated
Further population details	1. Age: Not applicable (Ave 57). 2. BMI: Not applicable (Ave 25). 3. DM: Not applicable (prev 35%). 4. Ethnicity: Not stated / Unclear
Extra comments	Extensive baseline info: Etiology - unknown 37%, diabetes 30%, HTN 10%, chronic g'nepritis 3.5%, other 19% Comorbidities - Diabetes 34.7%, smoking 24.9%, CV disease 26.4% Clinical - BMI 25, SBP 128, antihypertensive 13.6%, phosphate binder 83%, IV iron 57.7%, EPO 57.3%

	Vascular access - AV fistula 95.5%, ave blood flow 294 ml/min
Indirectness of population	Serious indirectness: Not RRT naive. Required to already be on HD
Interventions	(n=391) Intervention 1: Haemodialysis - HDF. OL-HDF procedure was performed in the postdilution mode using Fresenius 4008S dialysis machines, incorporating the ONLINEplus. The filtration rates were adjusted to be between 25 and 30% of the achieved blood flow rate and substitution volume was targeted to be above 15 L per session. The electrolyte composition of the infusate was the same as the composition of the dialysis fluid. The effective substitution volume (without the ultrafiltrate volume) used in analyses was calculated as mean of substitution volumes recorded in all sessions. The intended dialysis treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min. The dialysate flow rate was kept at 500 mL/min in both groups. The same high-flux dialysers, either FX60 or FX80 (Polysulfone-based Helixone Membrane) were used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 24 months. Concurrent medication/care: Not stated Comments: 110 dropped out due to - moved (58), switched (1), transplant (11), vascular access (40) (n=391) Intervention 2: Haemodialysis - HD (generic). High-flux haemodialysis using standard dialysate. The intended dialysis treatment duration for both modality arms of the trial was 240 min with a blood flow rate between 250 and 400 mL/min. The dialysate flow rate was kept at 500 mL/min in both groups. The same high-flux dialysers, either FX60 or FX80 (Polysulfone-based Helixone Membrane) were used during the entire study period. Dialysate composition was the same in >90% of subjects in both arms of the study. Duration 24 months. Concurrent medication/care: Not stated Comments: 90 dropped out - moved (81), switched (3), transplant (6)
Funding	Academic or government funding (European nephrology and dialysis institute)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Overall mortality at ave 23 months ; Group 1: 52/391, Group 2: 65/391
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98
- Actual outcome for General population: Overall mortality at ave 23 months ; Group 1: Observed events 52 n=391 ; Group 2: Observed events 65 n=391;

HR 1.04; Lower CI 1.02 to Upper CI 1.06 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98 - Actual outcome for People and children with diabetes: Death or non-fatal cardiovascular event at ave 23 months ; RR; 0.74 (95%CI 0.47 to 1.18) (n: 142 (HDF) 130 (HD)) ; Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, missing data unknown (will be high), summary data only reported; Indirectness of outcome: Serious indirectness, Comments: Not just mortality - includes myocardial infarction, stroke, coronary revascularisation and unstable angina pectoris; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months - Actual outcome for General population: Hospitalisation (count rate) at ave 23 months ; rate ratio: 1.10); Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98 Protocol outcome 3: AEs - vascular access issues - Actual outcome for General population: Withdrew due to VA issues at ave 23 months ; Group 1: 40/391, Group 2: 0/391 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Background care not detailed, around 25% data missing; Indirectness of outcome: No indirectness ; Baseline details: Age 56/56, female 40/42, htn cause 11.5/9.4, dm comorb 36/32, duration dialysis 57/58, av fistula 96/95, smoking 24/26, sbp 128/127; Group 1 Number missing: 110; Group 2 Number missing: 98	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study (subsidiary papers)	USRDS (transplant and dialysis data) trial: Merion 2005[288] (Abbott 2004[1], Glanton 2003[133])
Study type	Non randomised study
Number of studies (number of participants)	3 overlapping studies (n=Up to 157,969)
Countries and setting	Conducted in USA; Setting: USA using USRDS and CMS databases
Line of therapy	1st line
Duration of study	Other: 4-7y data: Glanton 1995-1999, Abbott 1995-2000, Merion 1995-2002
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with CKD entered onto kidney transplant list who also received dialysis through medicare or medicaid schemes
Exclusion criteria	Previous kidney transplant, waiting for another organ transplant, received transplant before starting dialysis
Recruitment/selection of patients	Retrospective
Age, gender and ethnicity	Age - Range: Merion - 0-17y 2.4%, 18-39y 25%, 40-59y 52%, >59y 21%. Gender (M:F): Merion - 59:41. Ethnicity: Using Merion - White 60%, African American 32%, Asian 5%, Other 2%
Further population details	1. Age: Not applicable (0-60+y age included). 2. BMI: Not stated / Unclear 3. DM: Not stated / Unclear 4. Ethnicity: Not applicable (White 60% (of which 14% Hispanic), African American 32%, Asian 5%).
Extra comments	. Etiology: GN 22%, Diabetes 29%, HTN 24%
Indirectness of population	No indirectness

Interventions	(n=45082) Intervention 1: Haemodialysis - HD (generic). On the transplant waiting list, receiving dialysis. Duration 2-7y. Concurrent medication/care: Uncontrolled Comments: PD:HD not stated (n=64045) Intervention 2: Transplant - Transplant (generic). Received dialysis while on transplant waiting list, and received a transplant within five years. Duration 2-7y. Concurrent medication/care: Uncontrolled Comments: 14% live donor, 38% deceased donor, 7% extended-criteria donor
Funding	Academic or government funding (USRDS is supported by US dept Health Resources and Service Administration)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSPLANT (GENERIC) versus DIALYSIS (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death - deceased (non-extended criteria donor) transplant vs remain on waiting list - adjusted (Merion 2005) at Ave 3y; RR; 0.28 (95%CI 0.27 to 0.3);
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern; Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: Death - deceased donor transplant vs remain on waiting list - adjusted (Abbott 2004) at Ave 3y; Group 1: n=16495 ; Group 2: n=17044; HR 0.47; Lower CI 0.44 to Upper CI 0.5
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern; Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: Death aged 65 and over - deceased donor transplant vs remain on waiting list - adjusted (Abbott 2004) at Ave 3y;
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern; Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for General population: Death for BMI≥30 kg/m² - deceased donor transplant vs remain on waiting list - adjusted (Glanton 2003) at Ave 2.5y; Group 1: n=1719 ; Group 2: n=5172; HR 0.39; Lower CI 0.33 to Upper CI 0.47
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Baseline differences and comparability of care concern;

Indirectness of outcome: No indirectness ; Baseline details: Age and aetiology; Key confounders: age, race/ethnicity, CKD aetiology, comorbidities; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Vonesh 2004[438]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=398940)
Countries and setting	Conducted in USA; Setting: US, Medicare patients, from CMS
Line of therapy	1st line
Duration of study	Intervention + follow up: 3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Post-hoc subgroup analysis
Inclusion criteria	Medicare patients starting dialysis between 1995 and 2000, survived first 90 days of ESRD, on modality for at least 60 days
Exclusion criteria	Nil else
Recruitment/selection of patients	Retrospective cohort analysis from CMS database
Age, gender and ethnicity	Age - Other: ~50% >65, 35% 45-64. Gender (M:F): 54:46. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=352706) Intervention 1: Haemodialysis - HD (generic). Nil else specified. Duration Maximum follow-up 3 years. Concurrent medication/care: Usual care

	(n=46234) Intervention 2: Peritoneal dialysis - PD (generic). Nil else specified. Duration Maximum follow-up 3 years. Concurrent medication/care: Usual care
Funding	Study funded by industry

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD (GENERIC) versus PD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for People and children without diabetes: RR, one or more comorbidities, aged 45-64, without diabetes at 3 year follow-up; RR; 1.01 (95%CI 0.92 to 1.11);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: RR, one or more comorbidities, aged 45-64, with diabetes at 3 year follow-up; RR; 0.96 (95%CI 0.91 to 1.01);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children without diabetes: RR, one or more comorbidities, aged at least 65, without diabetes at 3 year follow-up; RR; 0.82 (95%CI 0.77 to 0.87);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: RR, one or more comorbidities, aged at least 65, with diabetes at 3 year follow-up; RR; 0.80 (95%CI 0.76 to 0.85);
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Ward 2000[447]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=45)
Countries and setting	Conducted in Germany; Setting: Neuried KfH dialysis centre
Line of therapy	1st line
Duration of study	Intervention time: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Participants had previously been treated by conventional HD of high-flux HD and were stable on thrice weekly regimen for two months, with permanent vascular access
Exclusion criteria	Vascular access not capable of delivering a blood flow of at least 250ml/min
Recruitment/selection of patients	45 pts recruited. Protocol allowed for further pts to be recruited to replace any person dropping out before six months, which led to six more being recruited
Age, gender and ethnicity	Age - Mean (SD): HDF 61+/-3, HFH 52+/-3. Gender (M:F): 29:16. Ethnicity: Not stated
Further population details	1. Age: Not applicable (ave 56y). 2. BMI: Not applicable (ave 23). 3. DM: Not stated / Unclear 4. Ethnicity: Not stated / Unclear
Extra comments	All participants were paired on the basis of body size, existing treatment time and blood flow rate, and predialysis serum beta2-microglobulin concentration, and pair were allocated to different treatments. Baseline characteristics: Cause of ESRD - glomerulonephritis 6/9, PCKD 2/5, diabetes 3/3, HTN 4/0; Duration of

	dialysis (mo) 47/68; BMI 23/23.
Indirectness of population	Serious indirectness: Patients not RRT naive, as needed to be stabilised on HD prior to commencement
Interventions	(n=24) Intervention 1: Haemodialysis - HDF. Postdilution hemodiafiltration was performed using a specifically designed system incorporating on-line preparation. blood is passed through a high-flux filter, where it is subjected to dialysis with ultrafiltration at a rate in excess of that required to achieve the patient's dry weight. Fluid balance is maintained by infusing sterile, nonpyrogenic substitution solution into the venous blood line. The substitution solution is derived from ultrapure dialysate by passing it through a single-use ultrafilter immediately before its infusion into the venous blood line. The dialysate is prepared by proportioning ultrafiltered water, liquid acid concentrate, and liquid bicarbonate concentrate made on-line from a dry powder cartridge. This dialysate is then rendered ultrapure by passage through a second untrafilter. At entry to the study, the ultrafiltration rate for each patient was set at 25% of the patient's blood flow rate. The ultrafiltration rate was then increased until the rate that provided a stable transmembrane pressure of 200 mmHg was found. Typical substitution solution flow rates ranged from 65 to 85 ml/min, and actual dialysate flow rates during hemodiafiltration ranged from 415 to 435 ml/min. Duration 12 months. Concurrent medication/care: Other aspects of the patients' therapy prescription did not differ between the two groups. Anticoagulation was achieved using a loading dose and constant infusion of heparin. Net fluid removal was set on an individual basis according to the patient's clinical need. (n=21) Intervention 2: Haemodialysis - HD (generic). High-flux haemodialysis was performed using a dialyzer containing polyamide membrane and a dialysate flow rate of 500ml/min . Duration 12 months. Concurrent medication/care: Other aspects of the patients' therapy prescription did not differ between the two groups. Anticoagulation was achieved using a loading dose and constant infusion of heparin. Net fluid removal was set on an individual basis according to the patient's clinical need.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus HF-HD

Protocol outcome 1: Symptom scores/functional measures
- Actual outcome for General population: KDQ Physical symptoms at 12 months: Group 1: mean 4.8 pt (SD 0.3); n=24, Group 2: mean 4.8 pt (SD 0.4);

n=21; Kidney Disease Questionnaire, Physical symptoms dimension 1-7 Top=High is good outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HDF group older, shorter time on dialysis, more hypertensive kidney disease; difficult to understand why analysis of 45pts when the drop outs were replaced; Indirectness of outcome: No indirectness ; Baseline details: Age 61/52 (sd 3), aetiology HTN 4/0, duration of dialysis 47(sd9)/68(sd16); Group 1 Number missing: 1, Reason: 1 ?; Group 2 Number missing: 4, Reason: 3 hypertension worsened, 1 ? Protocol outcome 2: Psychological distress and mental wellbeing - Actual outcome for General population: KDQ Depression at 12 months; Group 1: mean 5.8 pt (SD 0.2); n=24, Group 2: mean 5.6 pt (SD 0.3); n=21; Kidney Disease Questionnaire, depression dimension 1-7 Top=High is good outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - HDF group older, shorter time on dialysis, more hypertensive kidney disease; difficult to understand why analysis of 45pts when the drop outs were replaced; Indirectness of outcome: No indirectness ; Baseline details: Age 61/52 (sd 3), aetiology HTN 4/0, duration of dialysis 47(sd9)/68(sd16); Group 1 Number missing: 1, Reason: 1 ?; Group 2 Number missing: 4, Reason: 3 hypertension worsened, 1 ?	
Protocol outcomes not reported by the study	Quality of life ; Mortality at >/= 6 months; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Weinhandl 2010[451]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=12674)
Countries and setting	Conducted in USA; Setting: USA
Line of therapy	1st line
Duration of study	Follow up (post intervention): Mean follow-up 2.3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Adult patients, started dialysis in US in 2003, started with HD/PD, in CMS database
Exclusion criteria	Nil else
Recruitment/selection of patients	Propensity score matched cohorts used for analysis
Age, gender and ethnicity	Age - Range of means: 59-64. Gender (M:F): 54:46. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=6337) Intervention 1: Haemodialysis - HD (generic). Nil else provided . Duration Mean follow-up 2.3 years . Concurrent medication/care: Usual care

	(n=6337) Intervention 2: Peritoneal dialysis - PD (generic). Nil else provided . Duration Mean follow-up 2.3 years. Concurrent medication/care: Usual care
Funding	Study funded by industry
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality, HR at Mean follow-up of 2.3 years; Group 1: n=6337 ; Group 2: n=6337; HR 0.92; Lower CI 0.86 to Upper CI 1 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Winkelmayer 2002[455]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=2539)
Countries and setting	Conducted in USA; Setting: New Jersey
Line of therapy	1st line
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	>65, began RRT between 1991 and 1996, either Medicare or Medicaid in New Jersey, renal insufficiency at least 1 year before starting dialysis, dialysis duration >1 month
Exclusion criteria	Transplantation within 1 month of starting RRT
Recruitment/selection of patients	Retrospective analysis of Medicare/Medicaid database
Age, gender and ethnicity	Age - Other: >65. Gender (M:F): 55:45. Ethnicity: ~80% white, ~15% black
Further population details	
Indirectness of population	No indirectness
Interventions	(n=1966) Intervention 1: Haemodialysis - HD (generic). HD as first mode of dialysis, no exclusion for switching but no detail provided on numbers switching, no other details specified (as entered on database). Duration 1

	year of follow-up. Concurrent medication/care: Usual care (n=537) Intervention 2: Peritoneal dialysis - PD (generic). PD as first mode of dialysis, no exclusion for switching but no detail provided on numbers switching, no other details specified (as entered on database). Duration 1 year . Concurrent medication/care: Usual care
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC) Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality at 1 year; Group 1: n=537 ; Group 2: n=1966; HR 1.24; Lower CI 1.09 to Upper CI 1.41; Comments: Principally driven by first and last 90 days of the year, violated proportional hazards assumption Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Wizemann 2000[457]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=44)
Countries and setting	Conducted in Germany; Setting: Appears to be from one HD centre
Line of therapy	1st line
Duration of study	Intervention time: 24 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	"Chronic patients" not preselected according to disease status, nutritional status or anaemia
Exclusion criteria	Nil described
Recruitment/selection of patients	Not described
Age, gender and ethnicity	Age - Mean (SD): HDF 60(12)y, HD 61(11)y. Gender (M:F): 25:19. Ethnicity: not stated
Further population details	1. Age: Not applicable (Ave around 60y). 2. BMI: Not applicable (Unselected). 3. DM: Not applicable (prev 18%). 4. Ethnicity: Not stated / Unclear
Extra comments	Sparse baseline data: DM 8/44, IHD 27/44
Indirectness of population	Serious indirectness: Not RRT naive as recruited from HD programme

Interventions	(n=23) Intervention 1: Haemodialysis - HDF. Received on-line haemodiafiltration. The HDF system differed in the use of an additional filter (total surface area 3.6m2) and substitution fluid running about a target of 60litre/pt/session. The dialysate flow was kept low in order to match the Kt/V of HD, and treatment duration was kept the same. Duration 24 months. Concurrent medication/care: Both processes used bicarbonate dialysate, with blood flow 400-500ml/min and dialysate flow 500ml/min. Biochemical and clinical parameters were reviewed every two months, and prescription altered if appropriate. Non-dialysis care not described Comments: Seven pt dropped out over 24m (n=21) Intervention 2: Haemodialysis - HD (generic). Low flux haemodialysis using polysulfone filter. Duration 24 months. Concurrent medication/care: Both processes used bicarbonate dialysate, with blood flow 400-500ml/min and dialysate flow 500ml/min. Biochemical and clinical parameters were reviewed every three months, and prescription altered if appropriate. Non-dialysis care not described
Funding	Funding not stated (One of the author's affiliation is to Fresnius MC)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HDF versus LF-HD

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for General population: Death at 24 months; Group 1: 1/23, Group 2: 2/21
Risk of bias: All domain - Low, Selection - High, Blinding - Low, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - No info re selection bias, high differential drop-out; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7, Reason: 2 transplant, 4 personal reasons, 1 febrile episode; Group 2 Number missing: 3, Reason: 3 personal reasons

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Woods 1996[463]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=3172)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up: Max follow up 4 years (median not stated)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Not applicable
Inclusion criteria	Started treatment for ESRD between 1986 and 1987, Medicare entitled, data contained in USRDS,
Exclusion criteria	Patients receiving home HD within 30 days of onset of ESRD as likely to be nurse provided and worse prognosis
Recruitment/selection of patients	Retrospective cohort analysis, randomly sampled after weighting for size of centres
Age, gender and ethnicity	Age - Range: 49-59. Gender (M:F): Define. Ethnicity: ~60% white
Further population details	
Indirectness of population	No indirectness
Interventions	(n=70) Intervention 1: Haemodialysis - HD at home. HD at home, nil else specified. Duration Max follow-up 4 years. Concurrent medication/care: Usual care

	(n=3102) Intervention 2: Haemodialysis - HD in centre. HD in centre, nil else specified . Duration Max follow-up 4 years . Concurrent medication/care: Usual care
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HD AT HOME versus HD IN CENTRE Protocol outcome 1: Mortality at >/= 6 months - Actual outcome for General population: Mortality, HR, median duration of follow-up not specified at Max follow-up 4 years; Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation or other healthcare resource use at >/= 6 months; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

Study	Yeates 2012[468]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=35265)
Countries and setting	Conducted in Canada; Setting: Canada
Line of therapy	1st line
Duration of study	Intervention + follow up: Maximum follow-up 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	General population
Subgroup analysis within study	Post-hoc subgroup analysis
Inclusion criteria	On dialysis (PD or HD) for at least 60 days, started dialysis in Canada between 1991 and 2007
Exclusion criteria	Died or censored within 90 days of starting dialysis
Recruitment/selection of patients	Retrospective cohort analysis from CORR
Age, gender and ethnicity	Age - --: >18. Gender (M:F): 58:42. Ethnicity:
Further population details	
Indirectness of population	No indirectness
Interventions	(n=32531) Intervention 1: Haemodialysis - HD (generic). Including hospital, community or home. Duration Maximum follow-up 5 years. Concurrent medication/care: Usual care

	(n=14308) Intervention 2: Peritoneal dialysis - PD (generic). Including home, satellite and hospital. Duration Maximum follow-up 5 years. Concurrent medication/care: Usual care
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PD (GENERIC) versus HD (GENERIC)

Protocol outcome 1: Mortality at >/= 6 months
- Actual outcome for People and children without diabetes: Mortality, HR, age 45 to 64, no DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: Mortality, HR, age 45 to 64, with DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children without diabetes: Mortality, HR, age at least 65, no DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for People and children with diabetes: Mortality, HR, age at least 65, with DM at Maximum follow-up 5 years;
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Hospitalisation or other healthcare resource use at >/= 6 months
- Actual outcome for General population: All-cause hospitalisation rate ratio (Quebec only) at Maximum follow-up 5 years; Rate ratio: 0.99, Comments: Length of stay = HD 37.5 days per 1000 pt/days of follow-up, PD 39.7 days per 1000 pt/days of follow-up);
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low, Comments - Based on LaFrance 2012; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing

Protocol outcomes not reported by the study	Quality of life ; Symptom scores/functional measures ; Hospitalisation - length of stay at >/= 6 months; Time to failure of RRT form ; Psychological distress and mental wellbeing ; Preferred location of death ; Cognitive impairment ; Patient/family/carer experience of care ; Growth ; Malignancy ; AEs - infections ; AEs - vascular access issues ; AEs - dialysis access issues ; AEs - acute transplant rejection episodes

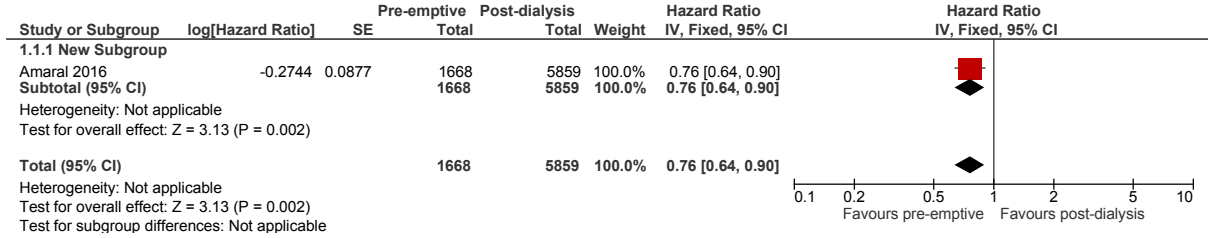
Appendix E: Forest plots

E.1 Infants and children aged under two years

No evidence

E.2 Children and young people aged 2 to 18

Figure 7: Pre-emptive transplant versus Transplant post-dialysis on mortality



E.3 Adults aged >18 to 70

Transplant vs dialysis (HD or PD)

Figure 8: Mortality (time to event) at 3y – NRS evidence

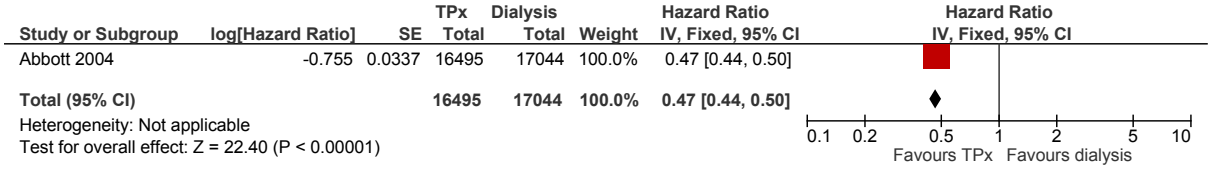


Figure 9: Mortality (time to event), people with BMI≥30, at mean 2.5y – NRS evidence

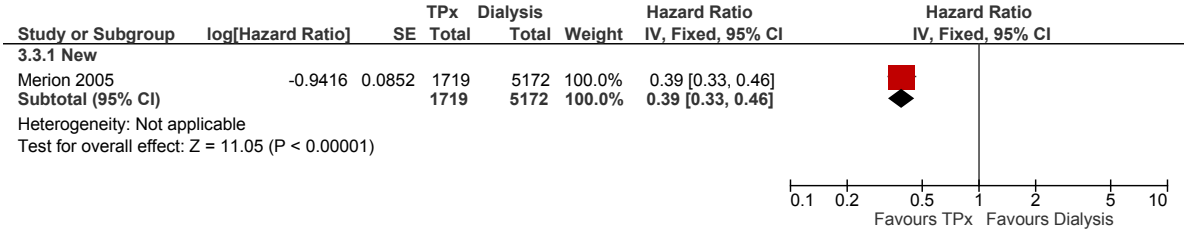
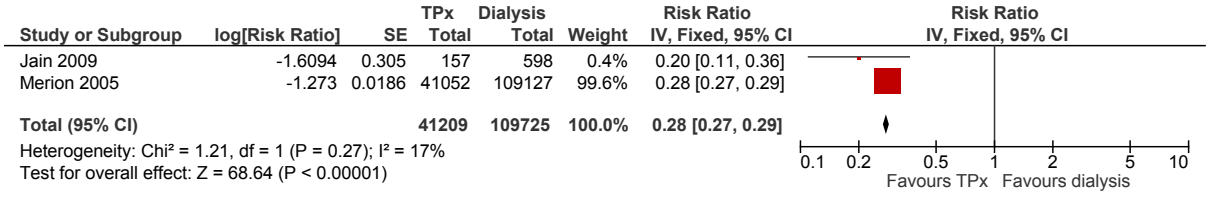


Figure 10: Mortality (relative risk) at 3-4y – NRS evidence



Peritoneal Dialysis (PD) vs Haemodialysis (HD), RCT

Figure 11: Mortality (time to event) at 2.5y – RCT evidence

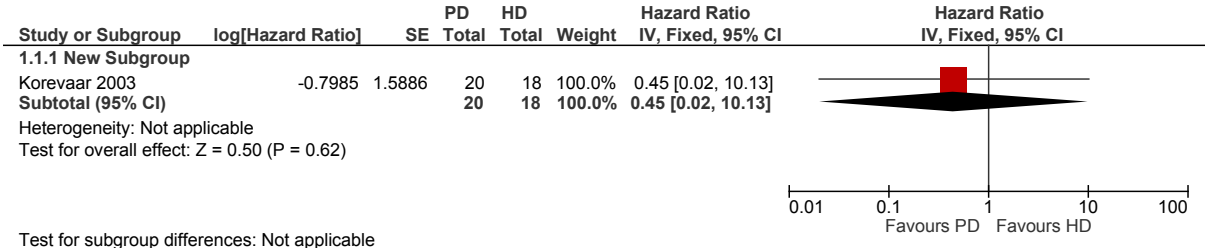
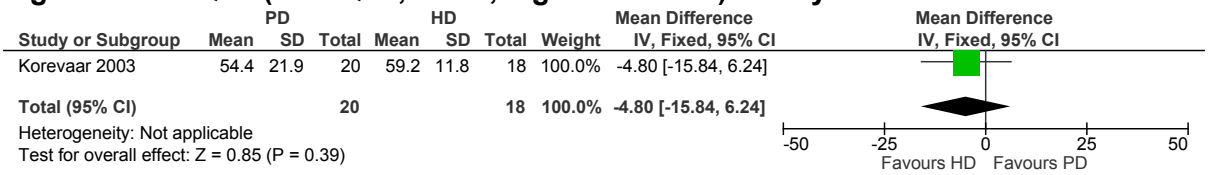


Figure 12: QoL (EuroQoL, 0-100, higher is better) at 2.5y – RCT evidence



Peritoneal Dialysis (PD) vs Haemodialysis (HD), NRS

Figure 13: Mortality (time to event), general population, average FU 2.5 years – NRS evidence

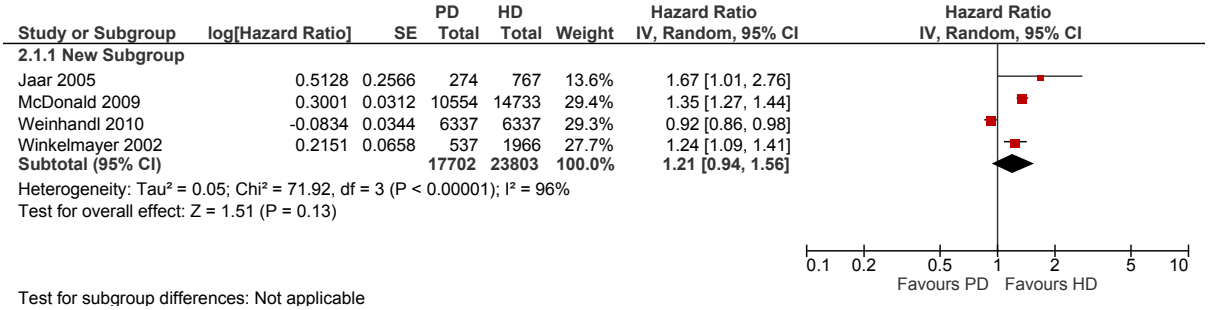


Figure 14: Mortality (time to event), people with diabetes (type 1 or 2), average FU 2.5 years – NRS evidence

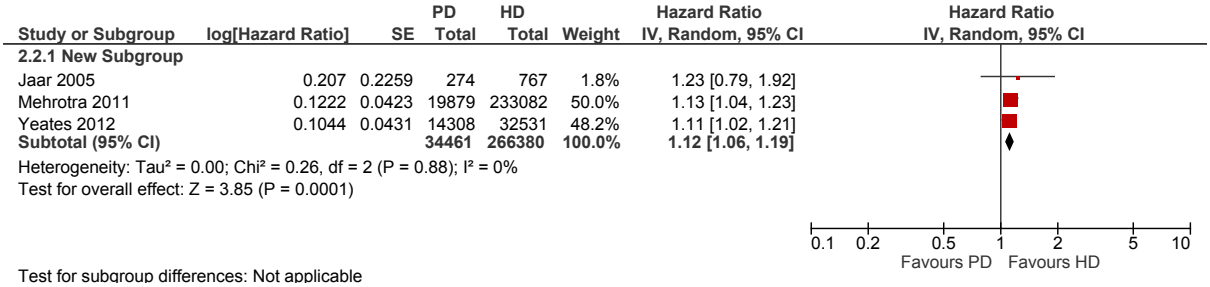


Figure 15: Mortality (time to event), people *without* diabetes, average FU 2.5 years – NRS evidence

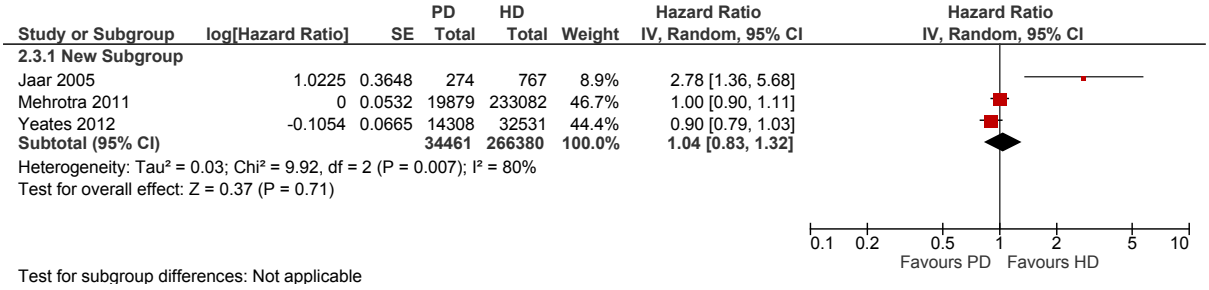


Figure 16: Mortality (time to event), people with residual urine output, average FU 2.5 years – NRS evidence

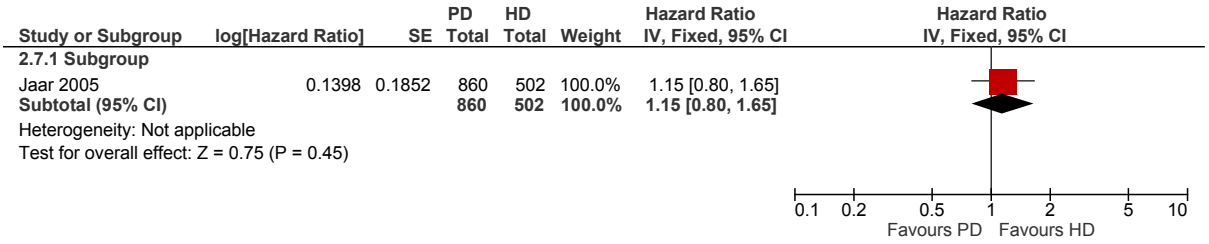


Figure 17: Mortality (relative risk), people with diabetes (type 1 or 2), average FU 2.5 years – NRS evidence

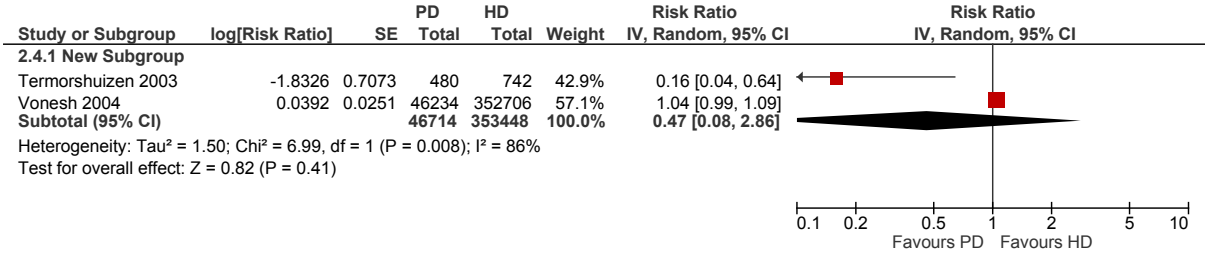


Figure 18: Mortality (relative risk), people *without* diabetes, average FU 2.5 years – NRS evidence

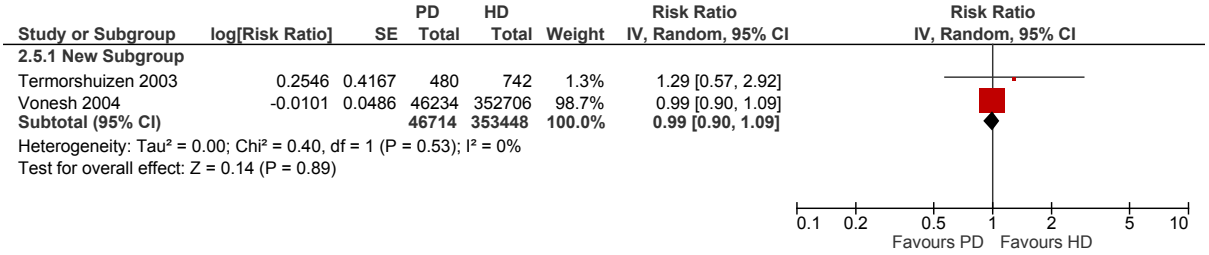


Figure 19: All-cause hospitalisation

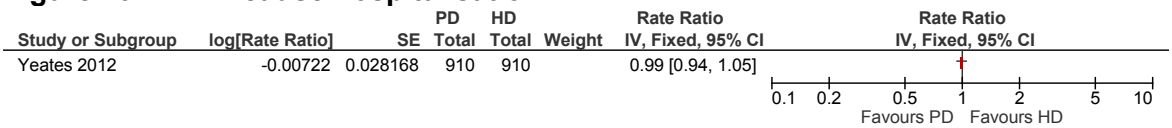
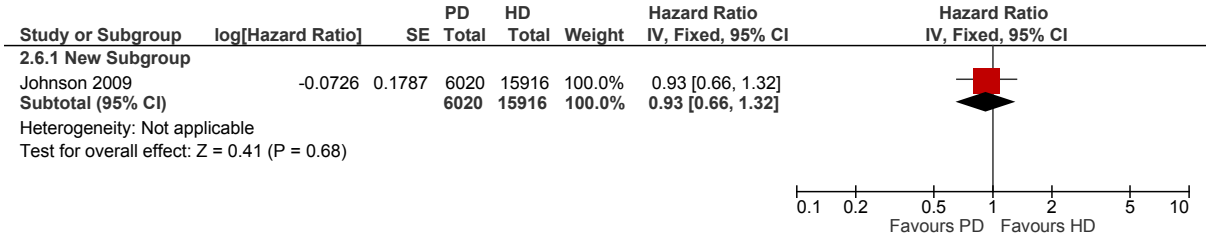


Figure 20: Adverse Events = deaths from infection (time to event) taking place 6 months to 2 years after start of dialysis



Transplant submodalities

Pre-emptive Transplant vs Transplant up to a year after dialysis (NRS evidence only)

Figure 21: Mortality (time to event), general population, average FU 3 years

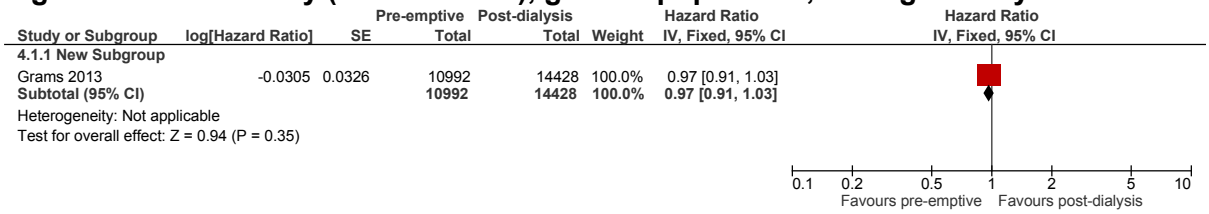
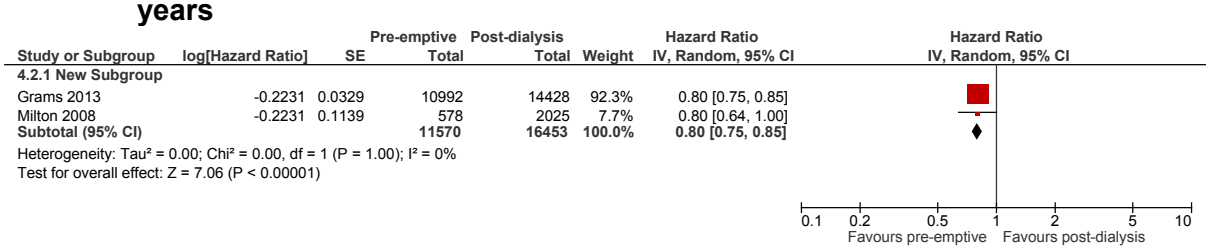


Figure 22: Modality/graft failure (time to event), general population, average FU 3 years



Transplant from Live Donor vs Transplant from deceased donor (NRS evidence only)

Figure 23: Mortality, general population, 5 yrs

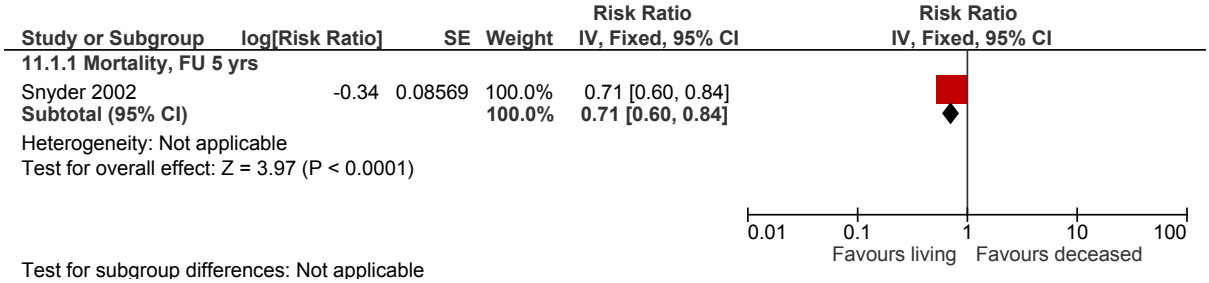
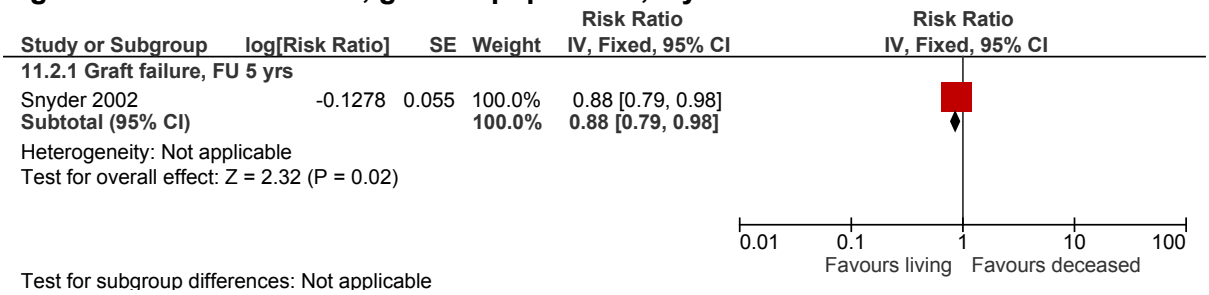


Figure 24: Graft failure, general population, 5 yrs



Test for subgroup differences: Not applicable

Haemodialysis submodalities

Haemodiafiltration (HDF) vs Haemodialysis (HD), RCT evidence only

Figure 25: Mortality, TTE, general population, average FU 2-3 years

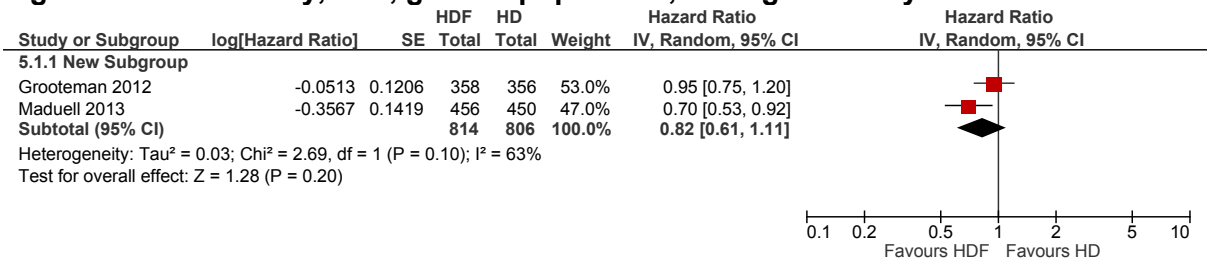


Figure 26: Mortality, RR, general population, average FU 2-3 years

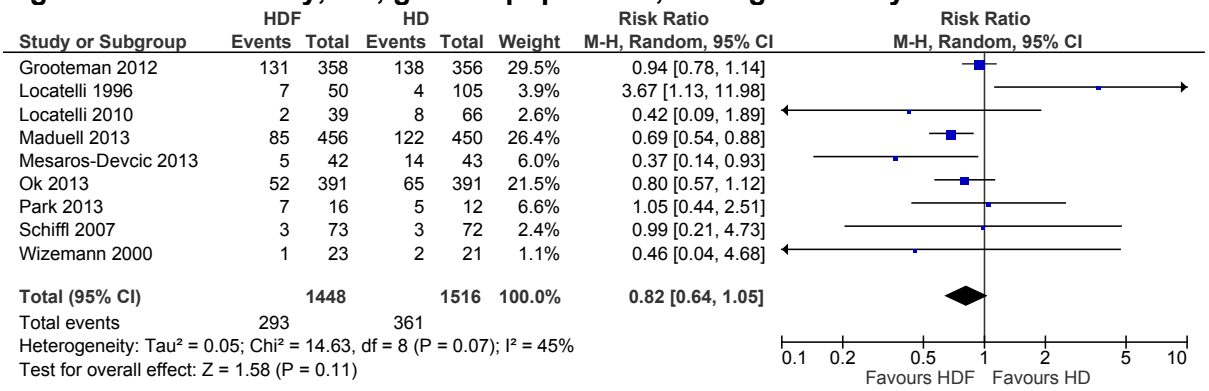
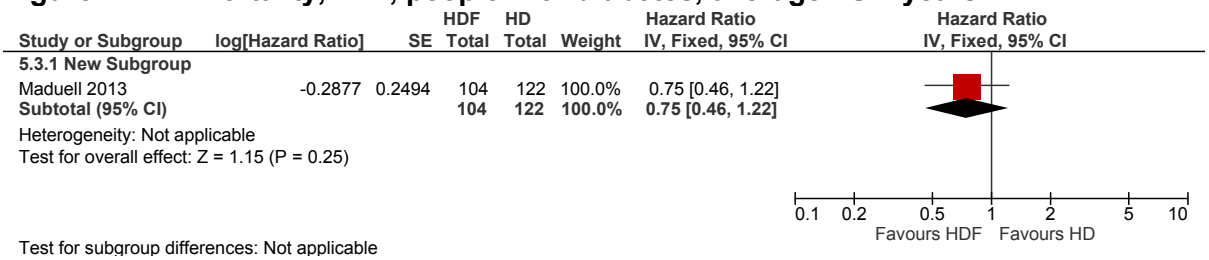


Figure 27: Mortality, TTE, people with diabetes, average FU 2 years



Test for subgroup differences: Not applicable

Figure 28: Mortality, RR, people with diabetes, average FU 2 years

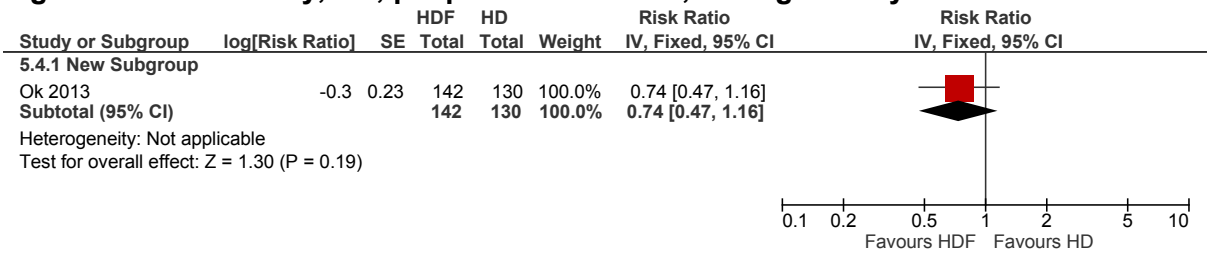


Figure 29: QoL (SF-36 PCS, 0-100, high is good outcome) average FU 2-3 months

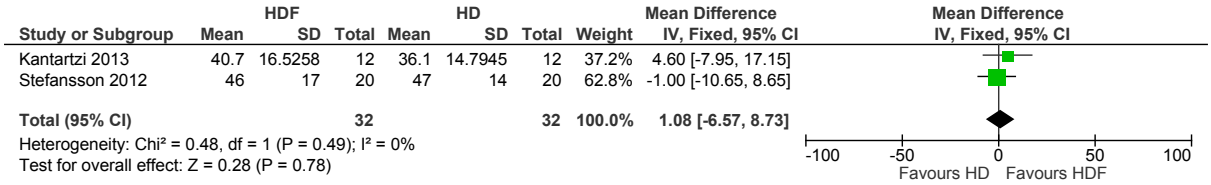


Figure 30: QoL (SF-36 MCS, 0-100, high is good outcome) FU 2 months

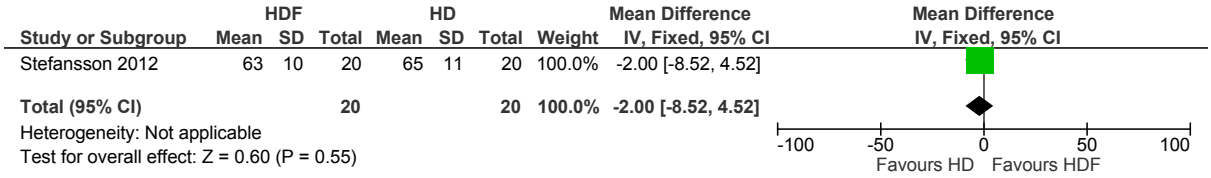


Figure 31: QoL (EQ5D, 0-1.0, high is good outcome) FU 5 yrs

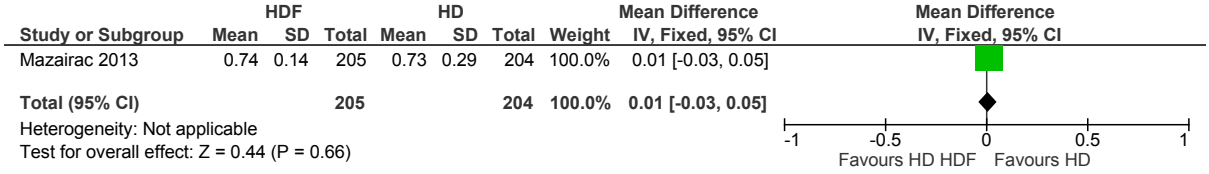


Figure 32: Hospitalisation, rate ratio, general population, average FU 2 years

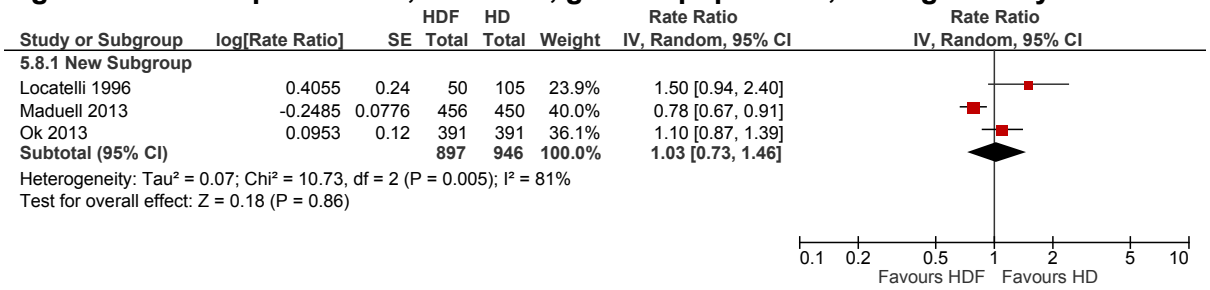


Figure 33: Symptom/function (KDQ physical symptoms, 1-7, high is good outcome), average FU 1 year

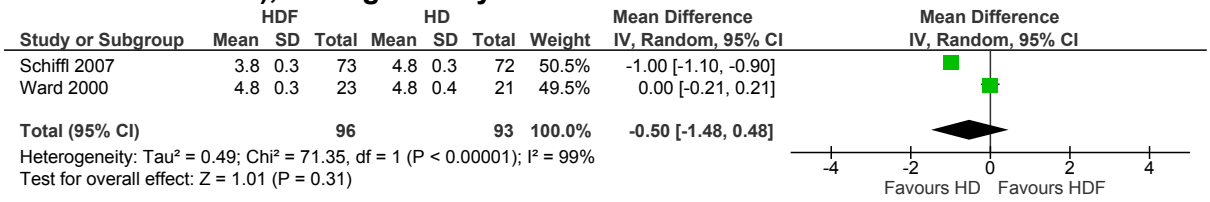


Figure 34: Mental wellbeing (KDQ depression, 1-7, high is good outcome), average FU 1 year

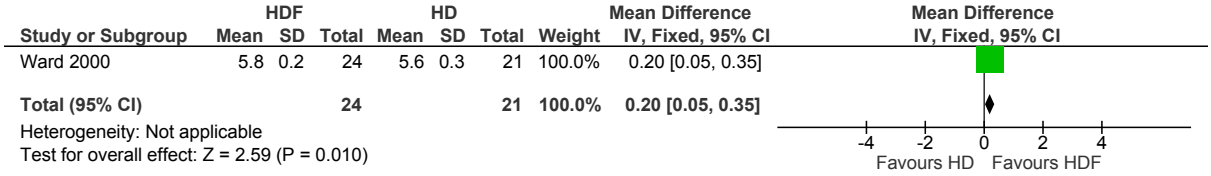


Figure 35: AE (all infections), average FU 2-3 years

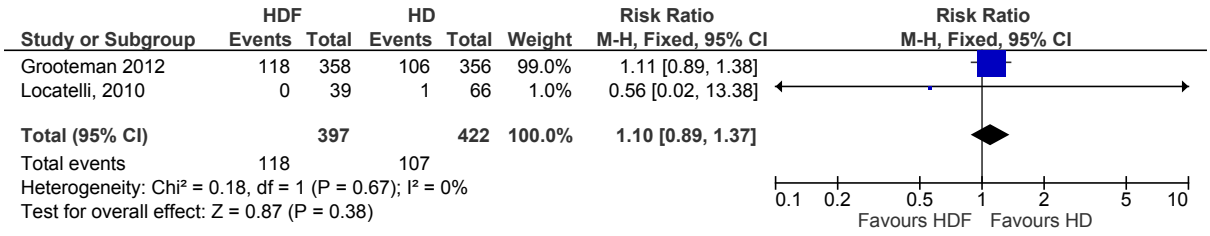
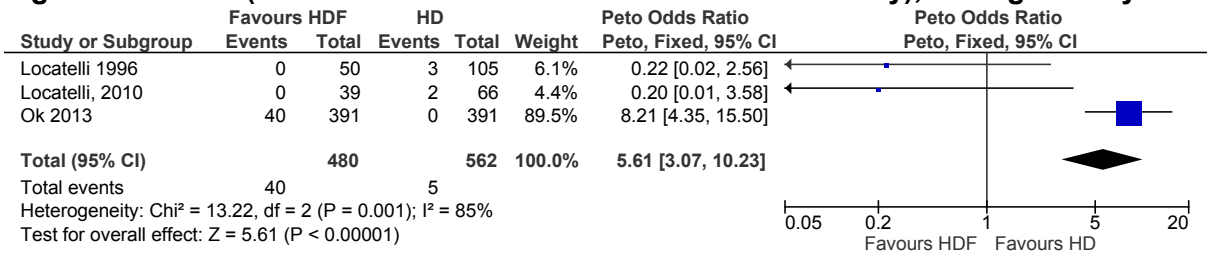


Figure 36: AE (vascular access related withdrawal from study), average FU 2 years



Haemodialysis submodalities continued

Haemodialysis three times a week (3xwk) vs More than three times a week (>3xwk), RCT evidence only

Figure 37: Mortality, RR, general population, average FU 3 years

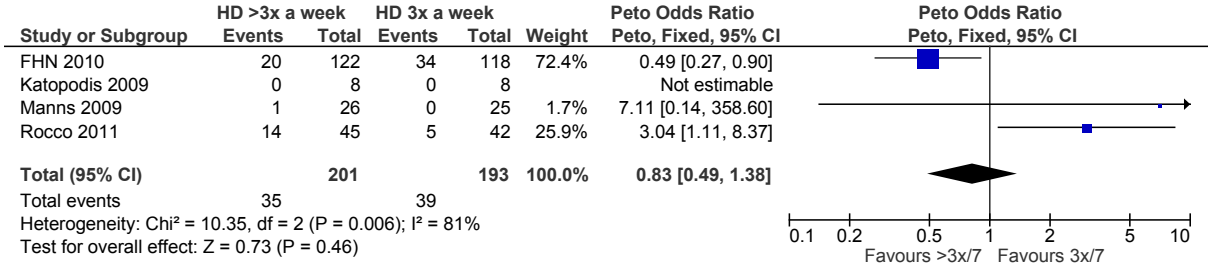


Figure 38: QoL (SF-36 MCS, 0-100, high is good outcome), average FU 1 year

Study or Subgroup	HD >3x a week Mean	SD	Total	HD 3x a week Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
FHN 2010	3.7	0.9	100	0.2	1	89	87.2%	3.50 [3.23, 3.77]
Manns 2009	0.71	12	26	0	11.9	25	0.2%	0.71 [-5.85, 7.27]
Rocco 2011	3	1.6	38	-0.7	1.6	39	12.7%	3.70 [2.99, 4.41]
Total (95% CI)			**164**			**153**	**100.0%**	**3.52 [3.27, 3.78]**

Heterogeneity: Chi² = 0.97, df = 2 (P = 0.62); I² = 0%
Test for overall effect: Z = 27.12 (P < 0.00001)

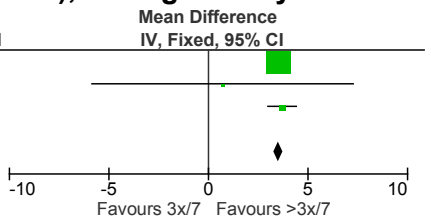


Figure 39: QoL (SF-36 PCS, 0-100, high is good outcome), average FU 1 year

Study or Subgroup	HD >3x a week Mean	SD	Total	HD 3x a week Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
FHN 2010	3.4	0.8	100	0.4	0.8	90	88.8%	3.00 [2.77, 3.23]
Manns 2009	1.24	8.7977	26	0	8.7977	25	0.2%	1.24 [-3.59, 6.07]
Rocco 2011	2.7	1.4	39	2.1	1.5	38	11.0%	0.60 [-0.05, 1.25]
Total (95% CI)			**165**			**153**	**100.0%**	**2.73 [2.52, 2.95]**

Heterogeneity: Chi² = 47.21, df = 2 (P < 0.00001); I² = 96%
Test for overall effect: Z = 24.95 (P < 0.00001)

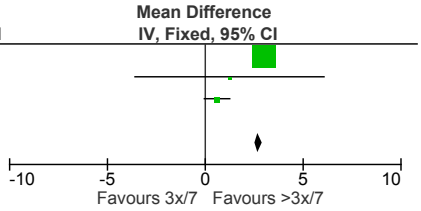


Figure 40: QoI (EQ-5D change score, high is good outcome), FU 6 months

Study or Subgroup	Mean Difference	SE	>3x a week Total	3x a week Total	Mean Difference IV, Fixed, 95% CI
Manns 2009	0.12	0.0587	27	25	0.12 [0.00, 0.24]

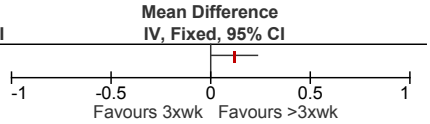


Figure 41: Hospitalisation, rate ratio, general population, average FU 1 year

Study or Subgroup	log[Rate Ratio]	SE	>3x/7 Total	3x/7 Total	Weight	Rate Ratio IV, Fixed, 95% CI
5.4.1 New Subgroup						
FHN 2010	-0.0943	0.133	125	120	68.1%	0.91 [0.70, 1.18]
Manns 2009	-0.30368	0.33114	25	26	11.0%	0.74 [0.39, 1.41]
Rocco 2011	0.2927	0.24	45	42	20.9%	1.34 [0.84, 2.14]
Subtotal (95% CI)			**195**	**188**	**100.0%**	**0.96 [0.78, 1.20]**

Heterogeneity: Chi² = 2.72, df = 2 (P = 0.26); I² = 27%
Test for overall effect: Z = 0.33 (P = 0.74)

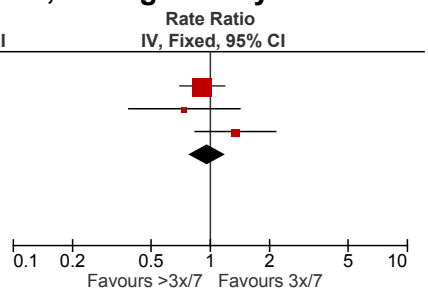


Figure 42: Symptom/function (SPPB, 0-12, high is good outcome), average FU 1 year

Study or Subgroup	HD >3x a week Mean	SD	Total	HD 3x a week Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
FHN 2010	-0.2	0.19	96	-0.4	0.21	81	92.1%	0.20 [0.14, 0.26]
Rocco 2011	-0.92	0.44	34	-0.41	0.43	37	7.9%	-0.51 [-0.71, -0.31]
Total (95% CI)			**130**			**118**	**100.0%**	**0.14 [0.09, 0.20]**

Heterogeneity: Chi² = 43.41, df = 1 (P < 0.00001); I² = 98%
Test for overall effect: Z = 4.94 (P < 0.00001)

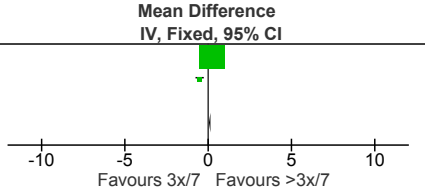


Figure 43: AE (vascular access procedure required), FU 1 year

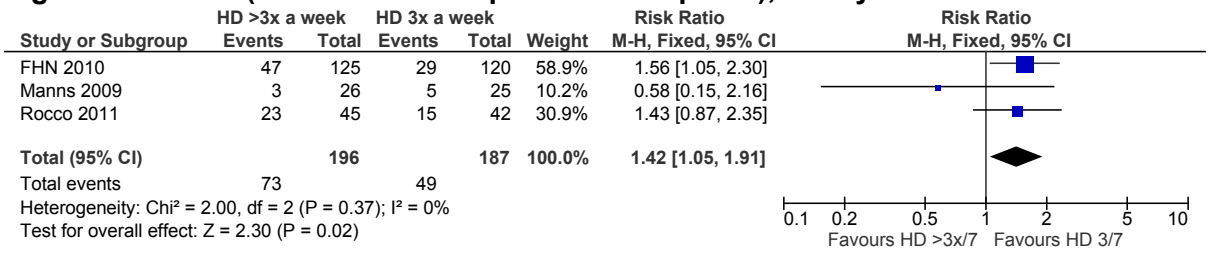
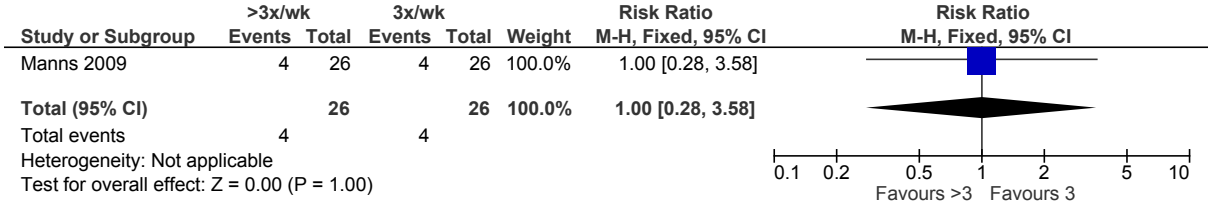


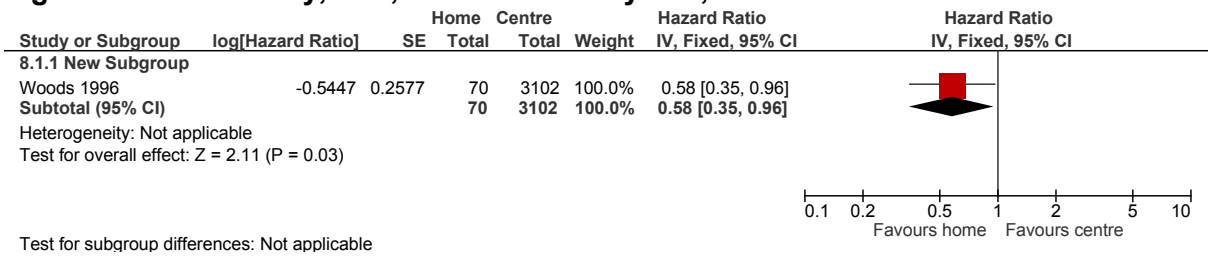
Figure 44: AE (bacteraemia), FU 6 months



Haemodialysis submodalities continued

HD at home vs HD in centre, NRS only

Figure 45: Mortality, TTE, maximum FU 4 years, NRS



Peritoneal Dialysis submodalities

Continuous Ambulatory Peritoneal Dialysis (CAPD) vs Automated Peritoneal Dialysis (APD/CCPD), all evidence

Figure 46: Mortality, RR, general population, average FU 1.5 years, RCT

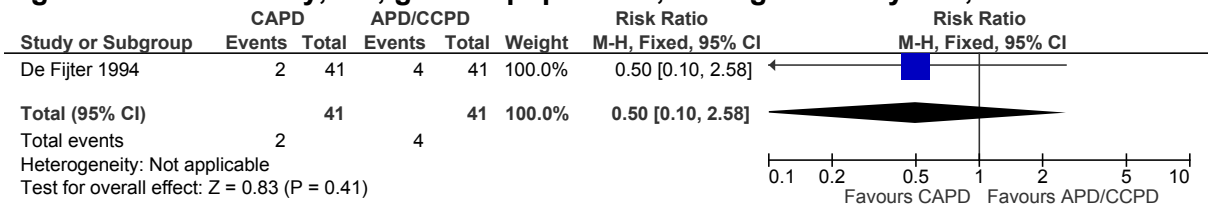


Figure 47: Hospitalisation, rate ratio, general population, average FU 2 years, RCT

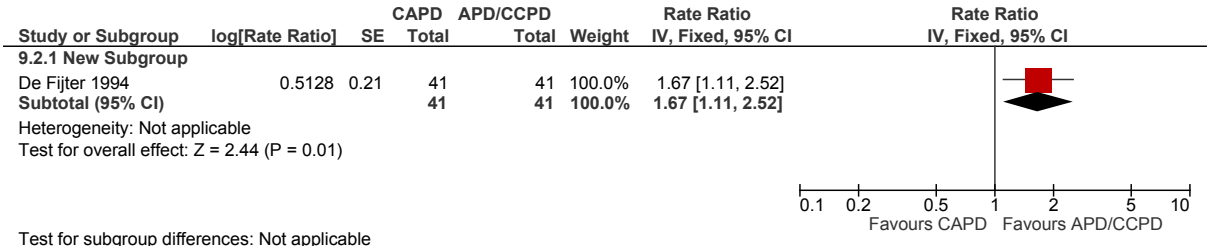


Figure 48: Symptom scores (physical discomfort, 1-5, high is poor), 6 months, RCT

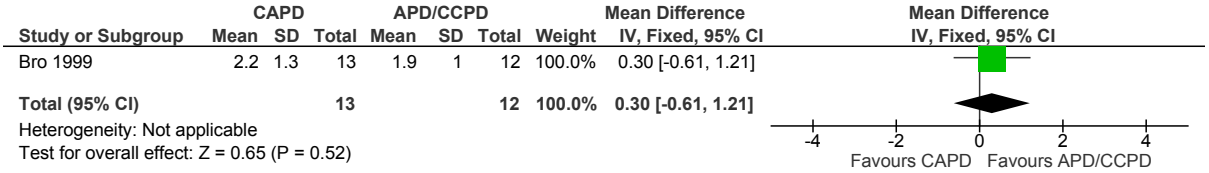


Figure 49: AE (Exit site infection), FU 6 months, RCT

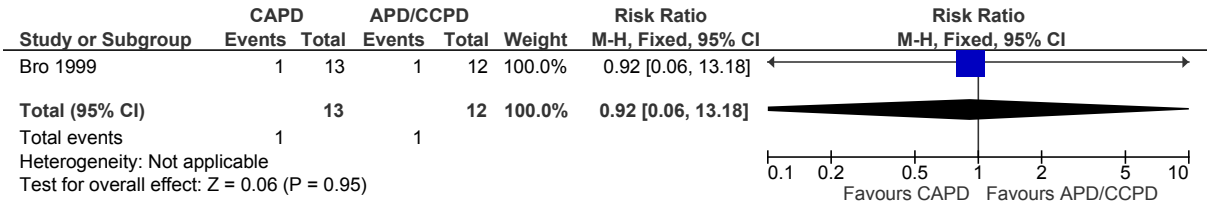


Figure 50: AE (Peritonitis), FU 0.5 -1.5 years, RCT

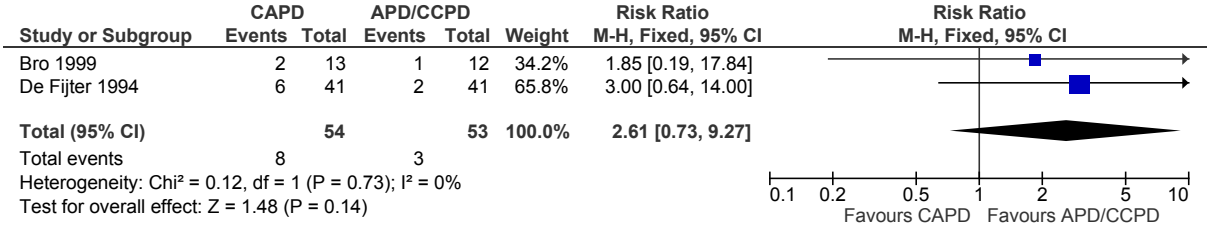


Figure 51: Mortality, TTE, average FU 5 years, NRS

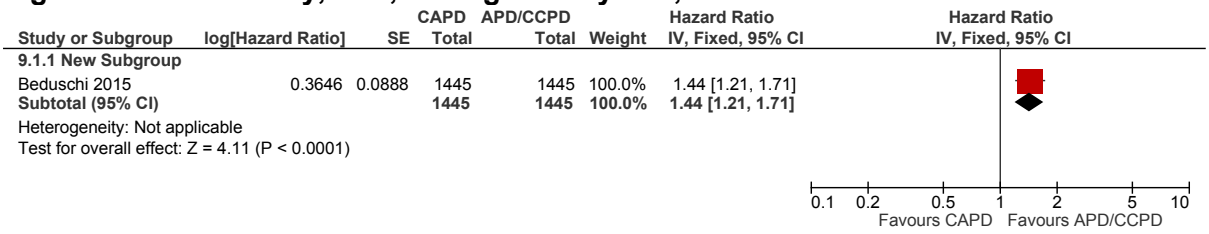


Figure 52: QoL (SF-36 PCS, 0-100, high is good outcome), average FU 1 year, NRS

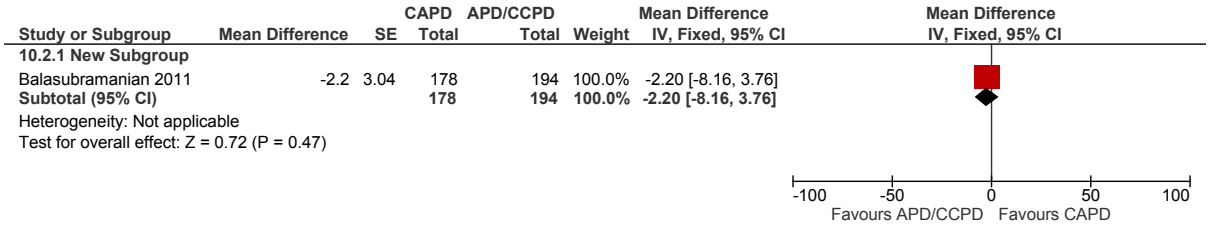


Figure 53: QoL (SF-36 MCS, 0-100, high is good outcome), average FU 1 year, NRS

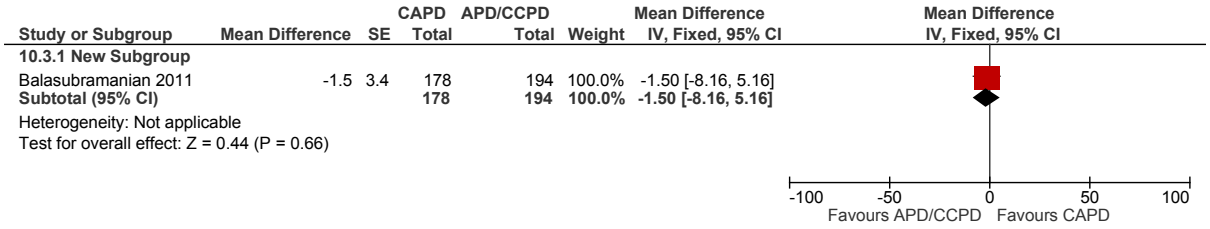
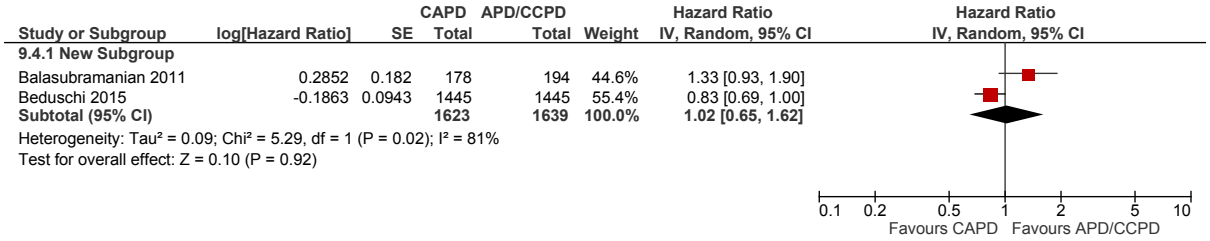


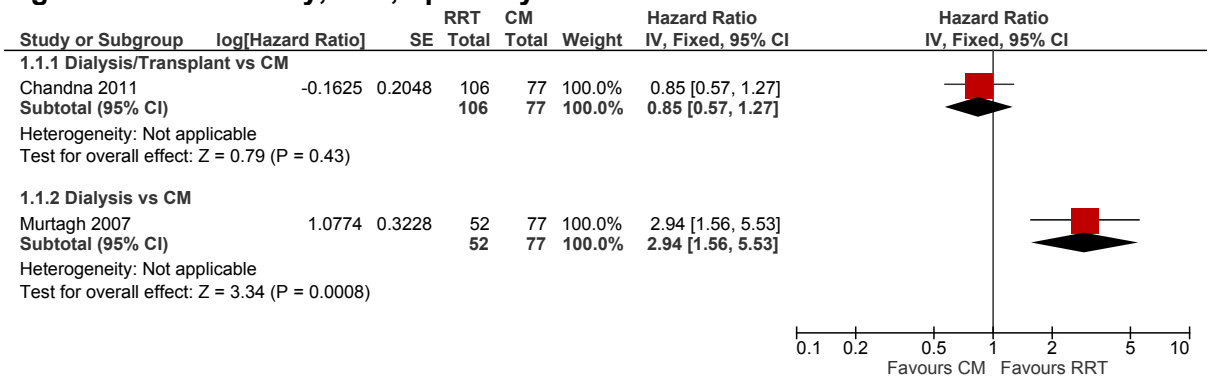
Figure 54: Modality failure, TTE, average FU 2-5 years, NRS



E.4 Adults aged >70

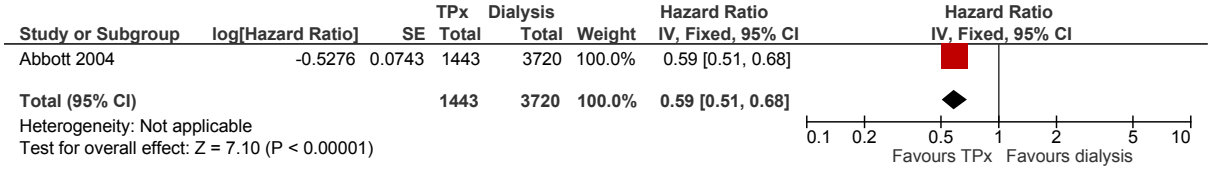
RRT vs Conservative Management

Figure 55: Mortality, TTE, up to 18y



Transplant vs dialysis (HD or PD), NRS only

Figure 56: Mortality, TTE, average FU 3 years



HDF vs HD, RCT

Figure 57 Mortality, RR, general population, average FU 2 years, RCT

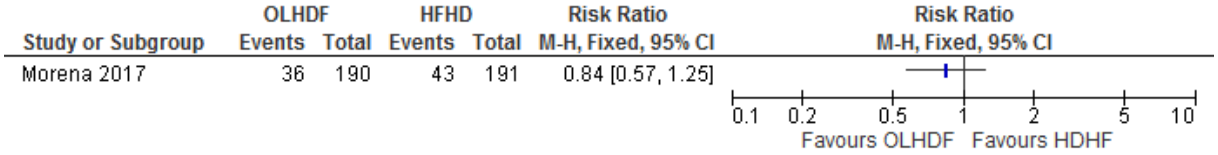
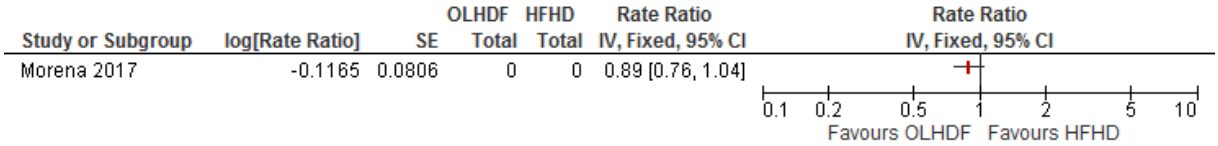


Figure 58 Hospitalisation, rate ratio, general population, average FU 2 years, RCT



Peritoneal dialysis vs Haemodialysis, NRS only

Figure 59: Mortality, TTE, general population, average FU 2.5 years

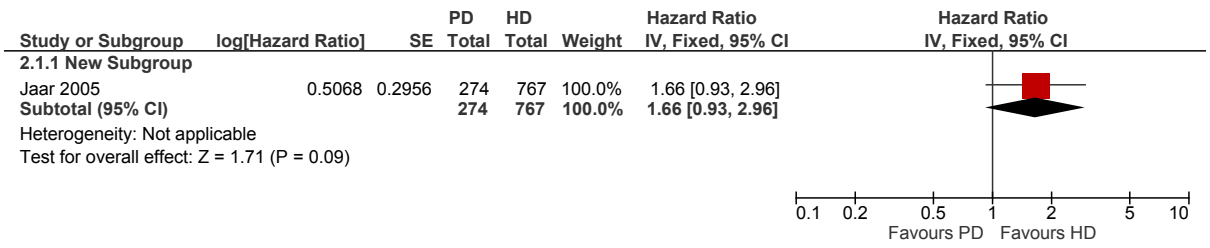
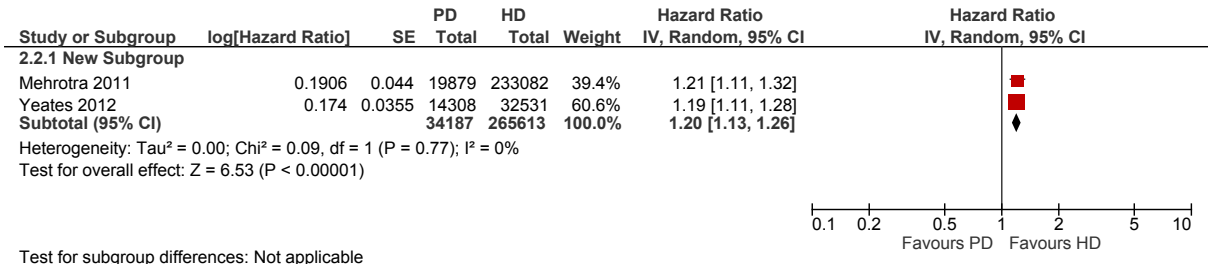


Figure 60: Mortality, TTE, people with, average FU 2.5 years



Test for subgroup differences: Not applicable

Figure 61: Mortality, TTE, people *without* diabetes, average FU 2.5 years

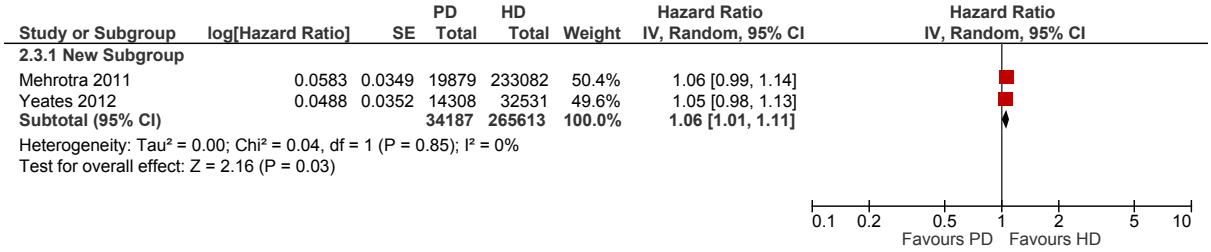


Figure 62: Mortality, RR, people with diabetes, average FU 2-3 years

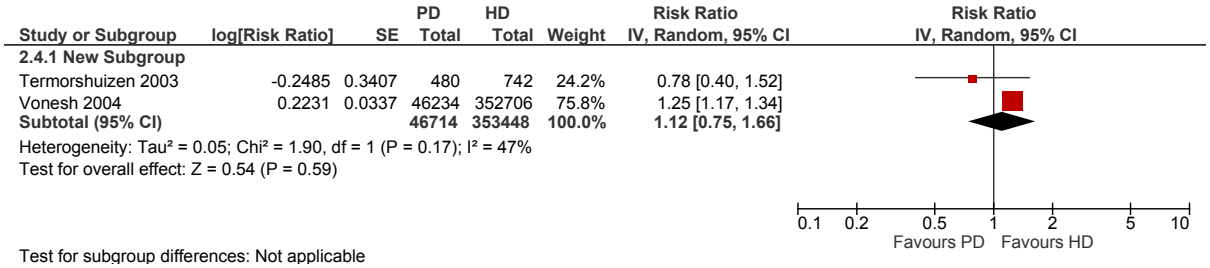
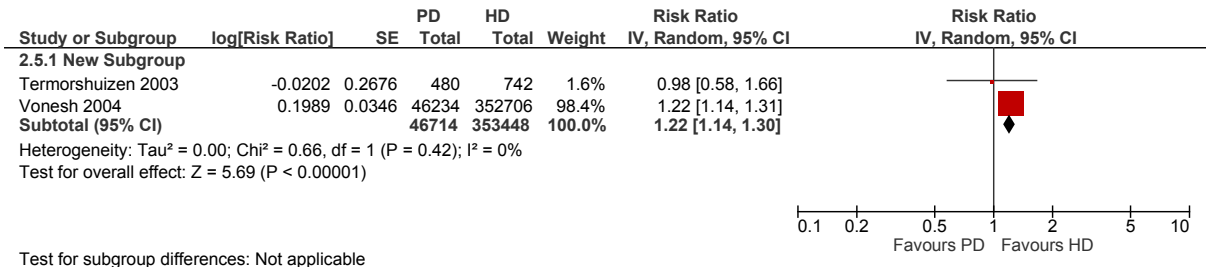


Figure 63: Mortality, RR, people *without* diabetes, average FU 2-3 years



Transplant submodality

Pre-emptive transplant vs Transplant after dialysis, NRS only

Figure 64: Mortality, TTE, general population, average FU 3 years

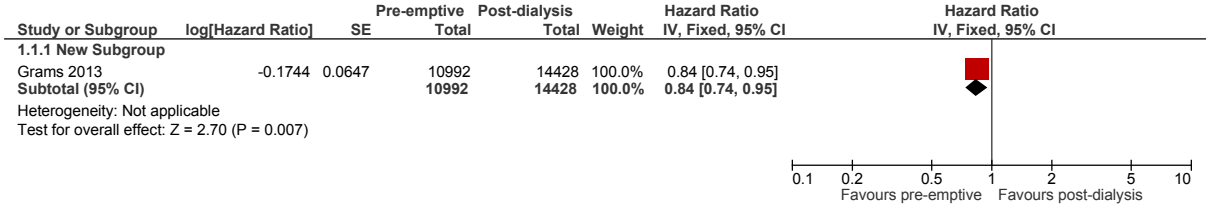
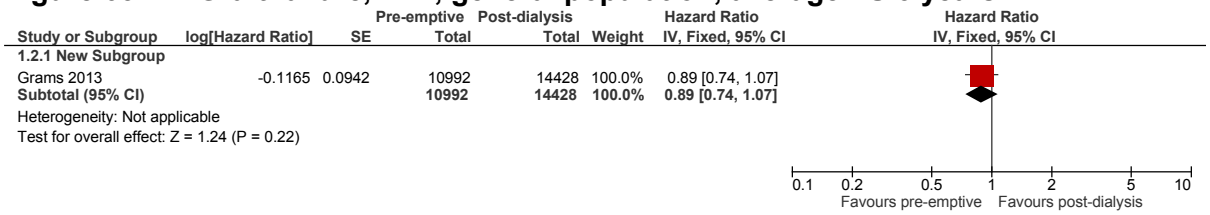


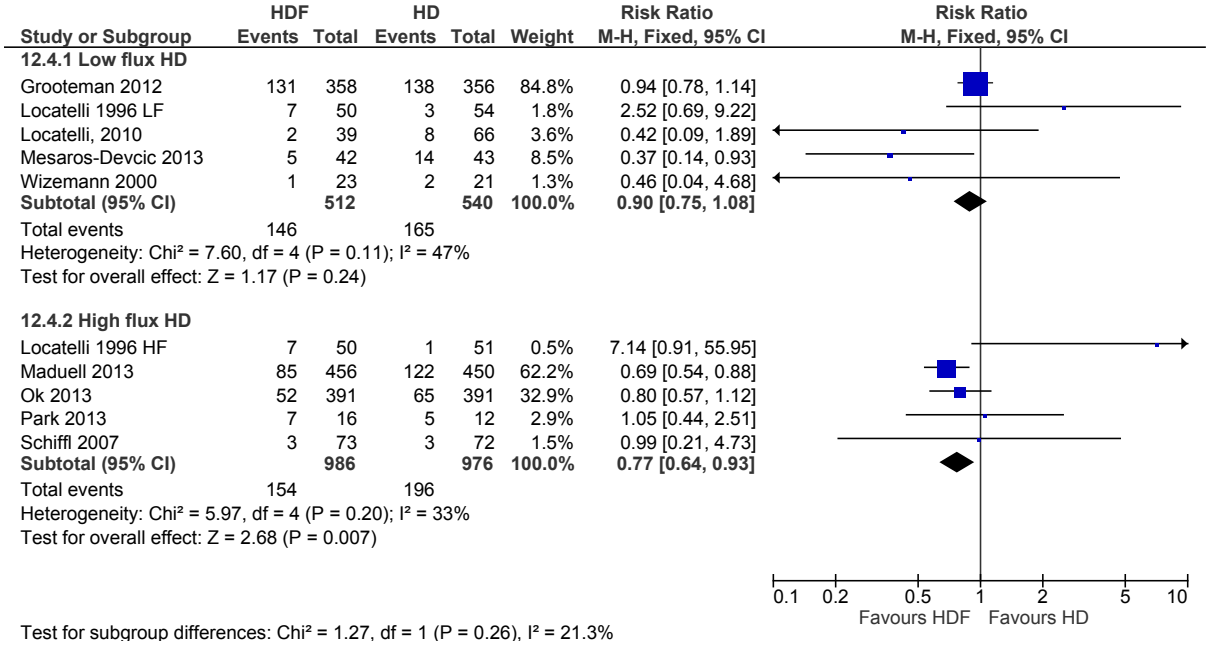
Figure 65: Graft failure, TTE, general population, average FU 3 years



E.5 Intervention subgroup analysis

HDF vs HD by type of HD in controls (low-flux and high-flux)

Figure 66: Mortality (RR), general population, average FU 2-3 years



HD >3x a week vs HD 3x a week

Figure 67: Mortality (RR), general population, average FU 3 years

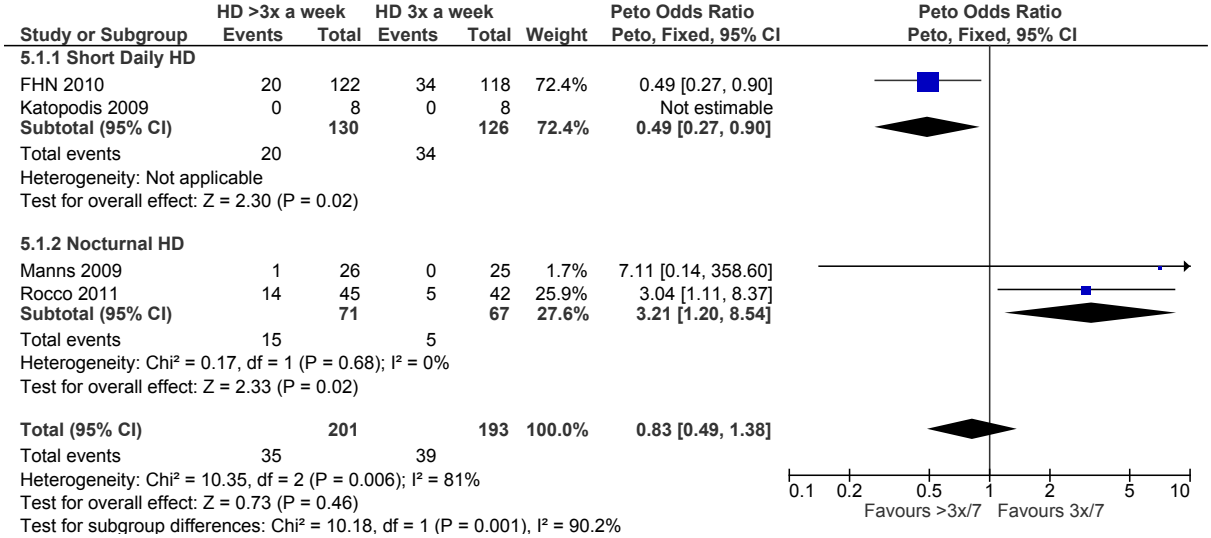


Table 35: Subgroup analysis report – HDF vs HD, mortality

Subgroup analysis	Subgroups	Test for subgroup differences	Committee prediction	Results
HD flux	Low flux (n=5 studies) High flux (n=5	I^2=21.3%, p=0.26	High flux HD is more similar to HDF than low flux HD, so likely to be less difference	High flux: RR

Subgroup analysis	Subgroups	Test for subgroup differences	Committee prediction	Results
	studies)		between high flux and HDF than low flux and HDF	0.77 (0.64 to 0.93) Low flux: RR 0.90 (0.75 to 1.08)
Frequent HD type	"Daily" HD (n=2 studies) Nocturnal HD (n=2 studies)	I^2=90.2%, p=0.001	Frequent daytime HD aims to deliver the same weekly duration of HD over more days, whereas nocturnal HD delivers a much increased number of hours HD, therefore they may have different effects	Short "daily" HD: RR = 0.49 (0.27-0.90) Nocturnal HD: RR = 3.21 (1.20-8.54)

Appendix F:GRADE tables

F.1 Children and young people aged 2 to 18

Table 36: Clinical evidence profile: Pre-emptive transplantation vs transplant after dialysis, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TPx - pre-emptive	After dialysis, NRS	Relative (95% CI)	Absolute		
Graft failure, TTE (follow-up 5 years)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	1668	5859	HR 0.76 (0.64 to 0.9)	-	⊕OOO VERY LOW	IMPORTANT

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

F.2 Adults aged >18 to 70

Table 37: Clinical evidence profile: TPx vs dialysis, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Modalities - TPx vs dialysis	Control	Relative (95% CI)	Absolute		
Mortality, TTE, general population (follow-up 3 years)												

1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	16495	17044	HR 0.47 (0.44 to 0.5)	-	⊕⊕OO LOW	CRITICAL
Mortality TTE, BMI>30 (follow-up mean 2.5 years)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none[3]	1719	5172	HR 0.39 (0.33 to 0.46)	-	⊕OOO VERY LOW	CRITICAL
Mortality, RR, general population (follow-up 3-4 years)												
2	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	strong association[3]	41209	109725	RR 0.28 (0.27 to 0.29)	-	⊕⊕⊕O MODERATE	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] Downgraded by one increment due to indirectness of intervention (those receiving transplant were not RRT naive)
[3] Large effect (ratio < 0.5 or > 2) and consistent across multiple studies

Table 38: Clinical evidence profile: PD vs HD, RCT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Modalities - PD**	**HD, RCTs**	**Relative (95% CI)**	**Absolute**		
Mortality, TTE (follow-up 2.5 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/20 (0%)	9/18 (50%)	HR 0.45 (0.02 to 10.13)	232 fewer per 1000 (from 486 fewer to 499 more)	⊕OOO VERY LOW	CRITICAL
QoL (EuroQoL, 0-100, higher is better) (follow-up 2.5 years; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	20	18	-	MD 4.8 lower (15.84 lower to 6.24 higher)	⊕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] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 39: Clinical evidence profile: PD vs HD, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Modalities - PD	Control	Relative (95% CI)	Absolute		
Mortality, TTE, general population (follow-up 2.5 years)												
4	observational studies	serious[1]	serious[2]	no serious indirectness	serious[3]	none	17702	23803	HR 1.21 (0.94 to 1.56)	-	⊕OOO VERY LOW	CRITICAL
Mortality, TTE, DM (follow-up 2.5 years)												
3	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	34461*	266380*	HR 1.12 (1.06 to 1.19)	-	⊕OOO VERY LOW	CRITICAL
Mortality, TTE, no DM (follow-up 2.5 years)												
3	observational studies	serious[1]	serious[2]	no serious indirectness	serious[3]	none	34461*	266380*	HR 1.04 (0.83 to 1.32)	-	⊕OOO VERY LOW	CRITICAL
Mortality, TTE, residual urine output (follow-up mean 2.5 years)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	860	502	HR 1.15 (0.8 to 1.65)	-	⊕OOO VERY LOW	CRITICAL
Mortality, RR, DM (follow-up 2-3 years)												
2	observational studies	serious[1]	serious[2]	no serious indirectness	very serious[3]	none	46714**	353448*	RR 0.47 (0.08 to 2.86)	-	⊕OOO VERY LOW	CRITICAL
Mortality, RR, no DM (follow-up 2-3 years)												

2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	46714**	353448*	RR 0.99 (0.9 to 1.09)	-	⊕OOO VERY LOW	CRITICAL
All-cause hospitalisation (follow-up 2.1 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2994/910	3147.910	HR 0.99 (0.94 to 1.05)	35 fewer per1000 (from 207 fewer to 173 more)	⊕OOO VERY LOW	CRITICAL
AE (deaths from infection) (follow-up 1 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	6020	15916	HR 0.93 (0.66 to 1.32)	-	⊕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 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup analysis
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

(and ** total study size. Size of DM:non-DM subgroup approx. 1:3)*

Table 40: Clinical evidence profile: Transplant – pre-emptive vs after dialysis, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Submodalities - TPx - pre-emptive**	**After dialysis, NRS**	**Relative (95% CI)**	**Absolute**		
Mortality, TTE, general population (follow-up 3 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10992	14428	HR 0.97 (0.91 to 1.03)	-	⊕OOO VERY LOW	CRITICAL
Modality failure, TTE, general population (follow-up 3 years)												

2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	11570	16453	HR 0.8 (0.75 to 0.85)	-	⊕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] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 41: Clinical evidence profile: Transplant – living vs deceased donor, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Submodalities - TPx, Living vs Deceased**	**Control**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up 5 years)												
1	observational studies	very serious[1]	no serious inconsistency	very serious[2]	no serious imprecision	none	22776		RR 0.71 (0.60 to 0.84)	-	⊕OOO VERY LOW	CRITICAL
Graft failure (follow-up 5 years)												
1	observational studies	very serious[1]	no serious inconsistency	very serious[2]	serious[3]	none	22776		RR 0.88 (0.79 to 0.98)	-	⊕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] Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 42: Clinical evidence profile: HD – HDF vs HD, RCT

Quality assessment							No of patients		Effect		Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Submodalities - HD - HDF**	**HD, RCTs**	**Relative (95% CI)**	**Absolute**		
Mortality, TTE, general population (follow-up 2-3 years)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	216/814 (26.5%)	33%	HR 0.82 (0.61 to 1.11)	50 fewer per 1000 (from 113 fewer to 29 more)	⊕OOO VERY LOW	CRITICAL
Mortality, RR, general population (follow-up 2-3 years)												
9	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	293/1448 (20.2%)	16.62%	RR 0.82 (0.64 to 1.05)	30 fewer per 1000 (from 60 fewer to 8 more)	⊕OOO VERY LOW	CRITICAL
Mortality, TTE, DM population (follow-up 2 years)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	104/456 (22.8%)	27.1%	HR 0.75 (0.46 to 1.22)	60 fewer per 1000 (from 136 fewer to 49 more)	⊕OOO VERY LOW	CRITICAL
Mortality, RR, DM population (follow-up 2 years)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	47/142 (33.1%)	36.9%	RR 0.74 (0.47 to 1.16)	96 fewer per 1000 (from 196 fewer to 59 more)	⊕OOO VERY LOW	CRITICAL
QoL (SF-36 PCS, 0-100, high is good outcome) (follow-up 2-3 months; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	32	32	-	MD 1.08 higher (6.57 lower to 8.73 higher)	⊕OOO VERY LOW	CRITICAL
QoL (SF-36 MCS, 0-100, high is good outcome) (follow-up 2 months; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	20	20	-	MD 2 lower (8.52 lower to 4.52 higher)	⊕OOO VERY LOW	CRITICAL
Qol (EQ5D, 0-1.0, high is good outcome) (follow-up 3 years; Better indicated by higher values)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	198	169	-	MD 0.01 higher (0.03 lower to 0.05 higher)	⊕⊕OO LOW	IMPORTANT
Hospitalisation, rate ratio, general population (follow-up 2 years)												
3	randomised trials	serious[1]	serious[4]	serious[2]	very serious[3]	none	412/897 (45.9%)	69.5%	Rate Ratio 1.03 (0.73 to 1.46)	21 more per 1000 (from 188 fewer to 320 more)	⊕OOO VERY LOW	IMPORTANT
Symptom/function (KDQ physical symptoms, 1-7, high is good outcome) (follow-up 1 years; Better indicated by lower values)												
2	randomised trials	very serious[1]	very serious[4]	serious[2]	no serious imprecision	none	96	93	-	MD 0.82 lower (0.91 to 0.73 lower)	⊕OOO VERY LOW	IMPORTANT
Mental wellbeing (KDQ depression, 1-7, high is good outcome), average FU 1 year (follow-up 1 years; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	24	21	-	MD 0.2 higher (0.05 to 0.35 higher)	⊕OOO VERY LOW	IMPORTANT
AE (all infections) (follow-up 3 years)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	118/397 (29.7%)	15.6%	RR 1.10 (0.89 to 1.37)	16 more per 1000 (from 17 less to 58 more)	⊕OOO VERY LOW	IMPORTANT
AE (vascular access related withdrawal from study) (follow-up 2 years)												
3	randomised trials	serious[1]	serious[4]	serious[2]	no serious imprecision	none	40/480 (8.3%)	2.9%	OR 5.61 (3.07 to 10.23)	70 more per 1000 (from 50 more to 100 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 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[4] Downgraded by 1 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup analysis

Table 43: Clinical evidence summary: HD – HD >3x a week vs HD 3x a week, RCT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Submodalities - HD - HD >3x a week	HD 3x a week, RCTs	Relative (95% CI)	Absolute		
Mortality, RR, general population (follow-up 3 years)												
4	randomised trials	serious[1]	serious[2]	serious[3]	very serious[4]	none	35/201 (17.4%)	11.9%	Peto Odds ratio 0.83 (0.49 to 1.38)	30 fewer per 1000 (from 100 fewer to 50 more)	⊕OOO VERY LOW	CRITICAL
QoL (SF-36 MCS, 0-100, high is good outcome) (follow-up 1 years; Better indicated by lower values)												
3	randomised trials	very serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	164	153	-	MD 3.52 higher (3.27 to 3.78 higher)	⊕OOO VERY LOW	CRITICAL
QoL (SF-36 PCS, 0-100, high is good outcome) (follow-up 1 years; Better indicated by lower values)												
3	randomised trials	very serious[1]	serious[2]	serious[3]	no serious imprecision	none	165	153	-	MD 2.73 higher (2.52 to 2.95 higher)	⊕OOO VERY LOW	CRITICAL
Hospitalisation, rate ratio (follow-up mean 1 years)												
3	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[4]	none	153/195 (78/5%)	95%	Rate Ratio 0.96 (0.78 to 1.2)	38 fewer per 1000 (from 209 fewer to 190 more)	⊕OOO VERY LOW	IMPORTANT
Symptom/function (SPPB, 0-12, high is good outcome) (follow-up 1 years; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[4]	none	130	118	-	MD 0.14 higher (0.09 to 0.2 higher)	⊕OOO VERY LOW	IMPORTANT
AE (vascular access procedure required) (follow-up 1 years)												
3	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[4]	none	73/196 (37.2%)	29.9%	RR 1.42 (1.05 to 1.91)	126 more per 1000 (from 15 more to	⊕OOO	IMPORTANT

										272 more)	VERY LOW	
AE (bacteraemia) (follow-up mean 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	very serious[4]	none	4/26 (15.4%)	16%	RR 1 (0.28 to 3.58)	0 fewer per 1000 (from 115 fewer to 413 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 or 2 increments because the point estimate and or the confidence intervals varied widely across studies, unexplained by subgroup analysis
[3] Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively
[4] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[5] Estimated

Table 44: Clinical evidence summary: HD – HD at home vs HD in centre, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Submodalities - HD - HD at home**	**HD in centre, NRS**	**Relative (95% CI)**	**Absolute**		
Mortality, TTE, general population (follow-up 4 years)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	70	3102	HR 0.58 (0.35 to 0.96)	-	⊕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] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 45: Clinical evidence summary: PD – CAPD compared to APD/CCPD, RCT

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Submodalities - PD - CAPD**	**APD/CCPD, RCTs**	**Relative (95% CI)**	**Absolute**		
Mortality, RR, general population (follow-up 1.5 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/41 (4.9%)	9.8%	RR 0.5 (0.1 to 2.58)	49 fewer per 1000 (from 88 fewer to 155 more)	⊕OOO VERY LOW	CRITICAL
Hospitalisation, rate ratio, general population (follow-up 1.5 years)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	27/41 (65.9%)	48.8%	Rate Ratio 1.67 (1.11 to 2.52)	327 more per 1000 (from 54 more to 742 more)	⊕OOO VERY LOW	CRITICAL
Symptom scores (physical discomfort, 1-5, high is poor), 6 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	13	12	-	MD 0.3 higher (0.61 lower to 1.21 higher)	⊕OOO VERY LOW	IMPORTANT
AE (Exit site infection) (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/13 (7.7%)	8.3%	RR 0.92 (0.06 to 13.18)	7 fewer per 1000 (from 78 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
AE (Peritonitis) (follow-up 0.5-1.5 years)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	8/54 (14.8%)	6.6%	RR 2.61 (0.73 to 9.27)	106 more per 1000 (from 18 fewer to 546 more)	⊕⊕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
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Downgraded by 1 or 2 increments because the majority of the evidence included an indirect or very indirect population respectively

Table 46: Clinical evidence summary: PD – CAPD compared to APD/CCPD, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Submodalities - PD - CAPD	APD/CCPD, NRS	Relative (95% CI)	Absolute		
Mortality, TTE (follow-up 5 years)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/1445 (0%)	0%	HR 1.44 (1.21to 1.71)	-	⊕OOO VERY LOW	CRITICAL
QoL (SF-36 PCS, 0-100, high is good outcome) (follow-up 1 years; Better indicated by lower values)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	178	194	-	MD 2.2 lower (8.16 lower to 3.76 higher)	⊕OOO VERY LOW	IMPORTANT
QoL (SF-36 MCS, 0-100, high is good outcome) (follow-up 1 years; Better indicated by lower values)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	178	194	-	MD 1.5 lower (8.16 lower to 5.16 higher)	⊕OOO VERY LOW	CRITICAL
Modality failure, TTE (follow-up 2-5 years)												
2	observational studies	serious[1]	serious[3]	no serious indirectness	serious[2]	none	0/1623 (0%)	0%	HR 1.02 (0.65 to 1.62)	-	⊕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
[3]Downgraded by 1 or 2 increments because the point estimate and the confidence intervals varied widely across studies, unexplained by subgroup analysis.

F.3 Adults >70

Table 47: Clinical evidence profile: RRT vs Conservative Management (over 75s)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	RRT	CM	Relative (95% CI)	Absolute		
Mortality in over 75s (RRT = Dialysis/Transplant) (follow-up 0-18 years)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	106	77	HR 0.85 (0.57 to 1.27)	-	⊕OOO VERY LOW	CRITICAL
Mortality in over 75s (RRT = Dialysis) (follow-up median 2 years)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	52	77	HR 2.94 (1.56 to 5.53)	-	⊕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] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 48: Clinical evidence profile: TPx vs dialysis

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Modalities - TPx vs dialysis	Control	Relative (95% CI)	Absolute		
Mortality, TTE, general population (follow-up 3 years)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1443	3720	HR 0.59 (0.51 to 0.68)	-	⊕⊕OO LOW	CRITICAL

Table 49: Clinical evidence profile: HDF vs HD

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**HDF**	**HD**	**Relative (95% CI)**	**Absolute**		
Deaths (follow-up mean 2 years)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	very serious[2]	none	36/190 (18.9%)	22.5%	RR 0.84 (0.55 to 1.25)	37 fewer per 1000 (from 100 fewer to 52 more)	⊕OOO VERY LOW	CRITICAL
Hospitalisation (all cause) (follow-up mean 2 years)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	309/190 (162.6%)	346/191 (181.2%)	Rate Ratio 0.89 (0.76 to 1.04)	199 fewer per 1000 (from 435 fewer to 72 more)	⊕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] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

[3] Downgraded by 1 increment if the population was indirect, by 2 increments if the population was very indirect

Table 50: Clinical evidence summary: PD vs HD, NRS (over 60/65y)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Modalities - PD**	**HD, NRS**	**Relative (95% CI)**	**Absolute**		
Mortality, TTE, general population (follow-up 2.5 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	274	767	HR 1.66 (0.93 to 2.96)	-	⊕OOO VERY LOW	CRITICAL
Mortality, TTE, DM (follow-up 2.5 years)												
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	34187*	265613*	HR 1.2 (1.13 to 1.26)	-	⊕OOO VERY LOW	CRITICAL
Mortality, TTE, no DM (follow-up 2.5 years)												
2	observational	serious[1]	no serious	no serious	no serious	none	34187*	265613*	HR 1.06 (1.01 to	-	⊕OOO	CRITICAL

	studies		inconsistency	indirectness	imprecision				1.11)		VERY LOW	
Mortality, RR, DM (follow-up 2-3 years)												
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	46714**	353448**	RR 1.12 (0.75 to 1.66)	-	⊕OOO VERY LOW	CRITICAL
Mortality, RR, no DM (follow-up 2-3 years)												
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	46714**	363448**	RR 1.22 (1.14 to 1.3)	-	⊕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] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
** and ** total study size. Size of DM:non-DM subgroup approx. 1:3*

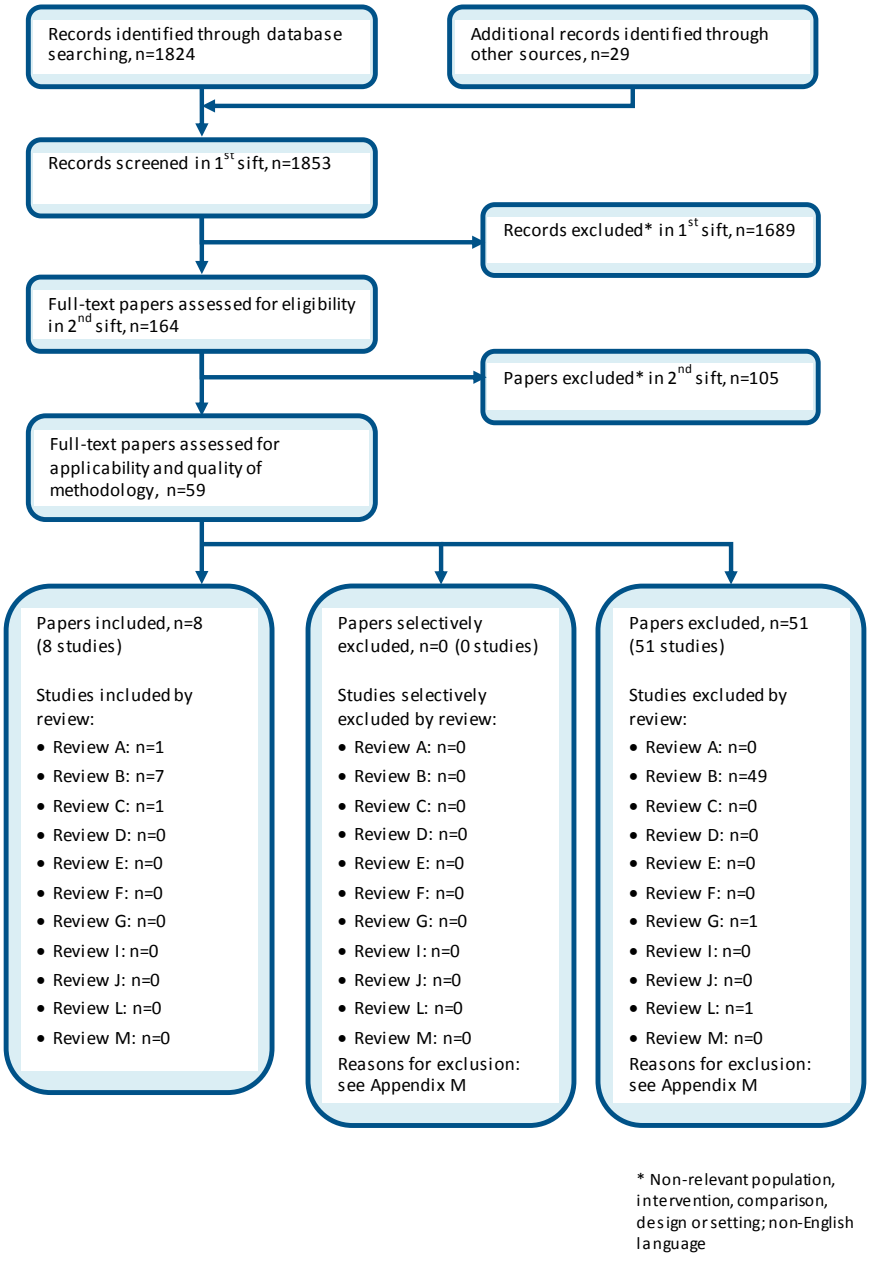
Table 51: Clinical evidence summary: Transplant – pre-emptive vs after dialysis, NRS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**TPx - pre-emptive**	**After dialysis, NRS**	**Relative (95% CI)**	**Absolute**		
Mortality, TTE, general population (follow-up 3 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	10992	14428	HR 0.84 (0.74 to 0.95)	-	⊕OOO VERY LOW	CRITICAL
Graft failure, TTE, general population (follow-up 3 years)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	10992	14428	HR 0.89 (0.74 to 1.07)	-	⊕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 68: 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

H.1 Transplant vs dialysis

None.

H.2 Conservative management versus RRT

None.

H.3 PD vs HD

Study	Chui 2013[74]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CC (health outcome: none) **Study design:** Cohort analysis with all cost models adjusted for age, sex, body mass index, race, comorbid conditions, cause of ESRD, and pre-dialysis care. **Approach to analysis:** multivariate regression **Perspective:** Canadian health care purchaser	**Population:** Adult patients who initiated long-term dialysis (PD or in-centre HD) for ESRD. **Patient characteristics:** HD / PD / HD>PD/ PD>HD N=1005 / 208 / 120 / 45 Male: 59% / 57% / 51% / 56% Age: 61.9 / 54.6 / 52.5 / 55.7 years **Intervention 1:** HD **Intervention 2:**	**Total 1 year costs (mean per patient):** Intervention 1: £50,310 Intervention 2: £19,214 Intervention 3: £35,832 Intervention 4: £43,818 Incremental (2−1): -£31,097 (95% CI: -£34,064 to -£28,130; p=NR) Incremental (3−1): -£14,478 (95% CI: -£18,692 to -£10,264; p=NR) Incremental (4−1): -£6,493 (95% CI: -£12,845 to -£140; p=NR) **Total 3 year costs (mean per patient):** Intervention 1: £99,656 Intervention 2: £33,252 Intervention 3: £64,836 Intervention 4: £98,134	n/a	n/a **Analysis of uncertainty:** 95% CI determined through bootstrapping. Effects of non-censoring of cost data and logarithmic transformations of costs used in multivariate regression models were

Follow-up: 3 years **Treatment effect duration:**[a] n/a **Discounting:** Costs: 0%; Outcomes: 0%	PD **Intervention 3:** HD then switched to PD in first year **Intervention 4:** PD then switched to HD in first year	Incremental (2−1): -£66,404 (95% CI: -£74,672 to -£58,136; p=NR) Incremental (3−1):-£34,820 (95% CI: -£45,117 to -£24,523; p=NR) Incremental (4−1): -£1,522 (95% CI: -£16,008 to £12,964; p=NR) **Cost breakdowns:** **HD>PD vs HD (1 year / 3 years)** Dialysis: -£16,220 (-£20,139 to -£12,301) / -£29,364 (-£37,120 to -£21,607) Inpatient: £333 (-£3,816 to £4,482) / £1,529 (-£6,738 to £9,795) Medication: -£13 (-£214 to £189) / -£31 (-£600 to £538) Physician fees: -£119 (-£655 to £417) / £488 (-£985 to £1,960) **PD>HD vs HD (1 year / 3 years)** Dialysis: -£7,667 (-£11,166 to -£4,067) / -£11,477 (-£21,253 to -£1,702) Inpatient: £2,283 (-£5,593 to £10,160) / £3,993 (-£6,119 to £14,104) Medication: £511 (-£3,425 to £4,448) / £1,259 (-£3,352 to £5,869) Physician fees: £993 (£37 to £1,949) / £2,652 (£493 to £4,811) **Currency & cost year:** 2010 Canadian dollars (presented here as 2010 UK pounds[b]) **Cost components incorporated:** Dialysis costs, inpatient costs, medication costs, and physician fees. It is unclear whether any transport costs are included.		explored in sensitivity analysis. Results not reported but authors state results are similar.

Data sources

Health outcomes: n/a **Quality-of-life weights:** n/a **Cost sources:** Resource use was based on an analysis of administrative records from the Northern and Southern Alberta Renal Programs. Unit costs for Alberta were applied.

Comments

Source of funding: Alberta Heritage Foundation for Medical Research, Alberta Health and Wellness and the Universities of Alberta and Calgary.
Limitations: Does not include all RRT modalities of interest. 2010 Canadian costs based on resource use from 1999-2006 may not reflect current NHS context. Discounting not applied. Health outcomes not incorporated. Within-trial analysis (cohort) so does not reflect the full body of evidence in this area

(note: no parallel clinical study, costs only). It is unclear whether any transport costs are included. **Other:** None.

Overall applicability:(c) Partially applicable **Overall quality:**(d) Potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; NR: not reported; QALYs: quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2010 purchasing power parities[324]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

H.4 APD vs CAPD

None.

H.5 Assisted PD

None.

H.6 HDF vs HD

Study	**Mazairac 2013 (CONTRAST)[276]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Markov model based on within-trial analysis of survival, utility and cost data from CONTRAST RCT[140] with probabilistic analysis. **Approach to analysis**: The model included 2	**Population:** People aged 18 years or above with ESRD undergoing chronic intermittent HD. Three age subgroups were analysed: 18–44 years; 45–64 years; and 65 years and older.	**Total costs (mean per patient):** ***45-64 years*** Intervention 1: £208,561 Intervention 2: £221,336 Incremental (2−1): £12,775 (95% CI: -£7984 to £33,528; p=NR) ***<45 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): £16,867 (95% CI: -£13,760 to £56,484; p=NR)	**QALYs (mean per patient):** ***45-64 years*** Intervention 1: 2.34 Intervention 2: 2.40 Incremental (2−1): 0.06 (95% CI: -0.19 to 0.32; p=NR) ***<45 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.12 (95% CI: -0.52	**ICER (Intervention 2 versus Intervention 1):** ***45-64 years*** £224,258 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): <10%/<10% ***<45 years*** £140,558 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NR ***≥65 years***

health states, 'ESRD' and 'Death'. Mortality, EQ5D utility and costs varied based on treatment and health state. 3 month cycle length. **Perspective:** Dutch societal perspective **Time horizon:** 5 years **Treatment effect duration:**[(a)] 5 years **Discounting:** Costs: 4%; Outcomes: 1.5%	**Cohort settings:** NR **Intervention 1:** HD (low-flux) **Intervention 2:** HDF	***≥65 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): £11,822 (95% CI: -£14,978 to £39,774; p=NR) **Currency & cost year:** 2009 Dutch Euros (presented here as 2009 UK pounds[(b)])] **Cost components incorporated:** Direct healthcare costs: dialysis and other medical staff, material (water installation, dialysis machines and disposables), vascular access, routine diagnostics of patients and dialysis water quality, meals during dialysis, hospitalisation, medication and overheads. Direct non-healthcare costs: travel expenses. Indirect non-healthcare costs: productivity losses.	to 0.81; p=NR) ***≥65 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.03 (95% CI: -0.27 to 0.35; p=NR)	£394,058 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NR **Analysis of uncertainty:** The following sensitivity analyses were undertaken in the 45-64 years subgroup: • 10 year time horizon: ICER £141,670 per QALY gained • Utility and survival data in model based on sub-analysis of HDF patients with high convection volume (CONTRAST data suggested that improved survival): ICER £44,052 per QALY gained • Discount rate to 3% for costs and outcomes: ICER £188,515 per QALY gained • Excluding standard dialysis costs in life years gained (life extending interventions may never be cost effective because the cost of dialysis itself may exclude cost effectiveness thresholds (survival differences removed from analysis): ICER £806,747 per QALY gained.

Data sources

Health outcomes: Survival probabilities and quality of life weights were based on a patient level analysis of a subset of CONTRAST RCT[140] (n=409; full CONTRAST RCT = 714). Probability of death per 3 months HD/HDF: overall 0.0315/0.0297; age <45 0.0019/0.0044; age 45-64 0.0221/0.0192; age >65 0.72/0.72. QOL EQ-5D scores HD/HDF: overall 0.73/0.74 (difference 0.01); age <45 0.77/0.81 (difference 0.04); age 45-64 0.73/0.76 (difference 0.03); age >65 0.72/0.72 (difference 0.00). **Quality-of-life weights:** EQ-5D Dutch tariff. **Cost sources:** a combination of bottom-up measurements using patient-level resource use collected during the CONTRAST trial and top down estimates for cost categories that were thought to be similar for all patients (e.g. disposables used during dialysis. Unit costs were from Dutch national sources where possible and the literature or local sources otherwise. 3 month total cost HD/HDF: £16,777/£17,271; annual total cost HD/HDF £67,108/£69,084 (higher cost of HDF mainly attributable to higher expenses for disposables and more frequent control of water purity). Medication and hospitalisation costs were similar.

Comments

Source of funding: This study was funded by ZonMw (the Netherlands Organization for Health Research and Development. The CONTRAST trial is financially supported by the Dutch Kidney Foundation (Nierstichting, the Netherlands, grant C02.2019), and unrestricted grants from Fresenius Medical

Care Netherlands and Gambro Lundia AB, Sweden. Additional support was received from the Dr E.E. Twiss Fund, Roche Netherlands and the International Society of Nephrology/Baxter Extramural Grant Programme. **Limitations:** Resource use from Netherlands, Canada and Norway between 2004 and 2010, and 2009 unit costs may not reflect current NHS context. The cost of productivity losses is included in the intervention costs which is not in line with the NICE reference case, however these costs are relatively small in relation to the total intervention costs in the analysis (a saving of £45 per 3 months with HDF vs HD; overall HDF costs £634 more than HD per 3 months in model); excluding these costs would makes HDF less cost effective. The discount rates used were not in line with the NICE reference case (4% of costs and 1.5% for outcomes, rather than 3.5% for both; a sensitivity analysis was done with 3% for both). QALYs are calculated using the EQ5D Dutch tariff. Analysis based on subset of a single study (CONTRAST[140]) and so does not reflect full body of available evidence for this area. 5 year time horizon; as survival varies between comparators the impact on QALYs and costs will not be fully captured (sensitivity analysis explores impact of extending to 10 years). Some sources of funding are from industry however primary funding is not. **Other:** None.

Overall applicability:[(c)] partially applicable **Overall quality:**[(d)] potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ESRD = end-stage renal disease; HD = haemodialysis; HDF = haemodiafiltration; ICER: incremental cost-effectiveness ratio; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2009 purchasing power parities[324]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Study	**Levesque 2015 (CONTRAST)[235]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** 1) Within-trial analysis from Canadian subset of CONTRAST RCT[140] incorporating survival, quality of life and resource use; 2) Markov model based on within-trial analysis data with probabilistic analysis. **Approach to analysis**:	**Population:** People aged 18 years or above with ESRD undergoing chronic intermittent HD. **Cohort settings:** **Intervention 1:** HD (low-flux)	**Total costs (mean per patient):** ***Within-trial analysis (74 months)*** Intervention 1: £115,884 Intervention 2: £125,211 Incremental (2−1): £9327 (95% CI: NR; p=NR) ***Model (lifetime)*** Intervention 1: £174,613 Intervention 2: £209,527 Incremental (2−1):	**QALYs (mean per patient):** ***Within-trial analysis (74 months)*** Intervention 1: 3.70 Intervention 2: 4.01 Incremental (2−1): 0.31 (95% CI: NR; p=NR) ***Model (lifetime)*** Intervention 1: 5.17	**ICER (Intervention 2 versus Intervention 1):** ***Within-trial analysis (74 months)*** £18,275 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): NR ***Model (lifetime)*** £30,316 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): ~40%/~50% **Analysis of uncertainty:**

The model included 2 health states, 'ESRD' and 'Death'. Mortality, EQ5D utility and costs varied based on treatment and health state. 1 year cycle length. **Perspective:** Canadian (Quebec) public healthcare system **Time horizon:** within-RCT analysis - 74 months/ with modelled extrapolation - lifetime **Treatment effect duration:**[(a)] same as time horizon **Discounting:** Costs: 3%; Outcomes: 3%	**Intervention 2:** HDF (high efficiency - HDF performed with an optimal convection fluid volume (that is the sum of substitution fluid volume and net ultrafiltration)	£34,914 (95% CI: NR; p=NR) **Currency & cost year:** 2013 Canadian dollars (presented here as 2013 UK pounds[(b)]) **Cost components incorporated:** Dialysis and other medical staff, material (water installation, dialysis machines and disposables), vascular access, routine diagnostics of patients and dialysis water quality, meals during dialysis, hospitalization, medication, transport.	Intervention 2: 6.21 Incremental (2−1): 1.04 (95% CI: NR; p=NR)	In the within-trial analysis, it is noted that when costs of additional survival time on HDF are disregarded there is a cost saving of £311. In the lifetime analysis one-way sensitivity analyses were undertaken using the upper and lower bounds of the 95% CI around model inputs. The authors report that the hazard ratio for death had the biggest impact on the ICER. • HR 0.440: £41,048 per QALY gained • HR 1.418: £82,915 per QALY gained Annual probability of death on HD: • 10%: £27,503 • 21%: £30,316 Assuming no difference in QOL increased the ICER to £46,707 per QALY gained. Use of the US value set for EQ-5D was also explored but is not reported here. Authors also calculate ICER compared to immediate death (no costs and no QALYs): HD £52,913; HDF £47,085. Including no treatment and immediate death as a comparator means HD is ruled out by extended dominance.
Data sources				
Health outcomes: Baseline mortality rate on HD, survival probabilities and quality of life weights were based on a patient level analysis of a subset of the CONTRAST RCT[140] consisting of the 80 participants from the Canadian centre in the CONTRAST study plus an additional 50 patients enrolled at the same centre in-line with the original trial protocol that all received high efficiency HDF (CONTRAST RCT = 714). Trial subgroup data used in model: Annual probability of death on HD 15.2%; HR for death with HDF vs HD 0.789 (0.440-1.418); QOL EQ-5D-5L scores for HD 0.64 (0.55-0.73) and HDF 0.72 (0.65-0.79); equates to differences of 0.08. **Quality-of-life weights:** EQ-5D-5L UK tariff. **Cost sources:** a combination of bottom-up measurements using patient-level resource use collected during the CONTRAST trial and top down estimates for cost categories that were thought to be similar for all patients (e.g. disposables used during dialysis. Unit costs were from the hospitals in the trial or from Canadian (Quebec) list prices. Intervention cost per session HD/HDF: £146/£153 (higher costs with HDF due to disposables, dialysis machine and water treatment).Total annual costs: £33,806/£33,752 (higher HDF intervention costs [£6860] and hospitalisation costs [£283] offset by lower drug costs [£7476 saving]).				
Comments				
Source of funding: Amgen Canada and Fresenius Medical Care. **Limitations:** Resource use from Canada between 2007 and 2010, and 2013 unit				

costs may not reflect current NHS context. The discount rate used was not in line with the NICE reference case (3% for costs and outcomes, rather than 3.5%). Analysis based on subset of a single study (CONTRAST) and so does not reflect full body of available evidence for this area. Methods for sensitivity analysis where remove costs of additional survival time are unclear. Funded by Amgen and Fresenius Medical Care. **Other:** None.

Overall applicability:(c) partially applicable **Overall quality:**(d) potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ESRD = end-stage renal disease; HD = haemodialysis; HDF = haemodiafiltration; ICER: incremental cost-effectiveness ratio; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years

(e) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(f) Converted using 2009 purchasing power parities[324]

(g) Directly applicable / Partially applicable / Not applicable

(h) Minor limitations / Potentially serious limitations / Very serious limitations

Study	**Ramponi 2016[354]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost-effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Markov model with probabilistic analysis. **Approach to analysis**: The model included 3 health states, 'Alive and under therapy' and 'Dead due to disease under therapy' and 'Dead due to other cause'. Mortality, EQ5D utility and costs varied based on treatment and health state. 1 year cycle length. **Perspective:** Italian	**Population:** People aged 18 years or above with ESRD undergoing HD. Subgroups analysis based on age 40, 50, and 50 years, sex and diabetic status. **Cohort settings:** **Intervention 1:** HD (high-flux) **Intervention 2:** HDF	**Total costs (mean per patient):** ***Male, 40 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): £1,551 (95% CI: NR; p=NR) ***Male, 50 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): £1,527 (95% CI: NR; p=NR) ***Male, 60 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): £1,421 (95% CI: NR; p=NR) ***Female, 40 years*** Intervention 1: NR	**QALYs (mean per patient):** ***Male, 40 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.293 (95% CI: NR; p=NR) ***Male, 50 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.237 (95% CI: NR; p=NR) ***Male, 60 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.112 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** ***Male, 40 years*** £5,296 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%(c) ***Male, 50 years*** £6,451 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%(c) ***Male, 60 years*** £12,628 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): ~60%/~65%(c) ***Female, 40 years*** £5,431 per QALY gained (pa) 95% CI: NR

societal perspective stated but only healthcare costs included as other costs assumed not to vary **Time horizon:** 10 years **Treatment effect duration:**[(a)] 10 years **Discounting:** Costs: 3.5%; Outcomes: 3.5%		Intervention 2: NR Incremental (2−1): £1,577 (95% CI: NR; p=NR) ***Female, 50 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): £1,572 (95% CI: NR; p=NR) ***Female, 60 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): £1,516 (95% CI: NR; p=NR) **Currency & cost year:** Italian Euros, cost year unspecified (presented here as UK pounds, assuming 2015 cost year[(b)])] **Cost components incorporated:** Direct healthcare costs that differ between HDF and HD focused only on the costs of equipment, disposables, ultrapure water testing, and water consumption.	***Female, 40 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.290 (95% CI: NR; p=NR) ***Female, 50 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.248 (95% CI: NR; p=NR) ***Female, 60 years*** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.120 (95% CI: NR; p=NR)	Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%[(c)] ***Female, 50 years*** £6,349 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): ~75%/~80%[(c)] ***Female, 60 years*** £12,655 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): ~60%/~65%[(c)] **Analysis of uncertainty:** • Using an alternative cost data source (Lebourg) ICERs increased (£7,146 to £18,368 across age groups). • Results were similar in a cohort of diabetic and non-diabetic patients. • Using a discount rate of 0% or 5% for costs and outcomes had very little impact on the ICER. • Using overall HRQoL coefficients (rather than the HRQoL coefficients linked to patient age) in the cohort of 50-year-old male patients increased the ICER to £17,945/QALY and increased uncertainty. ICERs for other groups not shown.

Data sources

Health outcomes: The survival function of HF-HD patients was estimated from the Membrane Permeability Outcome Study dataset – data itself not reported at all; the risk reduction with HDF was taken from the meta-analysis of Mostovaya et al (authors state that although it includes studies comparing HDF to low-flux HD, it was considered the best proxy with respect to other alternative meta-analyses available in the literature) - RR itself not reported. QOL life difference with HDF based on Mazairac 2013 (CONTRAST[140]). Coefficients linked to age were used.

Quality-of-life weights: EQ-5D, tariff not stated (Mazairac states Dutch tariff). **Cost sources:** Estimates of differences in cost with HDF and HD are based on the published literature. Oates 2012 converted from UK pounds to Euros was used in the base-case analysis. Lebourg 2013 was used in an

alternative analysis – French analysis.	
Comments	
Source of funding: Funding for this study is not stated. 2 of the 10 authors are employees of Fresenius Medical Care. **Limitations:** Italian costs, cost year not stated (published 2016) - may not reflect current NHS context. Societal perspective stated but only healthcare costs included in analysis. Unclear if EQ5D utilities are based on UK population values. 10 year time horizon; as survival varies between comparators the impact on QALYs and costs will not be fully captured. Costs other than those relating differences between HDF and HD intervention costs are assumed to be constant but as survival (and therefore life years) varies between HDF and HD this will not be true. Baseline mortality from non-UK clinical trial and so may not best represent general UK HD population. 2 of 10 authors are employees of Fresenius Medical Care; study funding not stated. **Other:** None.	
Overall applicability:(c) partially applicable	**Overall quality:**(d) potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ESRD = end-stage renal disease; HD = haemodialysis; HDF = haemodiafiltration; ICER: incremental cost-effectiveness ratio; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2015 purchasing power parities[324]

(c) Estimated from graph

(d) Directly applicable / Partially applicable / Not applicable

(e) Minor limitations / Potentially serious limitations / Very serious limitations

H.7 >3x weekly (home or in-centre) vs 3x weekly HD (in-centre)

Study	Klarenbach 2013[204]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Markov model based on primary data analysis from Manns RCT[271] with probabilistic analysis. **Approach to analysis:** Health states: Conventional HD, home nocturnal frequent HD, transplant, death. 6 month cycles. **Perspective:** Canadian healthcare payer **Time horizon/Follow-up:** lifetime **Treatment effect duration:**[(a)] lifetime **Discounting:** Costs: 5%; Outcomes: 5%	**Population:** Patients on conventional HD wishing to commence frequent nocturnal home HD. **Cohort settings:** Start age: Male: **Intervention 1:** Conventional HD (3x 4hr sessions per week, in-centre 61%, satellite 14%, home 25%) **Intervention 2:** Frequent home nocturnal (5-6 nights per week) HD (on average 5.7 nights per week for 6-9 hours per session)	**Total costs (mean per patient):** Intervention 1: £305,807 Intervention 2: £302,079 Incremental (2−1): saves £3728 (95% CI: NR; p=NR) **Currency & cost year:** 2012 Canadian dollars (presented here as 2012 UK pounds[(b)]) **Cost components incorporated:** Dialysis costs, NHD training/setup costs, medication, physician costs. Hospitalisation costs were excluded in base case analysis as RCT did not show a difference in the risk and duration of hospitalisation by modality (explored in SA).	**QALYs (mean per patient):** Intervention 1: 4.042 Intervention 2: 4.426 Incremental (2−1): 0.384 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Intervention 2 dominates (lower costs and higher QALYs) 95% CI: NR Probability Intervention 2 cost effective (£20K/30K threshold): NR **Analysis of uncertainty:** Extensive sensitivity analyses were undertaken including: baseline mortality rate, probability of transplant, annual treatment failure for NHD, mortality risk reduction with NHD, NHD training costs, cost of vascular access events, hospitalisation costs, quality of life treatment effect assumption, time horizon. Scenario analyses were also undertaken where the treatment mix in the conventional HD arm was varied. Frequent home nocturnal HD continued to dominate conventional HD or be considered cost effective except when: • Annual NHD technique failure was increased 0.19 (0.076 in base-case analysis): £43,357 per QALY gained • RR mortality with NHD 0.75 (1 in base-case analysis): £28,700 per QALY gained • NHD training costs are increased (8 weeks rather than 3.65): £21,214 per

				QALY gained • PD was incorporated into the conventional dialysis baseline in term of costs (78% conventional HD, 5% home conventional HD, 18% PD): £24,468 per QALY gained • Conventional HD as all home: £110,526 per QALY gained • Conventional HD as all PD: £236,858 per QALY gained

Data sources

Health outcomes: No mortality difference is assumed – authors state this is based on RCT evidence and reference Culleton 2007[87] and Rocco[365].Quality of life differences between interventions based on EQ5D data from Manns 2009 RCT. It is assumed that beyond 6 months the treatment difference is maintained. **Quality-of-life weights:** EQ-5D tariff not stated. **Cost sources:** microcosting analysis was undertaken in the RCT. Intervention costs used: in-centre HD (yr1/yr2+) £41,327/£41,326; satellite HD (yr1/yr2+) £34,807/£34,807; home HD (yr1/yr2+) £26,268/£25,271; Frequent home nocturnal HD (yr1/yr2+) £31,890/£29,897); PD (all items/health) £16,402/£21,029 (not from microcosting from literature). Frequent home nocturnal HD training and set up: £10,294. Medication costs (1st 6 months / 6 months +): Conventional HD £2,762/£2,734; Frequent home nocturnal HD £3,591/£3,028. Physician billing (1st 6 months / 6 months +): Conventional HD £1,440/£1,040; Frequent home nocturnal HD £1,285/£1,625.

Comments

Source of funding: Canadian Institutes of Health Research. One author is Baxter employee although not at the time of designing RCT or economic evaluation or conducting the RCT. **Limitations:** Resource use from Canada between 2004 and 2006, and 2012 unit costs may not reflect current NHS context. The discount rate used was not in-line with the NICE reference case (5% for costs and outcomes, rather than 3.5%). It is unclear whether or not the UK population tariff has been used for EQ5D. Analysis based on a single study (Manns 2009 RCT[271]) and so does not reflect full body of available evidence for this area (although only study that reported EQ-5D). Hospitalisation costs were excluded although justified on basis that RCT did not show a difference in the risk and duration of hospitalisation by modality and explored in sensitivity analysis. One author is a Baxter employee although not at the time of designing RCT or economic evaluation or conducting the RCT and study funding is not from industry. **Other:** None.

Overall applicability:(c) partly applicable **Overall quality:**(d) potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2012 purchasing power parities[324]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Study	Liu 2015[249]

Study details	Population & interventions	Costs	Health outcomes	Cost-effectiveness
Economic analysis: CUA (health outcome: QALYs) **Study design:** Markov model with probabilistic analysis **Approach to analysis:** Health states: High dose HD, conventional in-centre HD, Transplant, PD, death. In the model people start in either HD state and can stay on their current modality, change modality or die. 28 days cycles. Difference between interventions include survival, QOL and hospitalisations. **Perspective:** UK NHS **Time horizon:** lifetime (40 years) **Treatment effect duration:**[(a)] n/a **Discounting:** Costs: 3.5%; Outcomes: 3.5%	**Population:** Adult ESRD patients requiring RRT. **Cohort settings:** Start age: NR Male: NR **Intervention 1:** Conventional in-centre HD (3 sessions per week) **Intervention 2:** High dose in-centre HD (5 sessions per week)	**Total costs (mean per patient):** Intervention 1: £191,207 Intervention 2: £299,920 Incremental (2−1): £108,713 (95% CI: NR; p=NR) **Currency & cost year:** 2011-2014 UK pounds **Cost components incorporated:** In centre HD costs (using PBR tariff to account for staff costs and consumables per session), dialysis access establishment and maintenance, dialysis service, erythropoietin-stimulating agents, all cause hospitalisations, patient monitoring, transportation, kidney transplantation and maintenance.	**QALYs (mean per patient):** Intervention 1: 5.267 Intervention 2: 6.129 Incremental (2−1): 0.862 (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £126,106 per QALY gained (pa) 95% CI: NR Probability Intervention 2 cost-effective (£20K/30K threshold): 0%/0% **Analysis of uncertainty:** Number of sessions for intervention 1 increased from 3 to 3.5 per week: ICER reduced to £50,598 per QALY gained. No difference in survival: ICER increases to £396,614 per QALY gained. One way sensitivity analyses were undertaken where variables were individually varied within a plausible range from the literature or +/-25% if not. The conclusion that high dose in centre HD was not cost effective compared to conventional in centre HD robust to sensitivity analyses. When the comparator is changed to high dose HD given at home and compared to conventional in-centre HD, it is found to have lower costs (£522) and higher QALYs (1.273). Although if using a higher cost for home HD (£575/week rather than £456/week), the ICER was £17,404 per QALY gained. (Note: high dose home HD would also dominate the in-centre high dose HD with lower costs and higher QALYs in both these scenarios.) In one way sensitivity analyses for the home high dose HD comparison, results were most sensitive to the cost of home HD and the utility of home HD.
Data sources				
Health outcomes: Survival on HD from European Renal Association and European Dialysis and Transplant association Registry Annual Report 2009. It notes that 20% of incident population used is from UK and that assumes data is representative for UK. Doesn't discuss if UK only data available. Relative treatment effect for mortality with high dose HD compared to conventional in-centre-HD (0.76, CI 0.57 to 0.95) was based on Nesrallah 2012[312], Marshall				

2011[273] and Johansen 2009[181] (all excluded from clinical review). (Same rate appears to be applied for sensitivity analysis where home provision considered.) Hospitalisations rates based on Chertow 2010[70] (and Rocco 2011[365] for home provision comparison) (both included in clinical review). **Quality-of-life weights:** In base-case analysis QOL for conventional in centre HD from Liem et al. meta-analysis of EQ5D data. EQ-5D tariff not stated. Relative effect on QOL with frequent HD was informed by EQ-5D from RCT reported by Culleton 2007[87]; EQ5D tariff not stated. But as this was high dose at home they assumed half the benefit was from high dose and half from at home – applying a 8.8% improvement in the base-case analysis resulting in a 0.05 absolute difference with frequent HD. Methods for home high dose HD were somewhat unclear but seemed to include estimating conventional HD at home utility which was informed by de Witt 1998 (excluded from clinical review as NRS without adequate adjustment) and applying the same percentage increase as in the base-case analysis resulting in an absolute difference of 0.19 with home frequent HD compared with in centre HD 3x weekly. **Cost sources:** UK sources including UK PBR tariffs 2013-14 (in-centre dialysis per session £147), NHS Reference costs 2009-10, 2011-12 and 2012-13, British National Formulary. For analysis with home based

Comments

Source of funding: Baxter Healthcare. **Limitations:** Does not include all RRT modalities of interest. Cost year not stated and costs appear to be from various year from 2009 - 2014, therefore may not reflect current NHS context. Unclear if all EQ5D data is from patients and uses UK tariff; although relative treatment effect data is. Baseline data for survival on HD is from European registry (20% UK). Relative treatment effects are only partially based on studies included in the clinical review: differences in QOL are based on data from the Mann RCT of frequent home HD vs in-centre HD with an assumption that half the treatment difference is due to the frequency and half due to the home setting (resulting absolute difference in model 0.05); survival difference is based on studies excluded from the clinical review - a HR of 0.76 is applied; hospitalisation differences are based on Chertow 2010 which is included in the clinical review. For the sensitivity analysis where more frequent HD is provided at home Rocco 2011 (included in clinical review) is used for hospitalisations. QOL is based on a home HD baseline with the same relative treatment effect for more frequent HD as in the base case (resulting absolute difference 0.19 between home frequent HD and in centre HD). Costs are based on PBR tariff which may have included incentives. In addition for costs of frequent home HD the current PBR tariff for home HD was used in the base-case analysis which may not reflect the cost of frequent home HD. The study is funded by Baxter Healthcare. **Other:** None.

Overall applicability:[(c)] partly applicable **Overall quality:**[(d)] potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

Study	**Beby 2016[41]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs)	**Population:** Adults with ESRD requiring HD.	**Total costs (mean per patient):** **Analysis 1** Intervention 1: £178,209	**QALYs (mean per patient):** **Analysis 1** Intervention 1: 2.236	**ICER (Intervention 2 versus Intervention 1):** **Analysis 1** £231,028 per QALY gained

Study design: Markov model with probabilistic analysis. **Approach to analysis:** Health states: high dose ICHD, high dose HD at home, conventional HD at home, conventional ICHD, PD, transplant, death. 28 day cycles. **Perspective:** Dutch healthcare payer **Time horizon/Follow-up:** 5 years **Treatment effect duration:**[a] 5 years **Discounting:** Costs: 4%; Outcomes: 1.5%	**Cohort settings:** Start age: Male: **Intervention 1:** Conventional in-centre HD (3x 4hr sessions per week) **Analysis 1 – intervention 2:** High dose in-centre HD (5x 4hr sessions per week) **Analysis 2 – intervention 2:** High dose home HD (5x 7hr sessions per week) **Analysis 3 - intervention 2:** Conventional home HD (3x 4hr sessions per week)	Intervention 2: £273,500 Incremental (2−1): £95,290 (95% CI: NR; p=NR) **Analysis 2** Intervention 1: £178,209 Intervention 2: £179,870 Incremental (2−1): £1,660 (95% CI: NR; p=NR) **Analysis 3** Intervention 1: £178,209 Intervention 2: £175,644 Incremental (2−1): -£2,566 (95% CI: NR; p=NR) Additional comparison[c]: high dose home vs conventional home High dose home: £179,870 Conventional home: £175,644 Incremental (2−1): £4,226 (95% CI: NR; p=NR) **Cost breakdown – incremental (2-1)** **Analysis 1** Initiation: £181 Treatment: £87,387 Medication: -£2,654 Complications: £66 Transportation: £10,310 **Analysis 2** Initiation: £4,191 Treatment: £6,569 Medication: -£1,836	Intervention 2: 2.649 Incremental (2−1): 0.412 (95% CI: NR; p=NR) **Analysis 2** Intervention 1: 2.236 Intervention 2: 2.846 Incremental (2−1): 0.610 (95% CI: NR; p=NR) **Analysis 3** Intervention 1: 2.236 Intervention 2: 2.485 Incremental (2−1): 0.249 (95% CI: NR; p=NR) Additional comparison[c]: high dose home vs conventional home High dose home: 2.846 Conventional home: 2.485 Incremental (2−1): 0.361 (95% CI: NR; p=NR)	95% CI: NR Probability Intervention 2 cost effective (£20K/30K threshold): 0%/0% **Analysis 2** £2,721 per QALY gained 95% CI: NR Probability Intervention 2 cost effective (£20K/30K threshold): ~80%/~85%[d] **Analysis 3** Intervention 2 dominates (lower costs and higher QALYs) 95% CI: NR Probability Intervention 2 cost effective (£20K/30K threshold): ~70%/~75%[d] Additional comparison[c]: high dose home vs conventional home £11,706 per QALY gained Additional comparison[c]: Incremental analysis with all 4 comparators High dose home HD dominates all 3 other options (lower costs and higher QALYs) **Analysis of uncertainty:** • Various one way sensitivity analyses were undertaken for analyses 1 to 3 to explore how varying inputs within plausible ranges impacted the ICER.

		Complications: £152 Transportation: -£7,416 **Analysis 3** Initiation: £4,039 Treatment: £1,421 Medication: £10 Complications: -£247 Transportation: -£7,788 **Currency & cost year:** 2015 Dutch Euros (presented here as 2015 UK pounds[(b)]) **Cost components incorporated:** Initiation (including house adjustments), dialysis treatment, medication (blood pressure medication, phosphate binders), complications (access failure, hospitalisation), transportation.		However, results are only presented as net monetary benefit using the Netherland threshold of £67,000 to value QALYs and so are difficult to interpret.

Data sources

Health outcomes: Intervention differences were incorporated in terms of mortality, QOL and complications (hospitalisations and access failure).

Mortality: Baseline survival with conventional in-centre HD was based on survival analysis of European Renal Registry data. Mortality with conventional HD at home was assumed to be the same as conventional in-centre HD due to lack of evidence of difference. High dose HD (at home or in-centre) was attributed a relative risk of 0.56 based on FHN 2010 study comparing frequent with conventional in-centre HD[70, 110] – this is 1 of 4 studies with mortality data included clinical review (overall estimate from clinical review OR 0.83 [0.49 to 1.38]).

QOL: Conventional in-centre HD based on Liem et al EQ5D meta-analysis.[242] Conventional home HD QOL estimated by applying ratio between conventional in-centre HD and conventional home HD based on De Wit 1998 – evidence not included in clinical review. High dose QOL estimated by applying percentage difference estimated by assuming that half effect seen in Culleton et al is from treatment in the home setting and the rest is due to high dose treatment (comparison is frequent home nocturnal HD versus conventional HD in-centre or at home).[87] Study included in clinical review.

Complications: Vascular access failure rates varied between high dose and conventional HD - these appear to be based on rates from two different studies (11% vs 13.46%) rather than a comparative study. Hospitalisation rates varied between conventional and high dose HD based on two HDN RCTs: in-centre was based on FHN 2010[110] and home was based on Rocco 2011[365]. These studies were included in the clinical review.

Other transitions: Modality transitioning based on Dutch Renal Registry and Dutch transplantation Association.

Quality-of-life weights: ICHD value (0.56) from Liem et al EQ-5D meta-analysis, EQ-5D tariffs not stated. Home HD value (0.69) based on ratio between home and in centre HD QOL applied to ICHD value in model. This study was not included in clinical review. Improvement with high dose HD (8.8%) based

on Culleton et al.[87] This study was included in clinical review. **Cost sources:** Unit costs were from Dutch national sources or published literature. Dialysis treatment unit costs based on Dutch national data: ICHD £1,026; high dose ICHD £1,475; high dose home HD £1,039; conventional home HD £947. Blood pressure medication costs were varied between conventional and high dose HD based on Culleton 2007.[87] Study included in clinical review. Phosphate binder costs varied between conventional and high dose HD – although somewhat unclear this seems to be based on clinical practice.	
Comments	
Source of funding: Study funding is not stated but three of four authors are current or former Baxter employees and Baxter and publication and writing/editorial support was funded by Baxter. **Limitations:** Dutch 2015 costs may not reflect current NHS context. The discount rates used were not in line with the NICE reference case (4% of costs and 1.5% for outcomes, rather than 3.5% for both). QALYs are calculated using EQ5D values but it is unclear if the UK population tariff was used in the studies used. 5-year time horizon may not be sufficient to capture all difference in costs and outcomes given mortality is impacted by treatment. Baseline rates based on Dutch national data may not reflect the UK population. For frequency comparisons: Relative treatment effects are partially based on evidence included in clinical review: mortality benefit used for high dose HD greater than estimate from clinical review; QOL benefit with high dose HD based on study included in clinical review but with assumptions made about whether to attribute benefit to setting or frequency. Difference in vascular access failure rates appear to be based on rates from two different studies (11.00% vs 13.46%) rather than a comparative study. For home versus in-centre comparisons: relative treatment effects are based on studies excluded from clinical data or indirect evidence: QOL benefit with home HD based on study not included in clinical review (no mortality difference is applied); hospitalisation data for home and in-centre are from different studies. The weekly cost for high dose home HD is the lowest and lower than conventional HD and the reason for this is not explained given dialysis is for longer sessions and more often. Study funding is not stated but three of four authors are current or former Baxter employees and Baxter and publication and writing/editorial support was funded by Baxter. **Other:** None.	
Overall applicability:[(e)] partly applicable	**Overall quality:**[(f)] potentially serious limitations (frequency comparisons); very serious limitations (home versus in-centre comparison – therefore excluded and not presented in home versus in-centre review)

Abbreviations: 95% CI: 95% confidence interval; CUA: cost-utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ESRD – end-stage renal disease; HD: haemodialysis; ICER: incremental cost-effectiveness ratio; ICHD: in-centre haemodialysis; NR: not reported; pa: probabilistic analysis; PD: peritoneal dialysis; QALYs: quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.
(b) Converted using 2015 purchasing power parities[324]
(c) Calculated from data reported in paper.
(d) Estimated from graph.
(e) Directly applicable / Partially applicable / Not applicable
(f) Minor limitations / Potentially serious limitations / Very serious limitations

H.8 Home versus in-centre HD

None.

H.9 Live-donor transplant versus deceased-donor transplant

None.

H.10 Pre-emptive transplant versus non-pre-emptive transplant

None.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 52: Studies excluded from the clinical review

Study	Exclusion reason
Abbott 2004[1]	wrong intervention
Abou Ayache 2005[2]	NRS without adequate adjustment
Abramowicz 2016[3]	SR, checked for references
Aghakhani 2011[5]	NRS without adequate adjustment
Ahmadnia 2005[6]	NRS without adequate adjustment
Akkina 2008[7]	NRS without adequate adjustment
Akoglu 2013[8]	NRS study without adequate adjustment
Al Wakeel 2012[9]	Cross-sectional study
Alloatti 2000[10]	Review (not systematic)
Allon 2003[11]	Incorrect interventions
Altieri 2004[12]	Incorrect interventions
Alvares 2012[13]	Cross-sectional study
Alvestrand 1998[14]	Incorrect interventions
Amato 2005[16]	NRS without adequate adjustment
Andrikos 2008[17]	NRS without adequate adjustment
Anonymous 1973[18]	Commentary
Anonymous 1993[20]	Review (not systematic)
Anonymous 1993[19]	NRS without adequate adjustment
Anonymous 2005[21]	Commentary
Anonymous 2006[22]	Commentary
Apostolou 2007[23]	Cross-sectional study
Ardine de Wit 1998[24]	NRS without adequate adjustment
Arif 2017[25]	Wrong comparison
Asderakis 1998[26]	NRS without adequate adjustment
Atapour 2015[27]	NRS without adequate adjustment
Atapour 2016[28]	NRS without adequate adjustment
Avner 1979[30]	NRS without adequate adjustment
Avner 1981[29]	NRS without adequate adjustment
Ayus 2005[31]	NRS without adequate adjustment
Baboolal 2008[32]	No usable outcome
Bagdade 1977[33]	Wrong interventions
Baiardi 2002[34]	NRS without adequate adjustment
Bakris 2016[35]	SR, not matching PICO
Baldamus 1980[37]	NRS - RCTs available
Basile 2001[39]	NRS without adequate adjustment
Baykan 2012[40]	NRS without adequate adjustment
Becker 2006[42]	NRS without adequate adjustment
Bellien 2014[44]	No usable outcomes
Bergman 2008[45]	NRS without adequate adjustment

Study	Exclusion reason
Berthoux 1996[46]	NRS without adequate adjustment
Bolasco 2003[48]	Protocol only
Borthwick 2017[49]	SR, not matching PICO
Bourguignon 2016[50]	No usable outcomes
Bozkurt 2013[51]	NRS without adequate adjustment
Bremer 1989[52]	Not adjusted for confounders
Brown 2010[54]	Cross-sectional study
Brown 2013[55]	Protocol only
Brown 2014[56]	Systematic review checked for references
Brunner 1988[57]	NRS without adequate adjustment
Burton 1989[58]	No usable outcomes
Butani 2011[59]	NRS without adequate adjustment
Bzoma 2016[60]	NRS without adequate adjustment
Canaud 2015[61]	NRS (RCTs available)
Carson 2009[62]	NRS study without adequate adjustment
Castro 1971[63]	NRS study without adequate adjustment
Chandna 2011[65]	Wrong interventions
Chang 1985[66]	NRS (RCTs available)
Chang 2012[67]	NRS without adequate adjustment
Charytan 1986[68]	NRS without adequate adjustment
Chavers 2007[69]	Not adjusted for confounders
Chertow 2016[71]	Review (not systematic)
Chiu 2011[72]	Review (not systematic)
Choi 2013[73]	NRS without adequate adjustment
Churchill 1984[75]	No usable outcomes
Churchill 1987[76]	Not adjusted for confounders
Cogny-van Weydevelt 1999[78]	NRS without adequate adjustment
Copland 2016[79]	SR, not matching PICO
Couchoud 2007[83]	NRS without adequate adjustment
Courts 1998[84]	NRS without adequate adjustment
Cransberg 2006[86]	NRS without adequate adjustment
Czyzewski 2014[88]	NRS study without adequate adjustment
Daugirdas 2013[89]	No usable outcomes
De Abreu 2011[91]	No usable outcomes
De Fijter 1992[94]	NRS without adequate adjustment
De Fijter 1994[95]	Incorrect interventions
De Fijter 1995[93]	NRS study without adequate adjustment
De Jonge 2006[96]	Not Majority of population is RRT naive or using previous RRT mode and not selected on basis of "failure"
Dew 1997[101]	SR, checked for references
Diaz-Buxo 1996[102]	NRS without adequate adjustment
Dixon 2016[103]	NRS without adequate adjustment
Duric 2015[105]	NRS without adequate adjustment
El Hatw 2013[106]	Incorrect interventions
Eltawdy 2016[108]	NRS without adequate adjustment
Fagugli 2001[112]	NRS without adequate adjustment

Study	Exclusion reason
Fagugli 2006[111]	NRS without adequate adjustment
Farragher 2016[113]	NRS without adequate adjustment
Fenton 1977[114]	NRS without adequate adjustment
Ferguson 2015[115]	Review (not systematic)
Findlay 2016[116]	Incorrect comparisons
Fischbach 2004[117]	Incorrect interventions
Flanigan 2001[118]	Cross-sectional study
Fleming 1995[119]	Not review population
Flom 1992[120]	NRS without adequate adjustment
Floridi 2002[121]	NRS (RCTs available)
Foote 2012[123]	NRS without adequate adjustment
Foote 2016[122]	SR, checked for references
Francisco 2013[124]	No usable outcomes
Fytili 2002[125]	NRS without adequate adjustment
Garcia 2015[127]	Not adjusted for confounders
Garcia-Garcia 1985[126]	Not adjusted for confounders
Garg 2017[128]	No additional outcomes to previous publications
Gentil 1991[129]	NRS without adequate adjustment
Gill 2004[130]	No usable outcomes
Gjertson 1994[131]	No usable outcomes
Glabman 1979[132]	NRS (RCTs available)
Glanton 2003[133]	Wrong population
Gokal 1987[134]	NRS without adequate adjustment
Goldfarb-Rumyantzev 2005[135]	No usable outcomes
Goldfarb-Rumyantzev 2006[137]	Incorrect study design
Goldfarb-Rumyantzev 2006[136]	Wrong population
Gonzalez-Perez 2005[138]	No usable outcomes
Gudex 1995[142]	NRS without adequate adjustment
Gutman 1984[143]	Incorrect interventions
Habib 2016[144]	Not in English
Haller 2011[146]	HE model only
Han 2015[147]	SR, checked for references
Hanson 1999[148]	Wrong interventions
Harciarek 2009[149]	NRS without adequate adjustment
Harris 2002[150]	NRS without adequate adjustment
Heaf 2002[151]	NRS without adequate adjustment
Heaf 2014[152]	NRS study without adequate adjustment
Hecking 2004[153]	NRS (RCTs available)
Heidenheim 2003[154]	NRS without adequate adjustment
Held 1994[155]	No usable outcomes
Hellerstedt 1984[156]	NRS without adequate adjustment
Hill 2017[157]	NRS without adequate adjustment
Ho 2016[158]	SR, checked for references
Holtta 2000[159]	No usable outcomes
Hryszko 2001[162]	NRS without adequate adjustment

Study	Exclusion reason
Huang 2008[163]	NRS without adequate adjustment
Hufnagel 1999[164]	NRS without adequate adjustment
Huisman 2002[165]	Incorrect interventions
Hull 2008[166]	Commentary
Hussain 2013[167]	NRS study without adequate adjustment
Hwang 2016[168]	NRS without adequate adjustment
Iles-Smith 1999[169]	Not Majority of population is RRT naive or using previous RRT mode and not selected on basis of "failure"
Innocenti 2007[170]	NRS without adequate adjustment
Iseki 2003[171]	NRS without adequate adjustment
Jain 2009[173]	Not adjusted for confounders
Jardine 2015[174]	Protocol only
Jean 2015[176]	NRS (RCTs available)
Jeloka 2013[177]	Review (not systematic)
Jiang 2016[178]	No usable outcomes
Jimenez 2008[179]	NRS without adequate adjustment
Jin 2017[180]	NRS without adequate adjustment
Johansen 2009[181]	Wrong comparison (same number of dialysis sessions per week)
John 1998[182]	NRS without adequate adjustment
Johnson 2000[184]	NRS without adequate adjustment
Johnston 2013[185]	Not review population
Joly 2003[187]	No usable outcomes
Joo 2007[188]	NRS without adequate adjustment
Jung 2010[189]	NRS without adequate adjustment
Kaminota 2001[191]	HE model only
Kaplan 2016[194]	No usable outcomes
Kaplan de Nour 1994[193]	Review not systematic
Kasiske 2002[195]	NRS without adequate adjustment
Katz 1991[197]	NRS without adequate adjustment
Kaur 2014[198]	Review (not systematic)
Khanal 2012[200]	Not review population
Kir 2012[201]	NRS without adequate adjustment
Kirby 2001[202]	HE model only
Klarenbach 2014[205]	No usable outcomes
Knezevic 2012[206]	Incorrect study design
Koca 2012[207]	No usable outcomes
Kokkinos 2007[208]	Incorrect interventions
Korevaar 2000[212]	Cross-sectional study
Koshikawa 2003[213]	Incorrect study design
Kotanko 2015[214]	No usable outcomes
Kraus 2007[216]	No usable outcomes
Kraus 2016[217]	SR, not matching PICO
Kumar 2008[219]	NRS without adequate adjustment
Kute 2014[221]	NRS without adequate adjustment
Kuttykrishnan 2015[222]	Incorrect study design
Ladhani 2017[223]	Incorrect comparison

Study	Exclusion reason
Lang 2001[225]	No usable outcomes
Laudanski 2013[227]	NRS without adequate adjustment
Lassalle 2017[226]	Incorrect comparison
Laupacis 1996[228]	NRS without adequate adjustment
Leber 1980[229]	NRS (RCTs available)
Lebkowska 2003[230]	NRS without adequate adjustment
Lee 1996[234]	Review (not systematic)
Lee 2005[231]	NRS without adequate adjustment
Lee 2009[232]	NRS without adequate adjustment
Levy 1990[236]	NRS without adequate adjustment
Li 1997[241]	No usable outcomes
Li 2014[240]	Wrong population
Li 2016[239]	No usable outcomes
Li 2017[237]	Wrong comparison
Liem 2007[243]	NRS study without adequate adjustment
Lin 2001[244]	Less than minimum duration
Lindholm 1993[245]	No usable outcomes
Lindqvist 2000[246]	NRS without adequate adjustment
Lindsay 2003[248]	NRS without adequate adjustment
Liu 2001[250]	Not in English
Liu 2014[251]	Incorrect study design
Locatelli 2001[253]	NRS without adequate adjustment
Lowrie 1981[255]	NRS without adequate adjustment
Lukowsky 2013[256]	NRS study without adequate adjustment
Lunde 1991[257]	No usable outcomes
Ma 2014[258]	NRS without adequate adjustment
MacDonald 2009[259]	No usable outcomes
MacGregor 2007[260]	Review (not systematic)
MacLeod 1998[261]	SR, checked for references
Maggiore 2000[263]	No usable outcomes
Magoha 2001[264]	Review (not systematic)
Mailloux 1996[265]	NRS without adequate adjustment
Majkowicz 2000[266]	NRS without adequate adjustment
Malberti 1988[267]	NRS without adequate adjustment
Malyszko 2001[269]	NRS without adequate adjustment
Mange 2001[270]	NRS without adequate adjustment
Marshall 2006[272]	Incorrect interventions
Marshall 2011[273]	Incorrect line of therapy
Marshall 2015[274]	Wrong comparison (changes in mortality over time)
Martins 2015[275]	Not adjusted for confounders
McCullough 2016[277]	SR, not matching PICO
McEnery 1993[279]	NRS without adequate adjustment
McGregor 2001[283]	No usable outcomes
Meier-Kriesche 2000[286]	No usable outcomes
Meier-Kriesche 2002[285]	NRS without adequate adjustment

Study	Exclusion reason
Mercadal 2016[287]	NRS (RCTs available)
Merion 2005[288]	Wrong comparison
Merkus 1999[289]	NRS without adequate adjustment
Methven 2017[291]	Wrong comparison
Michels 2011[292]	NRS without adequate adjustment
Mircescu 2006[294]	NRS without adequate adjustment
Mircescu 2014[295]	NRS without adequate adjustment
Moreno 1996[297]	Incorrect interventions
Mostovaya 2014[298]	No usable outcomes
Mowatt 2004[299]	SR, checked for references
Murtagh 2007[301]	Wrong interventions
Naini 2016[302]	NRS without adequate adjustment
Najarian 1986[303]	NRS without adequate adjustment
Nemati 2014[310]	NRS without adequate adjustment
Nesrallah 2009[313]	NRS without adequate adjustment
Nesrallah 2011[311]	Commentary
Nesrallah 2012[312]	Incorrect interventions
Nistor 2015[316]	SR, checked for references
Nolph 1988[317]	NRS without adequate adjustment
Oates 2011[319]	NRS without adequate adjustment
Ochiai 1987[320]	NRS without adequate adjustment
Ohtake 2012[321]	No usable outcomes
Opelz 2010[323]	Incorrect interventions
Otero Gonzalez 2015[325]	Not in English
Palmer 2014[327]	SR, checked for references
Panichi 2015[328]	No usable outcomes
Papalois 2000[329]	NRS without adequate adjustment
Parvan 2015[331]	NRS without adequate adjustment
Pauly 2009[332]	NRS without adequate adjustment
Pavlakis 2012[333]	Review (not systematic)
Pedrini 2011[334]	No usable outcomes
Pesavento 2009[335]	Review (not systematic)
Peters 2016[336]	NRS study without adequate adjustment
Piccoli 2004[337]	NRS study without adequate adjustment
Pierratos 2008[338]	Commentary
Pitt 2013[340]	NRS without adequate adjustment
Poon 2015[341]	No usable outcomes
Port 1993[343]	Not adjusted for confounders
Port 1996[342]	Review (not systematic)
Postlethwaite 2002[344]	No usable outcomes
Potter 1986[345]	NRS without adequate adjustment
Povlsen 2007[346]	Review (not systematic)
Price 1978[347]	NRS without adequate adjustment
Pruijm 2006[348]	NRS without adequate adjustment
Pugh 1994[349]	Wrong comparison

Study	Exclusion reason
Punal 2008[350]	SR, checked for references
Rabbat 2000[351]	Not adjusted for confounders
Rabindranath 2007[352]	SR, checked for references
Rambod 2011[353]	Not adjusted for confounders
Rayner 2004[355]	Incorrect study design
Reichwald-Klugger 1984[356]	NRS without adequate adjustment
Richards 1998[357]	NRS without adequate adjustment
Riffaut 2015[358]	Cross-sectional study
Righetti 2010[359]	Incorrect study design
Rigo 2011[360]	NRS without adequate adjustment
Rivara 2016[361]	Incorrect interventions
Roake 1996[362]	NRS without adequate adjustment
Robinson 2006[363]	No usable outcomes
Rodriguez 1998[366]	NRS without adequate adjustment
Rose 2017[368]	NRS without adequate adjustment
Ross 2000[369]	SR, checked for references
Rubin 1983[371]	NRS without adequate adjustment
Rubin 1985[370]	Unable to access
Rubin 1989[372]	NRS without adequate adjustment
Ruggenenti 2001[373]	Review (not systematic)
Sacca 2006[374]	Review (not systematic)
Salomone 1995[375]	NRS without adequate adjustment
Salvadori 2009[378]	NRS without adequate adjustment
Sanabria 2008[379]	NRS without adequate adjustment
Saner 2005[382]	NRS without adequate adjustment
Santos 2015[383]	Not adjusted for confounders
Sattar 2012[384]	Incorrect interventions
Schaubel 1995[385]	NRS without adequate adjustment
Schiffl 1992[387]	Incorrect interventions
Schnitzler 2013[388]	No usable outcomes
Sebille 2016[389]	Protocol only
Sekercioglu 2017[390]	Incorrect population
Sennfalt 2002[391]	Cross-sectional
Sens 2011[392]	NRS without adequate adjustment
Sentveld 2008[393]	Less than minimum duration
Sharma 2013[394]	Review (not systematic)
Shimizu 1983[395]	Incorrect interventions
Shum 2014[397]	NRS without adequate adjustment
Simmons 1990[398]	NRS without adequate adjustment
Siriopol 2015[399]	NRS (RCTs available)
Slinin 2015[400]	SR, checked for references
Smith 2017[401]	No usable outcomes
Snyder 2006[403]	Wrong comparison
Son 2010[404]	NRS without adequate adjustment
Soskolne 1987[405]	NRS without adequate adjustment

Study	Exclusion reason
Soyupek 2013[406]	No usable outcomes
Suzuki 2003[409]	NRS without adequate adjustment
Takura 2015[410]	NRS (RCT evidence available)
Tanriover 2015[412]	No usable outcomes
Tanrisev 2015[413]	Wrong comparison
Tediosi 2001[414]	No usable outcomes
Terasaki 1976[415]	NRS without adequate adjustment
Thorsteinsdottir 2013[417]	SR, not matching PICO
Tokodai 2012[418]	NRS without adequate adjustment
Traeger 2004[420]	Incorrect interventions
Troidle 1998[422]	NRS without adequate adjustment
Tsai 2017[423]	SR, not matching PICO
Tucker 1991[424]	NRS without adequate adjustment
Uchida 2007[425]	NRS without adequate adjustment
Unruh 2008[427]	Incorrect interventions
Unsal 2015[428]	NRS without adequate adjustment
Vale 2004[429]	SR, checked for references
Van Arendonk 2015[430]	Incorrect study design
Van de Luijtgaarden 2011[431]	NRS study without adequate adjustment
Van der Heijden 2004[432]	NRS without adequate adjustment
Vaslaki 2005[434]	No usable outcomes
Vaslaki 2006[433]	No usable outcomes
Vejakama 2013[435]	Incorrect interventions
Vidal 2017[436]	NRS without adequate adjustment
Vollmer 1983[437]	Not adjusted for confounders
Waldum-Grevbo 2015[439]	NRS without adequate adjustment
Walker 2014[440]	HE model only
Walsh 2010[441]	No usable outcomes
Wang 2008[445]	Incorrect interventions
Wang 2013[443]	NRS without adequate adjustment
Wang 2014[442]	SR, checked for references
Wang 2017[446]	SR, not matching PICO
Wang 2017[444]	NRS without adequate adjustment
Wasserfallen 2004[448]	Cross-sectional
Weaver 2017[449]	NRS without adequate adjustment
Wei 1994[450]	No usable outcomes
Wiland 2004[452]	NRS without adequate adjustment
Williams 1990[453]	NRS without adequate adjustment
Williams 2004[454]	Incorrect study design
Wiseman 2013[456]	Review (not systematic)
Wolfe 1999[458]	Not adjusted for confounders
Wong 2012[461]	HE model only
Wong 2017[460]	NRS without adequate adjustment
Wongrakpanich 2017[462]	SR, not matching PICO
Wu 2004[464]	NRS without adequate adjustment

Study	Exclusion reason
Yaghoubifard 2016[465]	No usable outcomes
Yang 2009[467]	NRS without adequate adjustment
Yang 2015[466]	No usable outcomes
Yoo 2009[469]	NRS without adequate adjustment
Yoshimura 1994[470]	NRS without adequate adjustment
Younis 2015[471]	No usable outcomes
Zhu 2012[472]	Protocol only
Zimbudzi 2014[473]	NRS without adequate adjustment
Zimmerman 2014[474]	No usable outcomes

I.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2001 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 53: Studies excluded from the health economic review

Reference	Reason for exclusion
Agar 2005[4]	Excluded as rated very serious limitations. Intervention costs analysed but considered superseded by current NHS reference costs. Hospitalisation costs analysed but non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Australian setting may not reflect current UK NHS context.
Baboolal 2008[32]	Excluded as rated very serious limitations due to looking only at dialysis intervention costs (UK ~2005/6) and so superseded by current NHS reference costs.
Barnieh 2011[38]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Canadian setting may not reflect current UK NHS context.
Bevilacqua 2017[47]	Excluded as rated very serious limitations as cost analysis only includes intervention delivery costs (Canada 2014/15) and so superseded by current NHS reference costs. Outcomes analysis non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Canadian setting may not reflect current UK NHS context.
Cavallo 2014[64]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Italian setting may not reflect current UK NHS context.
Cleemput 2010[77]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Belgium setting.
Cortes-Sanabria 2013a[80]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Mexican setting.
Cortes-Sanabria	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol.

Reference	Reason for exclusion
2013b[81]	Also partially applicable, reasons include: Mexican setting.
Couchoud 2015[82]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: French setting may not reflect current UK NHS context.
Dominguez 2011[104]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Chilean setting may not reflect current UK NHS context.
Elgaard Jensen 2014[107]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Danish setting may not reflect current UK NHS context.
Eriksson 2016[109]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Norwegian setting may not reflect current UK NHS context.
Gonzalez-Perez 2005[138]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: UK resource use from before 2001 (various sources) and 2001/02 unit costs may not reflect current NHS context.
Grun 2003[141]	Excluded as rated not applicable. Resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Haller 2011[146]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Austrian setting may not reflect current NHS context.
Howard 2009[161]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Australian setting may not reflect current NHS context.
Jassal 2003[175]	Excluded as rated not applicable. US/Canadian costs and resource use from before 2001 judged unlikely to be applicable to current UK NHS context.
Kalo 2001[190]	Excluded as rated not applicable. Hungarian resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Kaminota 2001[191]	Excluded as rated not applicable. Japanese resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Kirby 2001[202]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Austrian setting may not reflect current NHS context.
Kitazawa 2017[203]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Japanese setting may not reflect current UK NHS context.
Kontodimopoulos 2008[209]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol.

Reference	Reason for exclusion
	Also partially applicable, reasons include: Greek setting may not reflect current UK NHS context.
Kontodimopoulos 2005[210]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Greek setting may not reflect current UK NHS context.
Koukou 2017[215]	Excluded as rated very serious limitations due to only looking at Greek 2013/14 intervention costs and so superseded by current NHS reference costs.
Kroeker 2003[218]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Canadian setting may not reflect current UK NHS context.
Lee 2002[233]	Excluded as rated not applicable. Canadian resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Li 2015[238]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: English resource use from 2003 to 2012 and 2011/12 unit costs may not reflect current UK NHS context; hospital costs not directly related to delivering intervention only.
Lindsay 2004[247]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Canadian setting may not reflect current UK NHS context.
Malmstrom 2008[268]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Finnish setting may not reflect current UK NHS context.
McFarlane 2003[280]	Excluded as rated not applicable. Canadian resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
McFarlane 2006[281]	Excluded as rated not applicable. Canadian resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
McFarlane 2002[282]	Excluded as rated not applicable. Canadian resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Mowatt 2003[300]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: UK resource use from before 2001 (various sources) and 2001/02 unit costs may not reflect current NHS context.
National Institute for Health and Clinical Excellence 2011[306]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: 2009 UK costs may not reflect current NHS context.
Oates 2012[318]	Excluded as primarily just intervention costs. Not presented in unit costs section as not current dialysis machine model in study and superseded by unit costs estimated for guideline economic model. Limited cost analysis excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol.

Reference	Reason for exclusion
Pacheco 2007[326]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Chilean setting may not reflect current UK NHS context.
Pike 2017[339]	Excluded due to combination of limited applicability and methodological limitations. Rated very serious limitations due treatment effects used in model: most studies used do not meet the guideline clinical review inclusion criteria: 2 study of 13 included for mortality estimate; 0 of 4 studies for complications PD vs HD). Difference in mortality applied in model 1.11 PD vs HD in hosp; 0.60 HD home vs HD satellite. It was assumed there was no diff between hospital and satellite HD to allow a common comparator and hence comparison between the different modalities. Committee concluded there was not good evidence of mortality differences based on guideline review therefore analysis not considered helpful to guideline decision making. Also partially applicable, reasons include: Norwegian setting may not reflect current NHS context; costs included cost of leisure time (not included in NICE reference case perspective) and these could not be separated from overall costs.
Roggeri 2017[367]	Excluded as rated very serious limitations due to being a non-randomised study without minimum adjustments specified in protocol. Also partially applicable, reasons include: Italian setting may not reflect current UK NHS context.
Salonen 2007[376]	Excluded as rated not applicable. Finnish resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Salonen 2003[377]	Excluded as rated not applicable. Finnish resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Sanchez-Escuredo 2015[380]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Spanish setting may not reflect current NHS context.
Sandoz 2004[381]	Excluded as rated not applicable. Primarily a cost of illness analysis although average costs per day also calculated for dialysis and transplantation; Swiss 2001 perspective with some data from earlier years judged unlikely to be applicable to current UK NHS context.
Sennfalt 2002[391]	Excluded as rated not applicable. Swedish resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.
Shimizu 2012[396]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Japanese setting may not reflect current NHS context.
Takura 2015[410]	Excluded as rated very serious limitations due to non-randomised evidence being excluded for this comparison as sufficient RCT evidence available (HDF vs HD). Also partially applicable, reasons include: Japanese setting may not reflect current UK NHS context.
Takura 2013[411]	Excluded as rated very serious limitations due to non-randomised evidence being excluded for this comparison as sufficient RCT evidence available (HDF vs HD). Also partially applicable, reasons include: Japanese setting may not reflect current UK NHS context.
Tediosi 2001[414]	Excluded as rated not applicable. Italian resource use and costs from before 2001 judged unlikely to be applicable to current UK NHS context.

Reference	Reason for exclusion
Treharne 2014[421]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: UK 2013/14 cost year may not reflect current NHS context.
Wong 2014[459]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Australian setting may not reflect current NHS context.

Appendix J: Research recommendations

J.1 CM vs RRT

Research question: What is the clinical and cost effectiveness of conservative management versus dialysis in frail, older people?

Why this is important:

The committee found only low quality, inconsistent evidence on the comparison of conservative management with RRT. For some groups of people with a poor prognosis, RRT may not offer an important degree of clinical benefit in terms of extending life and potentially may reduce the quality of life. However there are no randomised trials in these groups to confirm these theories. High quality research in this area would allow people with a poor prognosis to make a fully informed decision about whether RRT or conservative management is really the most appropriate choice for them.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Older people including with a poor prognosis (e.g., multimorbidity, high frailty index) in the later stages of CKD Intervention/comparison: • Conservative management • RRT (either HD/HDF/PD) Outcomes: Quality of life, mortality, hospitalisation, preferred place of death, mental wellbeing, cognitive impairment, experience of care, adverse events
Importance to patients or the population	High quality research in this area would allow older adults some may have a poor prognosis to make a fully informed decision about whether RRT or conservative management is really the most appropriate choice for them
Relevance to NICE guidance	There is current uncertainty and lack of evidence about conservative management compared with dialysis in this population
Relevance to the NHS	Research in this area will inform NICE recommendations around conservative management
Current evidence base	There is no randomised evidence on conservative management compared to dialysis and very low quality non-randomised evidence.
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	May be challenging to recruit a population of people willing to be randomised to either conservative management or RRT
Other comments	The committee consider this an important area for further research although they are aware of current research ongoing in the area
Importance	• Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.

J.2 Home haemodiafiltration vs home haemodialysis

Research question: What is the clinical and cost effectiveness of home haemodiafiltration versus home haemodialysis, taking into account the impact of frequency?

Why this is important:

The guideline found evidence that HDF is more clinically and cost effective than HD when done in centre. However there was no evidence available for the use of HDF at home. The committee were aware that HDF was being done at home at some centres in the UK and theoretically the same benefits of HDF over HD should hold true at home. The committee noted that potentially people doing HD more frequently than the standard 3 days a week could reduce the additional benefit of doing HDF instead of HD at home. Overall the committee agreed it was important for more research to be conducted before they could strongly recommend that HDF should be done instead of HD at home as well as in centre.

Criteria for selecting high-priority research recommendations:

PICO question	Population: People requiring RRT for CKD who have opted for dialysis via vascular access at home Intervention/comparison: • HDF done 3 days a week at home • HD done 3 days a week at home • HDF done >3 days a week at home • HD done >3 days a week at home Outcomes: Quality of life, mortality, resource use, time to failure of RRT form, symptom scores/functional measures, mental wellbeing, experience of care, adverse events
Importance to patients or the population	Research in this area could optimise the efficacy of dialysis via vascular access delivered at home
Relevance to NICE guidance	Research in this area will inform updates to the recommendations around whether HDF or HD should be done at home and also potentially allow for recommendations on increased frequency of dialysis
Relevance to the NHS	Research in this area may allow more people to opt for HDF, done at home which may be a cost saving intervention compared with dialysis via a vascular access done in centre
Current evidence base	There is no evidence comparing the efficacy of these 4 potential strategies for dialysis via vascular access
Equality	Not applicable
Study design	RCT
Feasibility	May require a large sample size in order to power the study given the requirements for 4 arms, however the need for 4 arms is key given the potential concern that the benefit of HDF may not be seen if dialysis is undertaken more frequently
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.

Appendix K: Unit costs

Additional unit cost information presented to the committee are included in this section. NHS reference costs presented are generally from 2015/16 reflecting the latest data available at the time of committee meetings. However, the renal dialysis costs were updated to 2017/18 as some of these are used in the cost effectiveness analysis undertaken as part of this guideline.

K.1 Dialysis costs

Table 54: UK NHS reference costs 2016/17 for renal dialysis, adults

Currency code	Renal dialysis	Currency description	No.of sessions	Unit cost[a]			Cost per week[b]	Cost per year[c]		
				National average	Lower quartile	Upper quartile				
Adults dialysis via vascular access										
LD01A	At base	Hospital Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 19 years and over	412,415	£150	£123	£165	*£449*	*£23,371*	*£23,362*	*£23,643*
LD02A	At base	Hospital Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 19 years and over	701,601	£161	£136	£172	*£483*	*£25,123*		
LD03A	At base	Hospital Haemodialysis or Filtration, with Access via Haemodialysis Catheter, with Blood-Borne Virus, 19 years and over	16,202	£177	£143	£218	*£530*	*£27,543*		
LD04A	At base	Hospital Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, with Blood-Borne Virus, 19 years and over	28,125	£184	£136	£236	*£551*	*£28,667*		
LD01A	Away from base	Hospital Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 19 years and over	404	£148	£118	£190	*£444*	*£23,095*		
LD02A	Away from base	Hospital Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 19 years and over	356	£232	£146	£251	*£697*	*£36,236*		
LD05A	At base	Satellite Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 19 years and over	539,870	£137	£124	£157	*£411*	*£21,375*		
LD06A	At base	Satellite Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 19 years and over	1,155,230	£148	£127	£165	*£443*	*£23,030*		
LD07A	At base	Satellite Haemodialysis or Filtration, with Access via Haemodialysis Catheter, with Blood-Borne Virus, 19 years and over	28,020	£148	£124	£171	*£443*	*£23,037*		
LD08A	At base	Satellite Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, with Blood-Borne Virus, 19 years and over	49,872	£150	£125	£161	*£451*	*£23,457*		
LD05A	Away from base	Satellite Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 19 years and over	142	£168	£177	£187	*£504*	*£26,206*		
LD06A	Away from base	Satellite Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 19 years and over	692	£153	£133	£163	*£458*	*£23,817*		

Currency code	Renal dialysis	Currency description	No.of sessions	Unit cost[a]			Cost per week[b]	Cost per year[c]		
				National average	Lower quartile	Upper quartile				
LD08A	Away from base	Satellite Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, with Blood-Borne Virus, 19 years and over	2	£160	£160	£160	*£480*	*£24,955*		
LD09A	At base	Home Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 19 years and over	38,467	£194	£163	£186	*£194*	*£10,106*	*£9,588*	
LD10A	At base	Home Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 19 years and over	121,988	£181	£103	£186	*£181*	*£9,425*		
LD10A	Away from base	Home Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 19 years and over	5	£208	£112	£112	*£208*	*£10,809*		
Adults peritoneal dialysis										
LD11A	At base	Continuous Ambulatory Peritoneal Dialysis, 19 years and over	380,887	£69	£49	£78	*£484*	*£25,144*	*£25,148*	*£26,857*
LD11A	Away from base	Continuous Ambulatory Peritoneal Dialysis, 19 years and over	4,710	£70	£70	£70	*£491*	*£25,514*		
LD12A	At base	Automated Peritoneal Dialysis, 19 years and over	579,804	£77	£57	£82	*£539*	*£28,005*	*£27,978*	
LD12A	Away from base	Automated Peritoneal Dialysis, 19 years and over	7,914	£71	£71	£71	*£500*	*£25,995*		
LD13A	At base	Assisted Automated Peritoneal Dialysis, 19 years and over	111,534	£93.60	£76	£93	*£655*	*£34,071*	*£33,950*	
LD13A	Away from base	Assisted Automated Peritoneal Dialysis, 19 years and over	1,566	£70	£70	£70	*£488*	*£25,353*		

Source: NHS reference costs 2016/17[100]
(a) Unit costs: per session for hospital/satellite haemodialysis or filtration; per week for home haemodialysis or filtration; per day for peritoneal dialysis
(b) Calculated assuming: hospital/satellite haemodialysis or filtration 3x per week; peritoneal dialysis 7 days per week
(c) Weighted average based on number of sessions

Table 55: UK NHS reference costs 2016/17 for renal dialysis, children

Currency code	Renal dialysis	Currency description	No.of sessions	Unit cost[a]			Cost per week[b]	Cost per year[c]		
				National average	Lower quartile	Upper quartile				
Children dialysis via vascular access										
LD01B	At base	Hospital Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 18 years and under	23,776	£385	£314	£425	*£1,156*	*£60,121*	*£61,673*	*£61,628*
LD02B	At base	Hospital Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 18 years and under	2,149	£623	£524	£727	*£1,870*	*£97,228*		
LD03B	At base	Hospital Haemodialysis or Filtration, with Access via Haemodialysis Catheter, with Blood-Borne Virus, 18 years and under	159	£709	£721	£721	*£2,127*	*£110,586*		
LD04B	At base	Hospital Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, with Blood-Borne Virus, 18 years and under	31	£167	£167	£167	*£502*	*£26,086*		
LD05B	At base	Satellite Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 18 years and under	664	£274	£134	£568	*£823*	*£42,801*		
LD06B	At base	Satellite Haemodialysis or Filtration, with Access via Arteriovenous	879	£165	£164	£164	*£495*	*£25,728*		

Currency code	Renal dialysis	Currency description	No.of sessions	Unit cost[a]			Cost per week[b]	Cost per year[c]		
				National average	Lower quartile	Upper quartile				
		Fistula or Graft, 18 years and under								
LD08B	At base	Satellite Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, with Blood-Borne Virus, 18 years and under	72	£213	£213	£213	*£638*	*£33,180*		
LD09B	At base	Home Haemodialysis or Filtration, with Access via Haemodialysis Catheter, 18 years and under	705	£381	£290	£290	*£381*	*£19,792*	*£19,985*	
LD10B	At base	Home Haemodialysis or Filtration, with Access via Arteriovenous Fistula or Graft, 18 years and under	36	£457	£457	£457	*£457*	*£23,761*		
Children peritoneal dialysis										
LD11B	At base	Continuous Ambulatory Peritoneal Dialysis, 18 years and under	12,056	£115	£85	£157	*£802*	*£41,715*	*£39,788*	
LD12B	At base	Automated Peritoneal Dialysis, 18 years and under	12,459	£104	£78	£117	*£729*	*£37,923*		
LD13B	At base	Assisted Automated Peritoneal Dialysis, 18 years and under	72	£65	£65	£65	*£454*	*£23,613*		

Source: NHS reference costs 2016/17[100]
(a) Unit costs: per session for hospital/satellite haemodialysis or filtration; per week for home haemodialysis or filtration; per day for peritoneal dialysis
(b) Calculated assuming: hospital/satellite haemodialysis or filtration 3x per week; peritoneal dialysis 7 days per week
(c) Weighted average based on number of sessions

K.2 Dialysis access-related costs

NHS reference costs for admissions related to dialysis access creation, removal and complications are summarised in Table 56.

Table 56: 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	

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

Currency description	Currency code	Admission	Number of FCEs	National average unit cost	Weighted average
		Regular Day or Night Admissions	80	£708	
HD access: AV fistula or graft					
Open Arteriovenous Fistula, Graft or Shunt Procedures	YQ42Z	Elective inpatient	2735	£2,451	£2,012
		Non-elective long stay	144	£3,661	
		Non-elective short stay	306	£1,826	
		Day case	5291	£1,763	
		Regular Day or Night Admissions	9	£665	
		Out-patient	28	£199	
Attention to Arteriovenous Fistula, Graft or Shunt	YR48Z	Elective inpatient	647	£1,715	£1,433
		Non-elective long stay	140	£2,824	
		Non-elective short stay	359	£2,079	
		Day case	2978	£1,235	
		Regular Day or Night Admissions	17	£523	
		Out-patient	3	£228	
PD access: PD catheter					
Renal Replacement Peritoneal Dialysis Associated Procedures	LA05Z	Elective inpatient	892	£1,819	£1,148
		Non-elective long stay	32	£5,701	
		Non-elective short stay	297	£1,288	
		Day case	1,588	£996	
		Regular Day or Night Admissions	46	£339	
		Out-patient	470	£71	

Source: NHS reference costs 2015/16[99]

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.

K.3 Nephrology outpatient costs

NHS reference costs for nephrology outpatient appointments are summarised in Table 57.

Table 57: UK NHS reference costs 2015/16 for nephrology outpatient appointments

Currency code	Currency description	No. of attendances	National average unit cost
Consultant led			
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	576,355	£153
WF01B	Non-Admitted Face to Face Attendance, First	88,492	£194
WF01C	Non-Admitted Non-Face to Face Attendance, Follow-Up	9,450	£86
WF01D	Non-Admitted Non-Face to Face Attendance, First	1,399	£72
WF02A	Multiprofessional Non-Admitted Face to Face Attendance, Follow-Up	29,964	£169
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	2,951	£206
WF02C	Multiprofessional Non-Admitted Non Face to Face Attendance, Follow-Up	11	£139
Non-consultant led			
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	92,331	£108
WF01B	Non-Admitted Face to Face Attendance, First	6,947	£130
WF01C	Non-Admitted Non-Face to Face Attendance, Follow-Up	8,587	£45
WF01D	Non-Admitted Non-Face to Face Attendance, First	328	£96
WF02A	Multiprofessional Non-Admitted Face to Face Attendance, Follow-Up	452	£135
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	24	£139

Source: NHS reference costs 2015/16[99]

K.4 CKD inpatient admission costs

NHS reference costs for CKD related inpatient admissions are summarised in Table 58. If a patient starts dialysis urgently requiring inpatient admission this will incur an additional inpatient stay cost (as well as the hospital dialysis costs recorded separately).

Table 58: UK NHS reference costs 2015/16 for CKD inpatient admissions

Admission	Currency code	Currency description	Number of FCEs	National average unit cost	Weighted average
Elective inpatient	LA08G	Chronic Kidney Disease with Interventions, with CC Score 6+	155	£6,344	£2,369
Elective inpatient	LA08H	Chronic Kidney Disease with Interventions, with CC Score 3-5	327	£4,420	
Elective inpatient	LA08J	Chronic Kidney Disease with Interventions, with CC Score 0-2	686	£3,475	
Elective inpatient	LA08K	Chronic Kidney Disease without Interventions, with CC Score 11+	74	£2,737	
Elective inpatient	LA08L	Chronic Kidney Disease without Interventions, with CC Score 8-10	151	£2,368	
Elective inpatient	LA08M	Chronic Kidney Disease without Interventions, with CC Score 5-7	317	£1,782	
Elective inpatient	LA08N	Chronic Kidney Disease without Interventions, with CC Score 3-4	437	£1,446	
Elective inpatient	LA08P	Chronic Kidney Disease without Interventions, with CC Score 0-2	1,362	£1,281	
Non-elective long stay	LA08G	Chronic Kidney Disease with Interventions, with CC Score 6+	764	£7,122	£3,398
Non-elective long stay	LA08H	Chronic Kidney Disease with Interventions, with CC Score 3-5	610	£5,083	
Non-elective long stay	LA08J	Chronic Kidney Disease with Interventions, with CC Score 0-2	541	£3,826	
Non-elective long stay	LA08K	Chronic Kidney Disease without Interventions, with CC Score 11+	480	£3,939	
Non-elective long stay	LA08L	Chronic Kidney Disease without Interventions, with CC Score 8-10	963	£3,405	
Non-elective long stay	LA08M	Chronic Kidney Disease without Interventions, with CC Score 5-7	1,655	£2,967	
Non-elective long stay	LA08N	Chronic Kidney Disease without Interventions, with CC Score 3-4	1,416	£2,446	
Non-elective long stay	LA08P	Chronic Kidney Disease without Interventions, with CC Score 0-2	1,761	£2,085	
Non-elective short stay	LA08H	Chronic Kidney Disease with Interventions, with CC Score 3-5	13	£988	£687
Non-elective short stay	LA08J	Chronic Kidney Disease with Interventions, with CC Score 0-2	13	£793	
Non-elective short stay	LA08K	Chronic Kidney Disease without Interventions, with CC Score 11+	126	£613	
Non-elective short stay	LA08L	Chronic Kidney Disease without Interventions, with CC Score 8-10	378	£570	
Non-elective short stay	LA08M	Chronic Kidney Disease without Interventions, with CC Score 5-7	923	£552	
Non-elective short stay	LA08N	Chronic Kidney Disease without Interventions, with CC Score 3-4	1,012	£592	
Non-elective short stay	LA08P	Chronic Kidney Disease without Interventions, with CC Score 0-2	2,234	£808	
Day case	LA08J	Chronic Kidney Disease with Interventions, with CC Score 0-2	2	£604	£379
Day case	LA08K	Chronic Kidney Disease without Interventions, with CC Score 11+	9	£670	
Day case	LA08L	Chronic Kidney Disease without Interventions, with CC Score 8-10	11	£311	
Day case	LA08M	Chronic Kidney Disease without Interventions, with CC Score 5-7	137	£331	
Day case	LA08N	Chronic Kidney Disease without Interventions, with CC Score 3-4	408	£340	

Admission	Currency code	Currency description	Number of FCEs	National average unit cost	Weighted average
Day case	LA08P	Chronic Kidney Disease without Interventions, with CC Score 0-2	1,940	£389	
Regular Day or Night Admissions	LA08L	Chronic Kidney Disease without Interventions, with CC Score 8-10	2	£359	£365
Regular Day or Night Admissions	LA08M	Chronic Kidney Disease without Interventions, with CC Score 5-7	7	£355	
Regular Day or Night Admissions	LA08N	Chronic Kidney Disease without Interventions, with CC Score 3-4	10	£337	
Regular Day or Night Admissions	LA08P	Chronic Kidney Disease without Interventions, with CC Score 0-2	1,652	£365	

Source: NHS reference costs 2015/16[99]

Abbreviations: FCE = finished consultant episodes

K.5 Kidney transplant-related costs

NHS reference costs related to transplant are presented in Table 59 to Table 65 below.

Table 59: UK NHS reference costs 2015/16 for inpatient episodes related to renal transplantation in adults

Type of admission	Currency description	Number of FCEs	National average unit cost	Weighted average[(a)]	
Pre-transplant					
Elective inpatient	Kidney Pre-Transplantation Work-up of Live Donor	1	£8,191	£895	
Non elective short stay	Kidney Pre-Transplantation Work-up of Live Donor	1	£768		
DAY CASE	Kidney Pre-Transplantation Work-up of Live Donor	80	£806		
Elective inpatient	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	2	£663	£727	
Non elective long stay	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	1	£1,211		
Non elective short stay	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	51	£720		
Donation					
Elective inpatient	Live Donation of Kidney	694	£7,733	£7,768	
Non elective long stay	Live Donation of Kidney	8	£10,793		

Type of admission	Currency description	Number of FCEs	National average unit cost	Weighted average[(a)]	
Transplant					
Elective inpatient	Kidney Transplant, 19 yrs and over, from Cadaver Non Heart-Beating Donor	55	£15,019	£15,065	£15,232
Non elective long stay	Kidney Transplant, 19 yrs and over, from Cadaver Non Heart-Beating Donor	448	£15,961		
Non elective short stay	Kidney Transplant, 19 yrs and over, from Cadaver Non Heart-Beating Donor	61	£8,522		
Elective inpatient	Kidney Transplant, 19 yrs and over, from Cadaver Heart-Beating Donor	123	£14,521	£15,239	
Non elective long stay	Kidney Transplant, 19 yrs and over, from Cadaver Heart-Beating Donor	811	£16,219		
Non elective short stay	Kidney Transplant, 19 yrs and over, from Cadaver Heart-Beating Donor	124	£9,547		
Elective inpatient	Kidney Transplant, 19 yrs and over, from Live Donor	683	£15,321	£15,351	
Non elective long stay	Kidney Transplant, 19 yrs and over, from Live Donor	36	£16,770		
Non elective short stay	Kidney Transplant, 19 yrs and over, from Live Donor	9	£11,926		
Post-transplant					
Day case	Examination for Post-Transplantation of Kidney of Recipient, 19 yrs and over	13	£417	£426	
Non elective short stay	Examination for Post-Transplantation of Kidney of Live Donor	1	£444		
Day case	Examination for Post-Transplantation of Kidney of Live Donor	1	£529		

Source: NHS reference costs 2015/16[99]

Abbreviations: FCE = finished consultant episodes

(a) Weighted by activity

Table 60: UK NHS reference costs 2015/16 for inpatient episodes related to renal transplantation in children

Type of admission	Currency description	Number of FCEs	National average unit cost	Weighted average[(a)]	
Transplant					
Elective inpatient	Kidney Transplant, 18 years and under, from Cadaver Non Heart-Beating Donor	4	£7,250	£9,312	£18,125

Type of admission	Currency description	Number of FCEs	National average unit cost	Weighted average[(a)]
Non elective long stay	Kidney Transplant, 18 years and under, from Cadaver Non Heart-Beating Donor	1	£17,560	
Non elective short stay	Kidney Transplant, 18 years and under, from Cadaver Non Heart-Beating Donor	3	£6,622	
Elective inpatient	Kidney Transplant, 18 years and under, from Cadaver Heart-Beating Donor	15	£15,257	£20,742
Non elective long stay	Kidney Transplant, 18 years and under, from Cadaver Heart-Beating Donor	22	£24,481	
Non elective short stay	Kidney Transplant, 18 years and under, from Cadaver Heart-Beating Donor	4	£7,968	
Elective inpatient	Kidney Transplant, 18 years and under, from Live Donor	60	£18,020	£18,309
Non elective long stay	Kidney Transplant, 18 years and under, from Live Donor	3	£24,096	
Non elective short stay	Kidney Transplant, 18 years and under, from Live Donor	1	£28,912	

Source: NHS reference costs 2015/16[99]

Abbreviations: FCE = finished consultant episodes

(a) Weighted by activity

Table 61: UK NHS reference costs 2015/16 for outpatient procedures relating to transplantation surgery in adults

Service description	Code	Currency description	Procedures	National average unit cost	Weighted average[(a)]
Pre-transplant					
Transplantation Surgery	LA10Z	Live Kidney Donor Screening	389	£208	£232
Upper GI Surgery	LA10Z	Live Kidney Donor Screening	1	£443	
Paediatric Transp. Surgery	LA10Z	Live Kidney Donor Screening	2	£200	
Cardiology	LA10Z	Live Kidney Donor Screening	1	£250	
Nephrology	LA10Z	Live Kidney Donor Screening	803	£244	
Neurology	LA10Z	Live Kidney Donor Screening	1	£144	
General Surgery	LA11Z	Kidney Pre-Transplantation Work-up of Live Donor	1	£61	£292
Transplantation Surgery	LA11Z	Kidney Pre-Transplantation Work-up of Live Donor	408	£229	
Clinical Haematology	LA11Z	Kidney Pre-Transplantation Work-up of Live Donor	7	£116	
Cardiology	LA11Z	Kidney Pre-Transplantation Work-up of Live Donor	2	£117	

Service description	Code	Currency description	Procedures	National average unit cost	Weighted average[a]
Nephrology	LA11Z	Kidney Pre-Transplantation Work-up of Live Donor	1,719	£308	
General Surgery	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	1	£22	£385
Urology	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	2	£116	
Transplantation Surgery	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	1,444	£245	
Vascular Surgery	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	1	£161	
Plastic Surgery	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	1	£70	
Clinical Haematology	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	1	£60	
Hepatology	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	1	£181	
Nephrology	LA12A	Kidney Pre-Transplantation Work-up of Recipient, 19 years and over	6,329	£418	
Post-transplant					
General Surgery	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	3	£115	£235
Urology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	2	£104	
Transplantation Surgery	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	29,487	£224	
Colorectal Surgery	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	2	£108	
Upper GI Surgery	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	1	£103	
Vascular Surgery	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	2	£126	
Ophthalmology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	1	£123	

Service description	Code	Currency description	Procedures	National average unit cost	Weighted average[a]
Paediatric Nephrology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	1	£241	
Clinical Haematology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	2	£11,414	
Hepatology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	1	£109	
Diabetic Medicine	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	3	£233	
Cardiology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	1	£165	
Dermatology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	2	£207	
Respiratory Medicine	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	3	£58	
Nephrology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	40,554	£242	
Neurology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	3	£288	
Rheumatology	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	6	£173	
Paediatrics	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	50	£442	
Obstetrics	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	1	£55	
Dietetics	LA13A	Examination for Post-Transplantation of Kidney of Recipient, 19 years and over	8	£56	
General Surgery	LA14Z	Examination for Post-Transplantation of Kidney of Live Donor	18	£95	£199
Transplantation Surgery	LA14Z	Examination for Post-Transplantation of Kidney of Live Donor	335	£155	
Paediatric Nephrology	LA14Z	Examination for Post-Transplantation of Kidney of Live Donor	33	£167	
Respiratory Medicine	LA14Z	Examination for Post-Transplantation of Kidney of Live Donor	1	£353	
Nephrology	LA14Z	Examination for Post-Transplantation of Kidney of Live Donor	2,187	£207	

Source: NHS reference costs 2015/16[99]

(a) Weighted by activity

Table 62: UK NHS reference costs 2015/16 for outpatient procedures relating to transplantation surgery in children

Service description	Code	Currency description	Procedures	National average unit cost	Weighted average[(a)]
General Surgery	LA12B	Kidney Pre-Transplantation Work-up of Recipient, 18 years and under	1	£340	£957
Transplantation Surgery	LA12B	Kidney Pre-Transplantation Work-up of Recipient, 18 years and under	7	£249	
Paediatric Nephrology	LA12B	Kidney Pre-Transplantation Work-up of Recipient, 18 years and under	7	£2,506	
Nephrology	LA12B	Kidney Pre-Transplantation Work-up of Recipient, 18 years and under	19	£681	
Transplantation Surgery	LA13B	Examination for Post-Transp. of Kidney of Recipient, 18 years and under	80	£392	£311
Paediatric Transp. Surgery	LA13B	Examination for Post-Transp. of Kidney of Recipient, 18 years and under	17	£371	
Paediatric Nephrology	LA13B	Examination for Post-Transp. of Kidney of Recipient, 18 years and under	80	£241	
Nephrology	LA13B	Examination for Post-Transp. of Kidney of Recipient, 18 years and under	153	£300	

Source: NHS reference costs 2015/16[99]

(a) Weighted by activity

Table 63: UK NHS reference costs 2015/16 for outpatient appointments relating to transplantation surgery in adults

Currency code	Currency description	Service code	Service description	Number of attendances	National average unit cost
Consultant led					
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	102	Transplantation Surgery	53,599	£306
WF01B	Non-Admitted Face to Face Attendance, First	102	Transplantation Surgery	5,269	£365
WF01C	Non-Admitted Non-Face to Face Attendance, Follow-Up	102	Transplantation Surgery	159	£50
WF01D	Non-Admitted Non-Face to Face Attendance, First	102	Transplantation Surgery	2	£184
WF02A	Multiprofessional Non-Admitted Face to Face Attendance, Follow-Up	102	Transplantation Surgery	2,549	£444
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	102	Transplantation Surgery	545	£388
Non-consultant led					
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	102	Transplantation Surgery	8,440	£241
WF01B	Non-Admitted Face to Face Attendance, First	102	Transplantation Surgery	535	£239
WF01C	Non-Admitted Non-Face to Face Attendance, Follow-Up	102	Transplantation Surgery	35	£43
WF01D	Non-Admitted Non-Face to Face Attendance, First	102	Transplantation Surgery	7	£32
WF02A	Multiprofessional Non-Admitted Face to Face Attendance, Follow-Up	102	Transplantation Surgery	3	£329
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	102	Transplantation Surgery	1	£164

Source: NHS reference costs 2015/16[99]

Table 64: UK NHS reference costs 2015/16 for outpatient appointments relating to transplantation surgery in children

Currency code	Currency description	Service code	Service description	Number of attendances	National average unit cost
Consultant led					
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	212	Paediatric Transplantation Surgery	773	£222
WF01B	Non-Admitted Face to Face Attendance, First	212	Paediatric Transplantation Surgery	92	£218
WF02A	Multiprofessional Non-Admitted Face to Face Attendance, Follow-Up	212	Paediatric Transplantation Surgery	65	£285
WF02B	Multiprofessional Non-Admitted Face to Face Attendance, First	212	Paediatric Transplantation Surgery	10	£333
Non-consultant led					
WF01A	Non-Admitted Face to Face Attendance, Follow-Up	212	Paediatric Transplantation Surgery	154	£130
WF01B	Non-Admitted Face to Face Attendance, First	212	Paediatric Transplantation Surgery	43	£217
WF01C	Non-Admitted Non-Face to Face Attendance, Follow-Up	212	Paediatric Transplantation Surgery	24	£83

Source: NHS reference costs 2015/16[99]

Table 65: UK unit costs of inpatient admissions for transplant failure

Admission	Code	Currency description	FCEs	National average unit cost	Weighted average[(a)]
Elective inpatient	WH01A	Transplant Failure and Rejection, with Multiple Interventions	100	£7,745	£3,862
Non-elective inpatient	WH01A	Transplant Failure and Rejection, with Multiple Interventions	190	£11,816	
Non-elective short stay	WH01A	Transplant Failure and Rejection, with Multiple Interventions	3	£5,263	
Day case	WH01A	Transplant Failure and Rejection, with Multiple Interventions	2	£675	
Elective inpatient	WH01B	Transplant Failure and Rejection, with Single Intervention	188	£5,235	
Non-elective inpatient	WH01B	Transplant Failure and Rejection, with Single Intervention	398	£6,053	
Non-elective short stay	WH01B	Transplant Failure and Rejection, with Single Intervention	5	£2,837	
Elective inpatient	WH01C	Transplant Failure and Rejection, without Interventions, with CC Score 2+	75	£3,682	
Non-elective inpatient	WH01C	Transplant Failure and Rejection, without Interventions, with CC Score 2+	252	£4,196	
Non-elective short stay	WH01C	Transplant Failure and Rejection, without Interventions, with CC Score 2+	103	£888	
Day case	WH01C	Transplant Failure and Rejection, without Interventions, with CC Score 2+	73	£358	
Regular Day or Night Admis.	WH01C	Transplant Failure and Rejection, without Interventions, with CC Score 2+	12	£418	
Elective inpatient	WH01D	Transplant Failure and Rejection, without Interventions, with CC Score 0-1	225	£2,903	
Non-elective inpatient	WH01D	Transplant Failure and Rejection, without Interventions, with CC Score 0-1	480	£3,212	
Non-elective short stay	WH01D	Transplant Failure and Rejection, without Interventions, with CC Score 0-1	327	£697	
Day case	WH01D	Transplant Failure and Rejection, without Interventions, with CC Score 0-1	232	£561	
Regular Day or Night Admis.	WH01D	Transplant Failure and Rejection, without Interventions, with CC Score 0-1	50	£624	

Source: NHS reference costs 2015/16[99]

Abbreviations: FCE = finished consultant episodes

(a) Weighted by activity