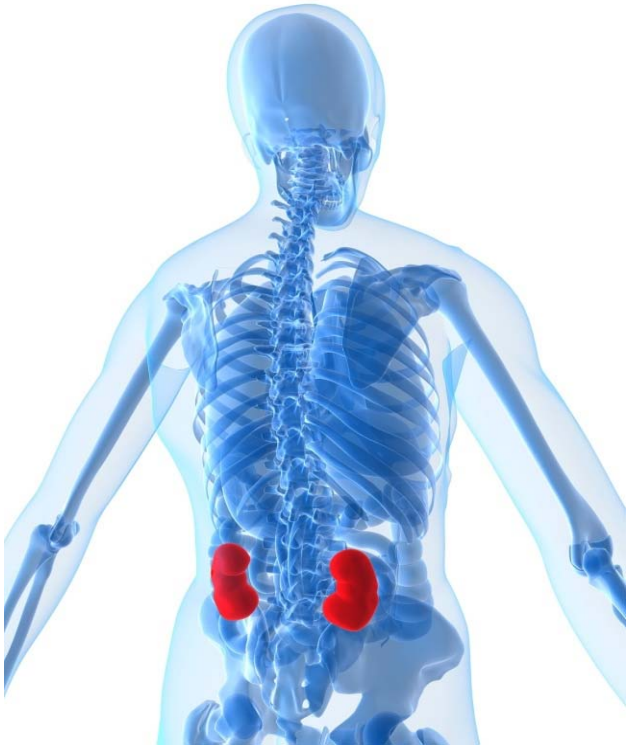
KCE REPORT 217S

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Center

MACHINE PERFUSION IN KIDNEYS FROM DECEASED DONORS – A RAPID ASSESSMENT

APPENDIX



KCE REPORT 217S
HEALTH TECHNOLOGY ASSESSMENT

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MACHINE PERFUSION IN KIDNEYS FROM DECEASED DONORS – A RAPID ASSESSMENT

APPENDIX

LORENA SAN MIGUEL, DOMINIQUE ROBERFROID, SABINE STORDEUR, NATHALIE SWARTENBROEKX

COLOPHON

Title :	Machine perfusion in kidneys from deceased donors – A rapid assessment – Appendix
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	and validators have a certain degree of conflict of interest to the main topic of this report.
Layout:	Ine Verhulst
Disclaimer:	• **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.** • **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.** • **Finally, this report has been approved by common assent by the Executive Board.** • **Only the KCE is responsible for errors or omissions that could persist. The policy recommendations are also under the full responsibility of the KCE.**
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APPENDIX REPORT

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1. SEARCH STRATEGIES

1.1. Search strategy for clinical studies

Date	16/05/2013
Database (name + access ; e.g.: Medline OVID)	Medline Ovid
Search Strategy (attention, for PubMed, check « Details »)	#1. ((machine* OR pulsat*) adj3 (perfus* OR preserv* OR system*)).ti,ab. #2. ((kidney or renal) adj3 (transplant* OR preserv*OR replace* OR dono* OR reciev*)).ti,ab. #3. (kidney OR renal).ti,ab. #4. Organ preservation/ #5.graft survival/ #6. #4 OR #5 #7. #3 AND #6 #8. #2 OR #7 #9. ((machine* OR pulsat* OR mechani*) adj3 (perfus* OR preserv* OR system*)).ti, ab. #10. RM3.ti,ab. #11. Lifeport.ti, ab. #12. #9 OR #10 OR #11 #13. #8 AND #12
Note	401 hits

Date	16/05/2013
Database (name + access ; e.g.: Medline OVID)	Embase
Search Strategy (attention, for PubMed, check « Details »)	#1. (machine* NEAR/3 (perfus* OR preserv* OR system*)): ab, ti #2. (pulsat* NEAR/3 (perfus* OR preserv* OR system*)): ab, ti #3. #1 OR #2 #4. ((kidney OR renal) NEAR/3 (transplant* OR preserv* OR replace* OR dono* Or reciev*)): ab, ti #5. Kidney: ab, ti OR renal: ab, ti #6.'kidney preservation'/de #7. 'graft survival'/de #8. #6 OR #7 #9 #5 AND #8 #10. #4 OR #9 #11. rm3: ab, ti OR lifeport: ab, ti #12. #3 OR #11 #13. #10 AND #9
Note	503 hits

Date	16/05/2013
Database (name + access ; e.g.: Medline OVID)	Cochrane Library
Search Strategy (attention, for PubMed, check « Details »)	#1. Machine perfusion #2.kidney OR renal #3. #1 AND #2
Note	60 hits

1.2. Search strategy for economic studies

Date	15/03/2013
Database	CRD NHS DATABASES
Search Strategy	1. MeSH DESCRIPTOR Kidney Transplantation EXPLODE ALL TREES (306) 2. MeSH DESCRIPTOR Perfusion EXPLODE ALL TREES (40) 3. 1 AND 2 (7)

Date	15/03/2013
Database	MEDLINE (OVID)
Search Strategy	Database: Ovid MEDLINE(R) <1946 to May Week 2 2013> Search Strategy: --- 1 exp Economics/ (472840) 2 exp "Costs and Cost Analysis"/ (172372) 3 exp Economics, Pharmaceutical/ (2440) 4 exp Economics, Hospital/ (18673) 5 exp Economics, Medical/ (13334) 6 exp Economics, Nursing/ (3871) 7 exp Health Care Costs/ (43329) 8 "Cost Savings"/ (8140) 9 exp "Value of Life"/ (5320) 10 exp Quality-Adjusted Life Years/ (6240) 11 Health Expenditures/ (13042) 12 "budget*".ab,ti. (16237) 13 (price or prices or pricing).ab,ti. (20607) 14 (cost-effectiveness or cost effectiveness).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary

	concept, unique identifier]	(29740)
	15 (cost-utility or cost utility).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	(2030)
	16 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 15	(493810)
	17 (machine* or pulsat*).ab,ti.	(94592)
	18 (perfus* or preserv* or system).ab,ti.	(1591970)
	19 lifeport.ab,ti.	(10)
	20 RM3.ab,ti.	(88)
	21 exp Perfusion/	(54985)
	22 exp Organ Preservation/	(7561)
	23 renal transplantation.mp. or exp Kidney Transplantation/	(78213)
	24 18 or 21 or 22	(1613031)
	25 17 or 19 or 20	(94671)
	26 24 and 25	(18546)
	27 16 and 26	(202)
	28 23 and 27	(13)

Date	15/03/2013	
Database	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations	
Search Strategy	1 cost*.mp.	(28087)
	2 (economic* or pharmacoeconomic*).mp.	(12438)
	3 (budget* or expenditure*).mp.	(3661)
	4 (price or prices or pricing).mp.	(1840)
	5 1 or 2 or 3 or 4 (41087)	
	6 (machine* or pulsat*).mp.	(8395)
	7 (perfus* or preserv* or system).mp.	(143208)
	8 (lifeport or RM3).mp.	(6)
	9 ((renal or kidney) and transplant*).mp.	(3052)
	10 perfusion.mp.	(3939)
	11 (organ adj preserv*).mp.	(120)
	12 7 or 10 or 11	(143208)
	13 6 or 8	(8399)
	14 5 and 12 and 13	(107)
	15 9 and 14	(2)

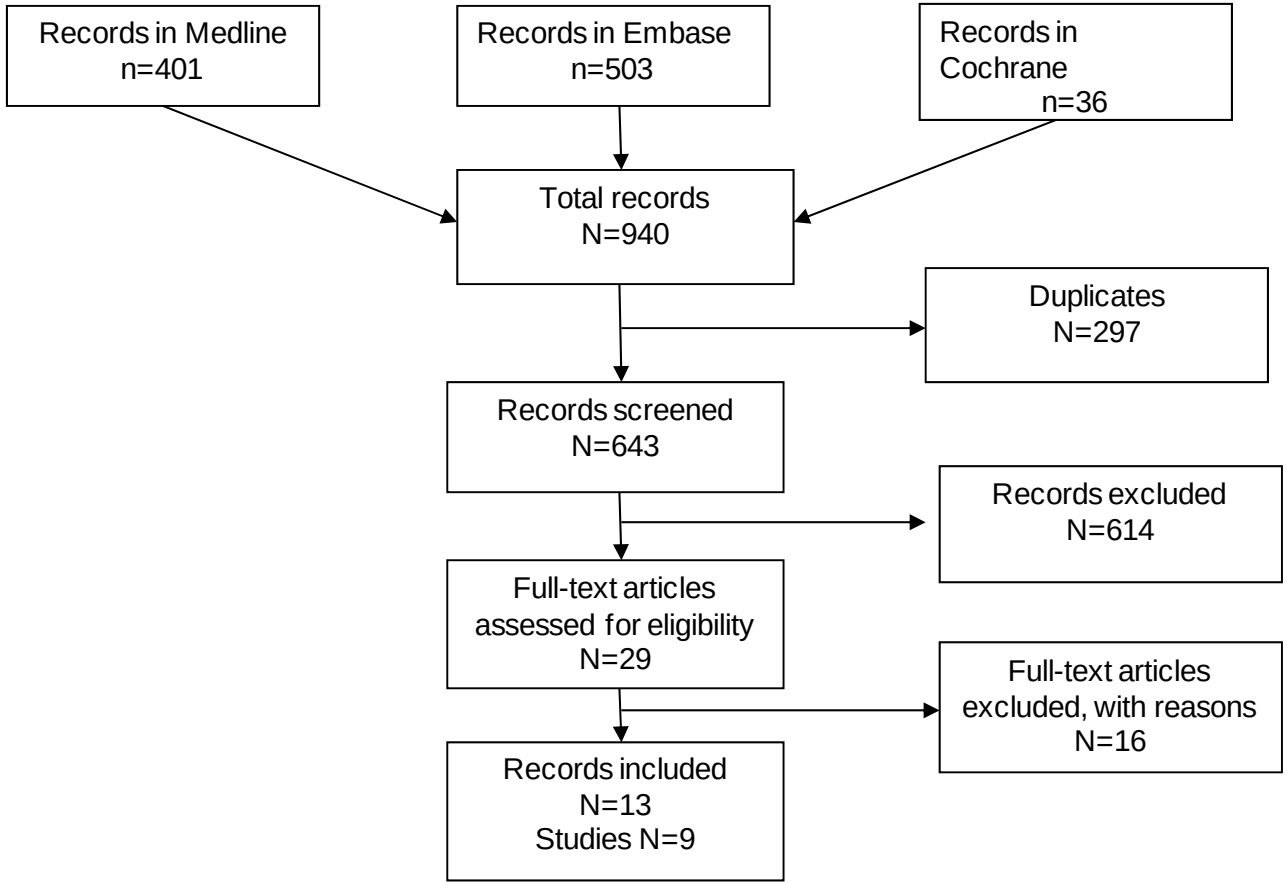
Date	15/03/2013	
Database	EMBASE	
Search Strategy	No. Query Results	Results
	#21. 14 AND 17 AND 20	
	#20. 18 OR 19	330,316
	#19. perfus*:ab,ti OR preserv*:ab,ti AND [embase]/lim	329,008
	#18. 'kidney perfusion'/exp AND [embase]/lim	5,062
	#17. 15 OR 16	89,365
	#16. lifeport:ab,ti OR rm3:ab,ti AND [embase]/lim	136

	#15. machine*:ab,ti OR pulsat*:ab,ti AND [embase]/lim	89,287
	#14. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13	396,439
	#13. budget* AND [embase]/lim	20,566
	#12. price OR prices OR pricing AND [embase]/lim	39,615
	#11. 'cost minimization analysis'/exp AND [embase]/lim	2,219
	#10. 'cost utility analysis'/exp AND [embase]/lim	4,599
	#9. 'hospital cost'/exp AND [embase]/lim	15,095
	#8. 'cost control'/exp AND [embase]/lim	25,973
	#7. 'cost of illness'/exp AND [embase]/lim	7,306
	#6. 'cost effectiveness analysis'/exp AND	86,745 [embase]/lim
	#5. 'cost benefit analysis'/exp AND [embase]/lim	40,541
	#4. 'health care financing'/exp AND [embase]/lim	10,915
	#3. 'health economics'/exp AND [embase]/lim	344,815
	#2. 'health care cost'/exp AND [embase]/lim	152,915
	#1. 'economics'/exp AND [embase]/lim	16,334

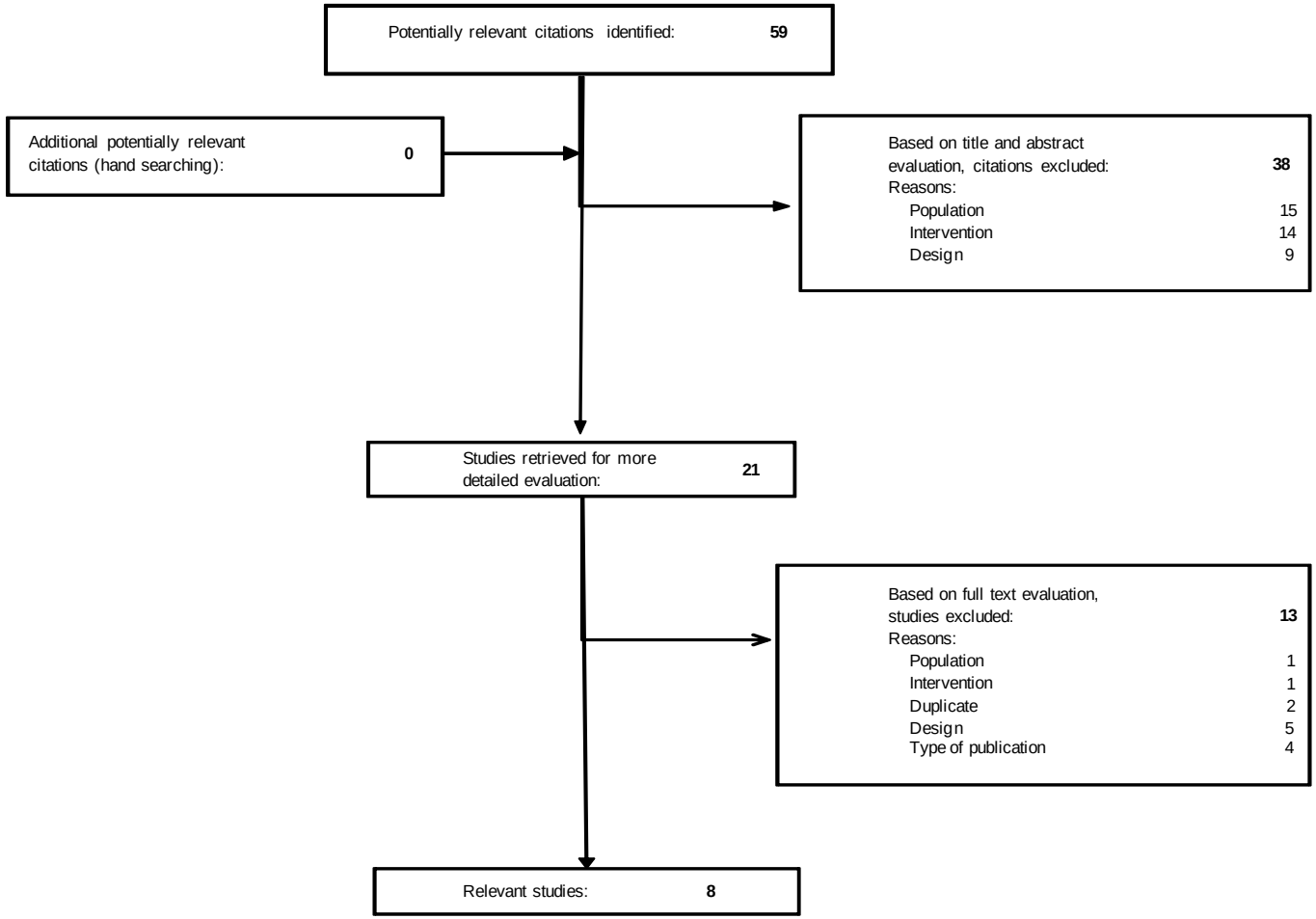
Date	**15/03/2013**	
Database	EconLit	
Search Strategy	((renal OR kidney) AND transplant*).mp.	(65)
	(perfus* OR preserv*).mp.	(4494)
	1 AND 2	(0)

2. FLOW CHARTS FOR SELECTION PROCEDURES

2.1. Flow chart for clinical studies



2.2. Flow chart for economic studies



3. EXCLUDED STUDIES

Author	Year	Reasons for exclusion
Amaduzzi[71]	2011	Only the abstract is available. Author has been contacted for reasons not to publish the full results (by Facebook on 24/08/2013). From October 2008 to February 2011, 59 pairs of kidney from consecutive 18 to 79 years old donors were included. One kidney was randomly assigned to HMP and the contralateral kidney to CS. Among the 59 kidneys enrolled in HMP group, 11 have been excluded for technical/logistic issues or renal artery unavailability. No statistical significant differences between groups were found (DGF was 37.8% in HMP versus 30% in CS).
Danielewicz[20]	1997	No randomization of intervention described, allocation concealment not described, no blinding of outcome assessment
Jaffers [23]	1989	The authors mentioned that "organs were randomly stored in slushed ice or by using perfusion machine". At the same time, they announced that "the records of 101 consecutive recipients" were reviewed, implying that the study was retrospective in nature. The huge imbalance of numbers between groups (68 versus 33) would have been impossible with a genuine randomization. Moreover, the authors used a different definition of DGF (lack of continuous decrease in serum creatinine over the first 4 days after transplantation).
Kumar[72]	1991	No randomization of intervention, allocation concealment not described, no blinding
Marshall[73]	1997	No randomization of intervention described. Moreover, kidneys of the MP group were first transported to the perfusion laboratory in ice, and retransported in ice when removed from the machine for subsequent transplantation
Matsuno[74]	1994	No randomization of intervention described, no blinding of outcome assessment, small sample
Merion[75]	1990	No randomization of intervention described, allocation concealment not described, no blinding of outcome assessment
Moers[76]	2008	This is a conference proceeding on the results published in 2009 in the New England Journal of Medicine
Moers[77]	2011	Abstract of results presented in 2012 in the New England Journal of Medicine
Nirmal[78]	2009	Comments on the study by Moers 2009
Paul[79]	2008	Abstract of results of a subgroup analysis (donors>55 years) from the Eurotransplant study (Moers 2009)
Paul[80]	2009	Abstract of results presented in full in Gallinat 2012 (although the abstract included only 52 donors versus 85 in the full paper)
Pirenne[81]	2009	Abstract of results presented in Jochmans 2010
Sheil[82]	1975	No randomization "kidneys which became available at night were preserved by machine perfusion, while those becoming available during the day were implanted directly after short-term storage

4. CLINICAL DATA EXTRACTION TABLES & RISK OF BIAS TABLES

Alijani 1985

Methods	
Participants	38 consecutive renal donors
Interventions	One kidney was preserved by cold storage (in Euro-Collins) and the opposite kidney with machine preservation Waters MOX-100 (with plasma protein fraction perfusate)
Outcomes	Acute tubular necrosis post transplantation defined as the requirement of hemodialysis during the 1st week after transplantation
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	A "randomized protocol" is mentioned only in the abstract.
Allocation concealment (selection bias)	Unclear risk	The authors mention that "kidneys were alternated: 38 right, 38 left for each preservation method"
Blinding of participants and personnel (performance bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias)	Unclear risk	The author report that "8 paired kidneys were deleted because one kidney was not transplanted, an in one pair the preservation mode was changed"
Selective reporting (reporting bias)	Low risk	
Other bias	Unclear risk	

Mozes 1985

Methods	
Participants	96 heart-beating donors
Interventions	Each of the paired kidneys from each donor was randomly assigned to CS in Euro-Collins pr to MP using the Waters Mox-100 and silica gel plasma perfusate.
Outcomes	Acute tubular necrosis (ATN) defined as the need for dialysis in the first week after transplantation Graft failure defined as a return to permanent dialysis or patient death
Notes	Matching not accounted for in analysis 6 participating centres + "outside centres". Clustering not accounted for in the analysis

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Generation of random sequence is not described
Allocation concealment (selection bias)	Unclear risk	Not described. Authors report that characteristics at baseline were similar in the 2 study arms (no table provided), which seems to discard the possibility of an important selection bias.
Blinding of participants and personnel (performance bias)	High risk	The recipient center was informed regarding the preservation method
Blinding of outcome assessment (detection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias)	Low risk	Five kidneys were not used because of recipients unavailability resulting with 94 kidneys in the CS and 93 kidneys in the MP group
Selective reporting (reporting bias)	Low risk	
Other bias	Unclear risk	The immunosuppressive protocols varied between centres and over time. Impact on results is unknown.

Heil 1987

Methods	
Participants	27 donors (not mentioned if they were DBD or DCD)
Interventions	The kidneys assigned to cold storage were submersed in Euro-Collins and sealed in a sterile jar and isolation bags. The mechanically perfused kidneys were placed into the Waters Mox-100 preservation unit primed with silica gel fractionated plasma
Outcomes	Delayed renal function (incidence and duration) Graft survival at 12 months
Notes	The report is less than 1 page and does not allow to judge quality of the evaluation

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	not described/evaluable ("sealed envelopes)"
Allocation concealment (selection bias)	Unclear risk	not described/evaluable
Blinding of participants and personnel (performance bias)	Unclear risk	not described/evaluable
Blinding of outcome assessment (detection bias)	Unclear risk	not described/evaluable
Incomplete outcome data (attrition bias)	Unclear risk	not described/evaluable
Selective reporting (reporting bias)	Unclear risk	not described/evaluable
Other bias	Unclear risk	not described/evaluable

Halloran 1987

Methods	
Participants	107 cadaver donors from January 1983 to January 1984 (in 9 centres). Type of patients is not reported.
Interventions	Donors were randomized (i.e. not kidneys) to CS or pulsatile perfusion (PP). CS kidneys were flushed with cold Collins'solution and stored in Collins' in a sterile container on ice. PP kidneys were flushed with Collins' and perfused on a Waters pulsatile perfusion machine using Plasmanate (Cutter Biological, Berkeley, Calif) + 10 kidneys perfused in a Gambro machine with albumin. Kidneys on PP were initially stored for an average of 3.3+/-2.0 hours on ice before placement on the perfusion machine.
Outcomes	1. Delayed graft function defined by: Method A: plama creatinine>500µmol/L during 1st week AND /OR requirement for more than 1 dialysis AND/OR urine output<1L/24 hr for more than 2 days immediately posttransplant Method B: requirement for dialysis in the 1st posttranslant week 2. Primary non function defined as never attaining plasma creatinine <500µmol/L AND/OR always requiring dialysis
Notes	No ITT. Cluster design not accounted for.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described/evaluable "randomization to CS or PP was performed by donor and was adjusted to obtain balanced numbers in each block of 20 patients"
Allocation concealment (selection bias)	Unclear risk	Not described/evaluable
Blinding of participants and personnel (performance bias)	Unclear risk	Not described/evaluable
Blinding of outcome assessment (detection bias)	Unclear risk	Not described/evaluable
Incomplete outcome data	High risk	The authors report that "107 donors were randomized yielding 208 kidneys (99 in the CS group and 109 in the

(attrition bias)		PP group). 12 kidneys were discarded after randomization. Follow-up information was available for 194 kidneys (90 in the CS group, 91 in the PP group, 13 randomized to PP but which received CS only). Complete data was available for 176 receivers. Data analysis was performed on those 176 patients"
Selective reporting (reporting bias)	Unclear risk	Not described/evaluable
Other bias	High risk	No intention-to-treat analysis (208 kidneys transplanted, analysis performed on 176) whereas: a. 13 kidneys allocated to PP received CS and were excluded from the study/analysis. b. 4 technical failures in the CS group and 3 in the PP group were also excluded. The nature of these technical failures were is not described.

Veller 1994

Methods	
Participants	18 DBD victims of trauma who were hemodynamically stable and who continued to pass urine, during the period 1989 to September 1992
Interventions	Kidneys were randomly allocated to CS in University of Wisconsin solution or to MP (Waters 1000 perfused with cooled cryoprecipitated plasma at 4-6 °C)
Outcomes	Acute tubular necrosis defined as the recipient requiring dialysis during the 1 st week post transplantation Delayed graft function defined as a creatinine which did not drop below 200µmol/l within 5 to 7 d after transplantation and ineffective passage of urine 1 year graft survival
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization procedure not described
Allocation concealment (selection bias)	Unclear risk	Authors state that "recipients were selected by individuals not directly involved in the study"
Blinding of participants and personnel (performance bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias)	Unclear risk	The authors state that " of the 30 donors, 12 were excluded from the study because one or both recipients had previously had a renal transplant". Whether this selection was decided post-hoc is unclear.
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	Pairing not accounted for in analysis

van der Vliet 2001

Methods	
Participants	38 consecutive DCD patients (2 Maastricht type 2, 34 Maastricht type 3, 2 Maastricht type 4)
Interventions	One kidney was randomly assigned to preservation with CS (University of Wisconsin solution) and the other underwent MP (Gambro pulsatile perfusion machine with Belzer solution).
Outcomes	Delayed graft function, primary nonfunction, serum creatine at 3 months after transplantation, 1-year graft survival
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described. Authors simply mentioned that "one kidney was randomly assigned to CS or MP"
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias)	Low risk	5/76 recipients were lost to follow up but number were balanced among trial groups (3 in the MP group, 2 in the CS group)
Selective reporting (reporting bias)	Low risk	
Other bias	Unclear risk	Analysis does not account for the matching on donors

Kwiatkowski 2009

Methods	
Participants	37 brain death donors
Interventions	74 kidneys were randomized to CS or to MP (Waters MOX-100 perfused with MPS II)
Outcomes	Delayed graft function
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described, only mentioned in the abstract
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias)	Unclear risk	Not described
Incomplete outcome data (attrition bias)	Unclear risk	37 pairs of kidneys were randomized, but outcomes are reported in only 34 pairs. Reasons for missing data are not explained
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	Pairing of kidneys not accounted for at the analysis stage

Moers 2009

Methods	Multi-center randomized controlled trial (the Netherlands, Belgium, the federal state of Norht Rhine-Westphalia)
Participants	Organ donors had to be 16 years of age or older. Only kidney pairs from deceased donors were included in the study, either from donation after brain death or donation after cardiocirculatory death. The category for donors without a heartbeat had to be Maastricht category III (awaiting cardiocirculatory death after withdrawal of treatment) or IV (cardiocirculatory death in a brain-dead donor). 594 potential donors were enrolled and 543 were eventually randomized. Eventually, the main set of cases consisted of 336 kidney pairs (672 recipients), of which 42 (84 recipients) came from non-heart beating donors (DCD). The trial was extended to include 40 more DCD, and eventually comprised a total of 376 kidney pairs (752 recipients).
Interventions	From each donor, one kidney was randomly assigned to machine perfusion and the contralateral organ to cold storage. LifePort Kidney Transporter machines (Organ Recovery Systems) were used for perfusion, delivering a pulsatile flow of University of Wisconsin machine preservation solution (Kidney Preservation Solution-1) at 1 to 8°C, with no changes in perfusion settings throughout the preservation period. The systolic perfusion pressure was fixed at 30 mm Hg, and the kidneys underwent machine perfusion from organ procurement until transplantation. No changes were made to the standard cold-storage protocols. After an initial vascular washout, kidneys were

	submerged in the preservation solution and stored on melting ice, according to the established Eurotransplant routine.
Outcomes	The primary end point was delayed graft function (DGF), defined as the requirement for dialysis during the first week after transplantation. The secondary end points were: • the duration of delayed graft function • primary nonfunction (PNF; permanent lack of function of the allograft from the time of transplantation; added post-hoc) • the area under the curve of the daily serum creatinine level at days 1 to 14 • the creatinine clearance at day 14 • biopsy-proven acute rejection • toxicity of the calcineurin inhibitor • the length of the recipient's hospital stay • survival of the graft and patient up to 1 year after transplantation (data on graft survival were censored at the time of death in patients who died with a functioning allograft) and up to 3 years after transplantation (Moers 2012). • functional delayed graft function defined as the absence of a decrease in the serum creatinine level of at least 10% per day for at least 3 consecutive days in the first week after transplantation, not including patients in whom acute rejection, toxicity of the calcineurin inhibitor, or both developed within the first week).
Notes	• If one kidney was transplanted into the same recipient together with another organ, this kidney pair was excluded. Reason for this is not explained. • Recipients dying in the first week after transplantation were excluded, since a follow- up of at least 1 week was required to determine the primary end point. • The organ could be transplanted into any recipient within the Eurotransplant region. Kidneys that underwent machine perfusion as well as those that were preserved with cold storage were transported to their respective recipient centre without any monitoring. • Follow-up data were provided by each participating transplantation centre through a secure online database hosted by Eurotransplant. • Statistical analysis: The primary analysis of the primary end point — delayed graft function — consisted of a logistic-regression model. Covariates for this model were pre-specified: 1.Panel-reactive antibody level (%); 2.recipient age (yr); 3.donor age (yr);

	4.expanded criteria donor (defined as a donor age of 60 years or more or a donor age between 50 and 60 years, with at least two of the following additional donor characteristics: history of hypertension, death due to a cerebrovascular cause, and a serum creatinine level of more than 132 ìmol per liter (1.5 mg per deciliter) before removal of the kidney) vs. standard criteria donor; 5.cold ischemic time (h); 6.HLA mismatches (no.); 7.duration of pretransplantation dialysis (yr); 8.retransplantation vs. first transplantation; 9.non-heart beating donor vs. heart beating donor. The final model was determined by entering all covariates together in the analysis, with a built-in normal gamma frailty term for the donor to account for the paired study design. For end-point variables, univariate differences between the groups were assessed with the use of McNemar's test or the Wilcoxon signed-rank test. The Kaplan–Meier method was used to analyze graft and patient survival. Differences between survival curves were determined with the use of log-rank tests.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A randomization scheme based on permuted blocks within regions was used with separate randomization lists for each of the three trial regions. Randomization lists were available only to the 24-hour Eurotransplant duty desk. Upon report of a kidney donor, the allocation officer first checked its eligibility and then assigned the left kidney to treatment with either machine perfusion or cold storage following one of the three randomization schemes, which automatically assigned the right kidney to preservation with the other method. Then both kidneys were offered according to the match list, without revealing the preservation method. Only if the kidney assigned to be machine perfused had a too small aortic patch or too many renal arteries preventing a reliable connection to the machine perfusion device were surgical teams allowed to switch preservation methods during organ procurement, thus frustrating randomization.
Allocation concealment (selection bias)	Low risk	Randomization with permuted block organized at central level
Blinding of participants and personnel (performance bias)	Low risk	Blinding of surgeons was impossible, but blinding of recipients and medical staff is not reported. However, this is unlikely to have influenced performance on the hard outcomes (DGF, graft survival)

Blinding of outcome assessment (detection bias)	Unclear risk	Procedures not described. No report of blinding medical staff is reported. High variation in practice among sites is plausible. Authors report a procedure of quality control but provide little details and results ("A random sample of 10% of all patients was audited externally; no relevant irregularities were found.", p9). However, it is unclear how this could have affected the reporting of hard outcomes (DGF, graft survival).
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	a.The crude odds ratio of the primary outcome is not reported, only the one from the multivariate logistic regression model. If we compute the OR for the main outcome based on the data provided in table 1 (p13), we obtain OR=0.73 (95%CI: 0.51; 1.04; p=0.085) The RR=0.79 (95%: 0.59; 1.03; p=0.09). However, we cannot account for the matching of kidneys when extracting data from the paper b. Transplantation failure could have been an outcome (4 kidneys rejected by transplantation centre in the MP group vs. 10 kidneys rejected and 1 death within 1 week post-transplant in the CS group). But it was not listed in protocol.
Other bias	Unclear risk	a. No ITT analysis was performed whereas: - in 25 donors (7.0% of the 359 pairs of kidneys), preservation methods were switched because of the aberrant vascular anatomy of the kidney assigned to machine perfusion - in 4 additional cases (1.1% of the kidneys in the CS group), the surgical team insisted on using machine perfusion for both kidneys. - in 7 cases (1.95% of the kidneys in MP group), there was a technical failure of the machine perfusion. When machine perfusion failed, the kidney was automatically preserved by means of cold storage inside the machine. These 7 cases (and their contralateral kidneys) were excluded from analysis. b. The exclusion of donors from whom one kidney was discarded may have resulted in a "better kidney donors" bias. The exclusion of donors providing one or both kidneys plus another organ (n=80, distribution per study arm not reported) may have resulted in a "worse kidney donors" bias. These 2 biases, if they were true, would affect the external validity of the results, not their internal validity. No sensitivity analysis of discarding data when the contralateral kidney was excluded is provided. c. Two authors, including the last author (Rutger J. Ploeg) of the paper, had a patent on a portable preservation apparatus for donor organs. Study sponsors is Organ Recovery Systems Inc. (USA), the producer of the perfusion machine Lifeport

Watson 2010

Methods	
Participants	90 transplant recipients between August 2006 and October 2007 in 5 centres. Donors were DCD (Maastricht 3 category).
Interventions	Following certification of donor death a period of at least 5 min was observed with no intervention. Organ retrieval then proceeded with initial in situ cold perfusion of the kidneys using the University of Wisconsin (UW) cold storage solution (ViaSpan). After removal the kidney allocated to CS was immersed in UW solution and placed in crushed ice in an insulated transport box until implantation. The kidney allocated to MP was placed on the Organ Recovery Systems LifePort kidney preservation machine using kidney preservation solution 1 (KPS-1). The perfusion machines were preprogrammed to pulsatile perfusion mode, and set to flow at 30 mmHg pressure. The perfusion pressure setting was not adjusted during the preservation period, and data on resistance and flow were not used to determine whether or not a kidney should be used; all kidneys were subsequently transplanted. Where organ retrieval occurred away from the base transplant hospital the kidney randomized to MP could first undergo a period of CS during transport to the base hospital with MP being started immediately upon return.
Outcomes	The primary endpoint for the study was the incidence of DGF, defined as the requirement for dialysis in the first 7 days following transplantation. Secondary endpoints included primary nonfunction (defined as a graft that failed to provide 1-month dialysis-free survival excluding losses attributable to rejection or vascular thrombosis), and other measures of DGF, including creatinine reduction ratio calculated as either the change in creatinine from day 1 (the first day posttransplant) to day 2 (CCR2), or from immediately pretransplant (day 0) to day 5 (CCR5). Other secondary endpoints included the incidence of acute rejection (biopsy-proven), patient survival (the time from transplant to death) and graft survival (the time from transplant to graft loss or return to dialysis) and graft function (glomerular filtration rate and serum creatinine).
Notes	Cluster design not accounted for in analysis. ITT analysis.

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Upon notification of a potential DCD kidney donor at a participating centre, the Duty Office at NHS Blood and Transplant randomized the donor kidneys to one of the two treatments, CS or MP. Randomization also dictated which kidney (right or left) was allocated to MP, and which kidney of the pair was to be transplanted first. The randomization sequence was generated using simple randomization based on a sequence of computer-generated random number integers from 1 to 4."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias)	Low risk	"The medical staff involved in the decision regarding the need for dialysis were not aware of the kidney preservation method used"
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	Novartis Pharmaceuticals UK provided an unrestricted research grant and Organ Recovery Systems provided an unrestricted research grant in addition to discounting the costs of disposables used for MP. Neither company was involved in protocol development, study conduct, data analysis or writing and approval of the manuscript.

Jochmans 2010

Methods	Multi-centre randomized controlled trial (the Netherlands, Belgium, the federal state of North Rhine-Westphalia). Extension of the study by Moers 2009, with inclusion of 40 DCD donors
Participants	204 DCD donors were enrolled, and 155 were eventually randomized. Eventually the main set of cases consisted of 82 kidney pairs
Interventions	See study by Moers 2009
Outcomes	See study by Moers 2009
Notes	See study by Moers 2009

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	See study by Moers 2009
Allocation concealment (selection bias)	Low risk	See study by Moers 2009
Blinding of participants and personnel (performance bias)	Unclear risk	See study by Moers 2009
Blinding of outcome assessment (detection bias)	Unclear risk	See study by Moers 2009
Incomplete outcome data (attrition bias)	High risk	See study by Moers 2009
Selective reporting (reporting bias)	High risk	See study by Moers 2009
Other bias	High risk	See study by Moers 2009

Treckmann 2011

Methods	Multi-centre randomized controlled trial (the Netherlands, Belgium, the federal state of North Rhine-Westphalia). Subgroup of the study by Moers 2009
Participants	200 Extended Criteria Donors (ECD) were enrolled, and outcomes were eventually studied in 91 pairs of donors. ECDs were defined as donor age>=60 years or 50-60 years with at least two of the following criteria: history of hypertension, cerebrovascular cause of death and serum creatinine 132µmol/L
Interventions	See Moers 2009
Outcomes	See Moers 2009
Notes	See Moers 2009

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	See Moers 2009
Allocation concealment (selection bias)	Unclear risk	See Moers 2009
Blinding of participants and personnel (performance bias)	Unclear risk	See Moers 2009
Blinding of outcome assessment (detection bias)	Unclear risk	See Moers 2009
Incomplete outcome data (attrition bias)	High risk	The original study reported 94 pairs in the dataset (vs. 91 pairs in this subgroup analysis). Moreover, the primary outcome (DGF) was assessed over 71 recipients in the intervention group and over 64 in the control group. The authors did not explain this discrepancy in numbers of participants.
Selective reporting (reporting bias)	Unclear risk	See Moers 2009
Other bias	Unclear risk	See Moers 2009

Gallinat 2012

Methods	
Participants	85 deceased heart-beating donors>=65 years of age, 39 of whom were included in Moers 2009
Interventions	See Moers 2009
Outcomes	See Moers 2009
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	See Moers 2009
Allocation concealment (selection bias)	Low risk	See Moers 2009
Blinding of participants and personnel (performance bias)	Unclear risk	See Moers 2009
Blinding of outcome assessment (detection bias)	Unclear risk	See Moers 2009
Incomplete outcome data (attrition bias)	High risk	127 kidney pairs underwent randomization but analysis is performed on 85 pairs. 25 pairs were excluded because one or both kidneys were not transplantable but no description is provided on how a kidney was deemed not transplantable nor if the rejection occurs more often in one of the 2 intervention groups. The latter remark also holds for 7 additional excluded pairs for unknown reasons.
Selective reporting (reporting bias)	Low risk	
Other bias	Unclear risk	- No ITT analysis whereas in 3 donors (3.4%), preservation methods were switched because of the aberrant vascular anatomy of the kidney assigned to machine perfusion

Moers 2012

Methods	Follow-up of study by Moers 2009 up to 3 years post-transplant
Participants	See Moers 2009
Interventions	See Moers 2009
Outcomes	See Moers 2009
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	See Moers 2009
Allocation concealment (selection bias)	Unclear risk	See Moers 2009
Blinding of participants and personnel (performance bias)	Unclear risk	See Moers 2009
Blinding of outcome assessment (detection bias)	Unclear risk	See Moers 2009
Incomplete outcome data (attrition bias)	Unclear risk	See Moers 2009
Selective reporting (reporting bias)	Unclear risk	See Moers 2009
Other bias		

5. ECONOMIC DATA EXTRACTION TABLES

Gómez 2012

1	Reference (including all authors)	Gómez V, Galeano C, Diez V, Bueno C, Díaz F, Burgos F J; Economic impact of the introduction of machine perfusion preservation in a kidney transplantation program in the expanded donor era: cost-effectiveness assessment; Transplantation Proceedings 2012; 44:2521-2524
2	Conflict of interest and/or study funding	No reporting
3	Country	Spain
4	Study question	Is machine perfusion (MP) cost-effective when compared to CS in the preservation of kidneys coming from ECD?
5	Type of analysis (analytic technique)	Cost-effectiveness
6	Design	Probabilistic decision-tree
7	Population	Kidneys coming from ECD
8	Intervention	Machine perfusion (LifePort) + solution (KPS-1)
9	Comparator	Static cold storage with preservation fluids (UW)
10	Time horizon	Up to patient discharge from the hospital following transplantation
11	Discount rate	NA
12	Perspective	Hospital
13	Costs	
	Cost items included	Direct medical costs for: human resources consumed, hospital stays, dialysis, diagnostic tests (ie biopsy and graft nephrectomy in case of PMF), technical equipment (MP) and consumables
	Measurement of resource use	Hospital accounting unit made calculations based on DRGs and acquisition costs for the equipment
	Valuation of resource use	DRGs (prospective payments) for services and interventions and purchasing prices for material
	Data sources	Internal accounting records and hospital DRGs
	Currency and cost year	€ of 2010 converted to US$ by using an exchange rate of 0,713US$/ €

14	Outcomes	
	Endpoints taken into account and/or health states	Immediate graft function (IGF), delayed graft function (DGF) and primary non function (PNF)
	Valuation of health states	Effects measured as “episodes of DGF and PNF avoided”
	Treatment effect and Extrapolation	For MP taken from RCT (European Machine Preservation Trial) For CS, hospital own historical records Extrapolation not required given the time frame of the study
	Utility assessment (Quality of Life)	NA
	Data sources for outcomes	Published literature and own hospital records
15	Uncertainty	
	Scenario analysis	NA
	Sensitivity analysis	NA
16	Assumptions	LifePort assumed to work for 10 years Cost calculations performed assuming 40 transplants per year
17	Results	
	Cost-effectiveness and/or cost-utility (base case)	MP appears to be cost effective when compared to CS (avoided cases of DGF and PNF versus CS=5,1). Incremental costs of MP over CS=17180.
	Scenario analysis	NA
	Sensitivity analysis	NA
18	Conclusions	Acquiring MP technology would be cost effective in renal transplantation when kidneys come from ECD
19	Remarks	Uncertainty not taken into consideration Short term time horizon (graft or patient survival not taken into consideration) QoL not considered

Groen 2012

1	Reference (including all authors)	Groen H, Moers C, Smits J M et al Cost-effectiveness of hypothermic machine preservation versus static cold storage in renal transplantation; American Journal of Transplantation 2012, 12:1824-1830
2	Conflict of interest and/or study funding	No conflict of Interest
3	Country	Belgium, Germany and the Netherlands
4	Study question	Is machine preservation cost-effective in renal transplantation when compared to cold storage?
5	Type of analysis (analytic technique)	Cost-effectiveness and cost-utility
6	Design	Economic evaluation alongside clinical trial and Markov model (3 health states: functioning graft, graft failure and death; cycle length: 1 yr).
7	Population	336 kidney pairs from consecutive deceased donors (>16yrs) transplanted into two different recipients from the Eurotransplant regions, after randomization to MP to one kidney and CS to its pair. Donor types included DCD, DBD and ECD.
8	Intervention	Hypothermic pulsatile machine (LifePort) perfusion with the modified University of Wisconsin preservation solution
9	Comparator	Cold storage (following the protocols of Eurotransplant)
10	Time horizon	Short term study: 1 yr Long term Markov model: 10 yrs
11	Discount rate	4% for both costs and outcomes
12	Perspective	Hospital perspective
13	Costs	
	Cost items included	LOS, dialysis and cost of complications Costs of surgical transplantation and immunosuppressant therapy was excluded from the analysis
	Measurement of resource use	Costs applied to clinical data captured during the study. Treatment costs calculated based on unit costs multiplied by individual health care consumption data
	Valuation of resource use	Public prices and hospital costs
	Data sources	Hospital costs for short term analysis For Markov model extrapolations: study results, published literature and expert opinion

	Currency and cost year	2007$ (costs captured in € but transformed to $ using the mean exchange rate from January to November 2011=0,713 $/€)
14	Outcomes	
	Endpoints taken into account and/or health states	DGF, PNF, Graft and patient survival
	Valuation of health states	Probabilities taken from the short term trial, published literature and registries (Organ Procurement and Transplantation Network – OPTN).
	Treatment effect and Extrapolation	Markov model
	Utility assessment (Quality of Life)	Quality of Life taken from the published literature
	Data sources for outcomes	Clinical trial for short term data and literature to help extrapolating that data to a 10-yr time horizon by use of the Markov model
15	Uncertainty	
	Scenario analysis	NA
	Sensitivity analysis	One way and probabilistic sensitivity analyses
16	Assumptions	Annual depreciation for the technical equipment (machine)=20% For hospitalisation, if there was a missing value, assumed that no hospital readmission had taken place Assumptions based on clinical practice had to be made to complete data gaps regarding return to dialysis after graft failure.
17	Results	
	Cost-effectiveness and/or cost-utility (base case)	Short term: MP showed to dominate, being both less costly and more effective (more functioning grafts at lower cost at year 1) than CS. Results were even more favourable for ECD. Long-term results: The dominance of MP compared to CS is confirmed in the long-term model.
	Scenario analysis	NA
	Sensitivity analysis	Sensitivity testing showed a probability for MP to dominate of 86%. Important increases in the cost of MP disposables (organ cassette and preservation solution) could affect the short term cost-effectiveness results.

18	Conclusions	The use of MP in renal transplantation is likely to be cost-effective when compared to CS preservation with lower costs per life-year saved and lower costs per QALY
19	Remarks	First economic evaluation on this area performed alongside an RCT. Relatively high number of patients Some missing values – assumptions had to be made. No robust data available on long-term survival In the short-term analysis, the low number of graft failures does not allow for clear conclusions for the DCD population. Some sensitivity of results to high increases in the cost of disposables. Main results contradict a previous model for the DCD population (UK PPART study)

Bond 2009

1	Reference (including all authors)	Bond M, Pitt M, Akoh J et al. The effectiveness and cost-effectiveness of methods of storing donated kidneys from deceased donors: a systematic review and economic model; Health Technology Assessment 2009; 13(38):1-156
2	Conflict of interest and/or study funding	One of their investigators took part in the PPART study
3	Country	UK
4	Study question	Is Machine Perfusion cost-effective in the preservation of kidneys for transplantation when compared to static cold storage?
5	Type of analysis (analytic technique)	Cost-utility analysis
6	Design	Markov model
7	Population	Mixed-age group (18-34, 35-44, 45-54, 55-64, 65+) of end stage renal disease patients who received kidney transplantation
8	Intervention	Machine perfusion (LifePort)
9	Comparator	Cold storage with ViaSpan solution Cold storage with Marshall's Soltran solution
10	Time horizon	Lifetime
11	Discount rate	3,5% for both costs and outcomes (NICE guidelines)

12	Perspective	UK's NHS
13	Costs	
	Cost items included	Storage solutions Machine or containers Post-transplantation dialysis while inpatient (for DGF) Explantation operations (for PNF) Ongoing care for successful transplants (check-ups, immunosuppresants and treatment of acute rejection episodes) Ongoing care for failures (regular HD or PD, check-ups, pharma treatment for anaemia)
	Measurement of resource use	Taken from national registries (NHSBT and UKRR)
	Valuation of resource use	The machines, containers and solutions and drugs were valued at public prices (purchasing costs) Rest of costs represented by average NHS reference cost
	Data sources	National registries (NHSBT and UKRR) Purchasing prices: submissions to NICE for LifePort and cold storage containers/solutions Routine check-ups or cost of acute rejection including hospitalization: NHS reference costs Immunosuppressants: Drug Tariff
	Currency and cost year	GBP2007
14	Outcomes	
	Endpoints taken into account and/or health states	DGF PNF Graft survival Patient survival
	Treatment effect and Extrapolation	Graft and patient survival from trials, extrapolated by means of national registry data
	Utility assessment (Quality of Life)	QALYs
	Data sources for outcomes	Published literature complemented with expert opinion and registry data
	Uncertainty	

15	Scenario analysis	NA
	Sensitivity analysis	One-way and probabilistic sensitivity analyses performed
	Assumptions	PNF determined in the first cycle of the model All PNF patients have to go through an explant operation Graft survival not modelled as a function of age Patients who receive a second transplant (after initial graft failure) modeled as homogeneous group (aggregated costs and graft survival) No differentiation between DBD and DCD (no clear data available) Within each age group modelled patients are treated as homogeneous Other potentially interesting factors not modelled because of lack of data included CIT or the age of the donor Impact of complications during or after transplant not included
16	Results	
17	Cost-effectiveness and/or cost-utility (base case)	Contradicting results depending on data modeled (two separate trials in two different donor populations): • When the comparison of LifePort versus ViaSpan (using PPART study data - DCD): ViaSpan dominates • When the comparison of LifePort versus ViaSpan (using MPT study data – different types of donors but mainly SCD): LifePort dominates Comparison between LifePort and Marshall's Soltran solution showed that MP is both less costly and more effective (more QALYs).
	Scenario analysis	NA
	Sensitivity analysis	The sensitivity analysis performed on the comparison of LifePort versus ViaSpan using PPART data showed a 27% probability for LifePort to be cost-effective The sensitivity analysis performed on the comparison of LifePort versus ViaSpan using EMPT data showed a 78% probability for LifePort to provide a cost-effective alternative to cold storage. The sensitivity analysis performed on the comparison of LifePort versus Marshall's Soltran solution showed a 87% probability for LifePort to provide a cost-effective alternative to cold storage
	Conclusions	MP is an alternative to CS which could be considered in the preservation of kidneys prior to their transplantation
18	Remarks	Contradicting results for DCD depending on model/source of data chosen (PPART versus EMPT data) Uncertainty surrounding the parameters DGF and graft survival (lack of robust evidence)
19		

Garfield 2009

1	Reference (including all authors)	Garfield S S, Poret A W, Evans R W; The cost-effectiveness of organ preservation methods in renal transplantation: US projections based on Machine Preservation Trial; Transplantation Proceedings 2009; 41:3531-3536
2	Conflict of interest and/or study funding	Industry sponsored
3	Country	USA
4	Study question	Is Machine perfusion (MP) a cost-effective alternative to CS in the preservation of kidneys for renal transplantation?
5	Type of analysis (analytic technique)	Cost-utility
6	Design	Decision analytic model
7	Population	Organs from standard criteria donors (SCD) and extended criteria donors (ECD)
8	Intervention	Machine perfusion (Life-Port Kidney Transporter)
9	Comparator	CS
10	Time horizon	1-year
11	Discount rate	NA
12	Perspective	Health care system
13	Costs	
	Cost items included	Material and capital equipment acquisition costs, dialysis, hospitalization, transplant, follow-up costs for a year after transplantation
	Measurement of resource use	Based on reimbursement payments publicly available per transplant
	Valuation of resource use	Reimbursement rates for Medicare and Private payers
	Data sources	Published literature
	Currency and cost year	US$. Year not specified
14	Outcomes	
	Endpoints taken into account and/or health states	Success (functioning graft), failure (PNF) or delayed graft function (DGF)
	Valuation of health states	From European Machine Preservation Trial

	Treatment effect and Extrapolation	NA
	Utility assessment (Quality of Life)	Taken into consideration as follows: Utility score of 1 if graft is functioning after a year Utility score 0 if primary non function Utility of 0,5 if DGF
	Data sources for outcomes	European Machine preservation trial
15	Uncertainty	
	Scenario analysis	Best and worst case scenarios linked to clinical outcomes were tested (best and worst values taken from the published literature).
	Sensitivity analysis	Not clear what type of sensitivity analyses were performed
16	Assumptions	All patients suffering from a DGF or PNF require dialysis Graft failure has additional costs over those of dialysis Patients with functioning grafts incur in maintenance costs (eg immunosuppressant therapy) Short term dialysis costs are associated with DGF
17	Results	
	Cost-effectiveness and/or cost-utility (base case)	C/E ratios for CS: ECD=114,530US$; SCD=104,118US$ C/E ratios for MP: ECD=106,012US$; SCD=92,561US$
	Scenario analysis	Robust results
	Sensitivity analysis	Robust results. Most sensitive to assumptions regarding the standard acquisition costs for kidneys and the overall costs associated with transplants of kidneys coming from ECD.
18	Conclusions	MP is more cost-effective than CS in kidney preservation from both SCD and ECD
19	Remarks	Uncertainty not covered in detail. No quantitative reporting on the actual type of analysis performed or its results Costs included not specified in enough detail QoL assumptions highly simplified and not taken from published data or valid sources of information.

Wszola 2009

1	Reference (including all authors)	Wszola M, Kwiatkowski A, Latek M et al; Long term medical and economical benefit of machine perfusion (MP) kidney storage in comparison with cold storage (CS)
2	Conflict of interest and/or study funding	Not reported
3	Country	Poland
4	Study question	Is MP cost-effective when compared to CS in kidney transplantation?
5	Type of analysis (analytic technique)	Regression analysis
6	Design	Retrospective case review 1994-1999
7	Population	429 ESRD patients receiving transplants from 242 brain-dead deceased donors. 234 kidneys were stored using MP and 195 were stored with CS
8	Intervention	Machine Perfusion (MOX-100 perfusion system with MPS-II perfusion fluid and cassettes)
9	Comparator	Cold storage (CS)
10	Time horizon	5-10 years follow-up following transplantation
11	Discount rate	NA
12	Perspective	Hospital costs – based on the registry for just one centre
13	Costs	
	Cost items included	Short term : cost of MP, post-transplantation hemodialysis, cost of hospitalisation (including lab tests). Not included: Organ procurement, transportation, surgical and anesthetic procedures, episodes of acute rejection and their treatment; since these were considered to be similar for both arms.
	Measurement of resource use	Cumulative costs taken over the transplantation period and follow-up
	Valuation of resource use	NA
	Data sources	Not clearly explained
	Currency and cost year	US$
14	Outcomes	
	Endpoints taken into account	DGF, duration of DGF, mean number of hemodialysis post transplantation, LOS, incidence of acute rejection

	and/or health states	
	Valuation of health states	Not made explicit
	Treatment effect and Extrapolation	No extrapolation made. Data taken (probably) from a registry
	Utility assessment (Quality of Life)	NA
	Data sources for outcomes	Probably from a registry but not made explicit
15	Uncertainty	
	Scenario analysis	NA
	Sensitivity analysis	NA
16	Assumptions	None made explicit
17	Results	
	Cost-effectiveness and/or cost-utility (base case)	Long graft survival: 68% in MP versus 54% in CS group (p=0,02) Return to dialysis treatment 20% in MP versus 36% in the CS group (p=0,01) Cumulative costs per patient at year 5: US$43 787 with MP versus 46 484 for CS
	Scenario analysis	NA
	Sensitivity analysis	NA
18	Conclusions	Despite higher costs for MP versus CS in the first month post-transplantation, MP is cost saving in the long-term
19	Remarks	Kidneys not randomized Imbalances on baseline characteristics between groups Not clear whether (and for how long) the kidneys of the MP group were first preserved with CS Incremental cost-effectiveness ratios not calculated – Outcomes and costs savings presented separately

Buchanan 2008

1	Reference (including all authors)	Buchanan P M, Lentine K L, Burroughs T E et al; Association of lower costs of pulsatile machine perfusion in renal transplantation from expanded criteria donors; American Journal of Transplantation 2008; 8:2391=2401
2	Conflict of interest and/or study funding	No funding from the industry reported. Grants were received from the American Society of Transplantation
3	Country	USA
4	Study question	Is Machine Perfusion cost effective in ECD kidney transplants?
5	Type of analysis (analytic technique)	Cost and outcome evaluation
6	Design	Retrospective case review
7	Population	Adults ECD renal transplant recipients included in the USRDS registry from 1995-2004 with Medicare as their primary payer Patients with multiple organ transplants or recipients from previous transplants were excluded.
8	Intervention	Pulsatile MP
9	Comparator	Cold storage
10	Time horizon	3 years post transplant follow up
11	Discount rate	NA
12	Perspective	Third party payer
13	Costs	
	Cost items included	Any hospitalization costs related to transplantation over the study period
	Measurement of resource use	All costs taken as reimbursement claims
	Valuation of resource use	From DRGs
	Data sources	Medicare claims
	Currency and cost year	US$. Year not specified
14	Outcomes	
	Endpoints taken into account and/or health states	Secondary outcomes (cost taken as primary outcome): DGF, LOS for transplantation, creatinine levels at discharge, rejection (within 3 years post-transplant, Death censored

		graft failure, mortality.
	Valuation of health states	
	Treatment effect and Extrapolation	No extrapolation performed from the data. Follow-up registry data used for the analysis
	Utility assessment (Quality of Life)	NA
	Data sources for outcomes	Organ Procurement and Transplantation Network (OPTN) registry
15	Uncertainty	
	Scenario analysis	NA
	Sensitivity analysis	NA
16	Assumptions	Medicare was considered to be the primary payer in cases in which initial hospitalization costs for transplantation exceeded US$15000 and HCFA indicated Medicare as the primary payer for that transplant Cost data was censored at 3 yrs
17	Results	
	Cost-effectiveness and/or cost-utility (base case)	
	Scenario analysis	NA
	Sensitivity analysis	NA
18	Conclusions	MP provides immediate cost savings linked to hospitalisation for transplantation but it does not improve long-term outcomes or costs
19	Remarks	No consideration of uncertainty No calculations on incremental cost effectiveness ratios, costs analysed as an outcome separate from all others Retrospective review based on US registry data – weak generalizability Imbalances in baseline characteristics that may have affected the results, although adjustments were done.

Costa 2007

1	Reference (including all authors)	Costa V, McGregor M, Brophy J; Pulsatile machine perfusión compared to cold storage in kidney preservation ; Montreal: Technology Assessment Unit of the McGill University Health Centre (MUHC). Report #30. 2007
2	Conflict of interest and/or study funding	Not reported
3	Country	Canada
4	Study question	Is machine perfusion (MP) a cost-effective alternative to CS?
5	Type of analysis (analytic technique)	Cost-effectiveness
6	Design	Decision-analytic model
7	Population	Kidneys from DBD, DCD and ECD
8	Intervention	Machine perfusion
9	Comparator	Static cold storage
10	Time horizon	1 year
11	Discount rate	NA
12	Perspective	Hospital perspective
13	Costs	
	Cost items included	Equipment and disposable costs linked to MP or CS In-hospital resource consumption associated with DGF Excluded: physicians' fees
	Measurement of resource use	Unit costs from proposal for purchase of MP
	Valuation of resource use	From the literature and internal data information (Finance department of health centre)
	Data sources	Proposal for purchase of MP, published literature and finance department of the health centre
	Currency and cost year	2006 CAN$
14	Outcomes	
	Endpoints taken into account and/or health states	Delayed graft function (DGF)

	Valuation of health states	Not clearly explained
	Treatment effect and Extrapolation	For machine perfusion: taken for the short term from a meta analysis For CS: taken as the mean DGF observed in the hospital over the previous 5 years in transplantations from deceased donors in which CS was used as the preservation method
	Utility assessment (Quality of Life)	NA
	Data sources for outcomes	Own MA of published literature on DGF rates (17 studies included) and hospital records for CS
15	Uncertainty	
	Scenario analysis	One scenario including machine costs and one without them (since funding for the equipment could come from outside the institution)
	Sensitivity analysis	Probabilistic sensitivity analysis
16	Assumptions	Each machine used for 30 transplants/year
17	Results	
	Cost-effectiveness and/or cost-utility (base case)	MP dominates with savings over CS of $841 (95%CI $1406-$262) and a mean 0,059 DGF episodes avoided (95%CI: 0,0209; 0,0957)
	Scenario analysis	NA
	Sensitivity analysis	Robust results – PSA showed that 99.7% of simulations MP would be the dominant strategy
18	Conclusions	The available evidence appears to show that MP is likely to be cost-saving
19	Remarks	Time horizon limited to 1 year (long-term graft/patient survival not studied) QoL not included Conflicts of interest not well covered

Wight 2003

1	Reference (including all authors)	Wight J, Chilcott J, Holmes M, Brewer N; The clinical and cost-effectiveness of pulsatile machine perfusion versus cold storage of kidneys for transplantation retrieved from heart-beating donors and non-heart-beating donors Health Technology Assessment 2003; 7(25)
2	Conflict of interest and/or study funding	No conflicts of interest
3	Country	UK
4	Study question	Is machine perfusion cost-effective when compared to CS in kidney preservation for renal transplantation
5	Type of analysis (analytic technique)	Cost-utility analysis
6	Design	Decision analytic model
7	Population	Kidneys coming from both heart-beating-donors (HBD) and non-heart-beating-donors (NHBD)
8	Intervention	Machine perfusion (MP)
9	Comparator	Cold storage (CS). Solution not specified
10	Time horizon	10 years for long-term analysis
11	Discount rate	6% for costs and 1,5% for outcomes
12	Perspective	Health services perspective
13	Costs	
	Cost items included	Direct costs including: Graft loss, short-term costs of DGF and cost of MP system (purchasing costs for machine, disposables, maintenance and personnel)
	Measurement of resource use	From literature and public costing sources
	Valuation of resource use	Short term costs of DGF estimated from the marginal cost of DGF multiplied by the number of days with DGF Long-term graft loss: graft years gained multiplied by the annual marginal costs of graft loss
	Data sources	Dialysis costs from UK prospective diabetes study group Transplant maintenance costs from a Trent Institute Guidance note and the UK medicines information service. MP costs: based on the cost for RM3 in an international price list 2002 from Waters Corporation Number of transplants,
	Currency and cost year	GBP 2002

14	Outcomes	
	Endpoints taken into account and/or health states	QALYs based on graft survival. Graft survival derived from long-term impact of DGF on graft survival
	Valuation of health states	
	Treatment effect and Extrapolation	Inputs from the published literature (MA) taken and modeled
	Utility assessment (Quality of Life)	Scores: 0,84 for a functional transplant and 0,65 for dialysis after graft failure
	Data sources for outcomes	QoL scores taken from the published literature
15	Uncertainty	
	Scenario analysis	NA
	Sensitivity analysis	PSA separated for NHBD and HBD
16	Assumptions	Machine functioning for 5 years Number of transplants from hospital data
17	Results	
	Cost-effectiveness and/or cost-utility (base case)	MP dominates (both more effective and less costly than CS)
	Scenario analysis	NA
	Sensitivity analysis	MP dominates CS in 80% of simulations when kidneys are coming from NHBD and in 50-60% of the simulations when kidneys are coming from HBD
18	Conclusions	The analysis appears to show that MP could offer benefits both in terms of effectiveness and cost savings in kidney preservation prior to transplantation when compared to CS
19	Remarks	Model primarily based on observational data. Most recent RCT evidence not included in here since this was published before the CTs were completed and published Link between DGF and graft survival not clear DGF is a surrogate point of what they authors are truly trying to capture (graft loss). More evidence would be needed from CTs to truly validate the findings from this model and in particular the effect of MP on graft loss