# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Overview

## Machine perfusion systems and cold static storage of donated kidneys from deceased donors

The overview is written by members of the Institute's team of technical analysts. It forms part of the information received by the Appraisal Committee members before the first committee meeting. The overview summarises the evidence and views that have been submitted by consultees and evaluated by the Assessment Group, and highlights key issues and uncertainties. To allow sufficient time for the overview to be circulated to Appraisal Committee members before the meeting, it is prepared before the Institute receives consultees' comments on the assessment report. These comments are therefore not addressed in the overview.

A list of the sources of evidence used in the preparation of this document is given in appendix A.

# 1 Background

### *1.1 The condition*

End-stage renal disease, or established renal failure (ERF), is defined as an irreversible decline in kidney function that is severe enough to be fatal without renal replacement therapy.

The most common causes of chronic renal damage leading to ERF are diabetes mellitus, arteriosclerosis, hypertension, glomerulonephritis, and microscopic vasculitis. Acute renal failure from traumatic injury or infection may also lead to ERF. In children, it is usually caused by congenital structural abnormalities, but may be genetic or the result of glomerulonephritis.

People with ERF become tired and nauseated and lose their appetite, leading to weight loss. Pruritus may also be a problem. Signs of ERF include fluid retention, pallor and raised blood pressure, which are accompanied by lowered haemoglobin levels and abnormality of biochemical markers. ERF leads to death unless renal replacement therapy is provided.

In the UK in 2005 there were 41,776 adults and 748 children (younger than 18 years) on renal replacement therapy. This is a 28% increase in patient numbers since 2000. In 2005, the median age in the UK at which people started renal replacement therapy was 65 years. Survival in the first year after starting renal replacement therapy was 79%. Five-year survival rates vary depending on age. 58% of people aged 18–34 years are alive 5 years after starting renal replacement therapy. This figure falls to 12% in people aged 75 years or older.

## *1.2 Current management*

End-stage kidney disease is managed with renal replacement therapy, either through haemodialysis, peritoneal dialysis or kidney transplantation. Kidney transplantation is the preferred therapeutic option where it is possible.

Haemodialysis and peritoneal dialysis are methods of removing waste products from the body. In haemodialysis the person is connected to a dialysis machine containing a semi-permeable membrane. Their blood is passed into the machine and excess salts and fluid in the blood pass across the semipermeable membrane into the dialysis fluid. The waste products are retained in the dialysis fluid. People may attend specialist centres three times a week for 3 or 4 hours each session.

Peritoneal dialysis uses the person's peritoneal membrane as the semipermeable membrane for removal of waste products. A fluid is run into the peritoneal cavity, left there for a time and then drained out. Peritoneal dialysis may be preferred because it can take place at home, either continuously during the day with the fluid being exchanged four times a day (continuous ambulatory peritoneal dialysis) or overnight, using a machine to automatically change the fluid (automated peritoneal dialysis). Dialysis is time consuming and has a significant effect on quality of life. Medication is required to prevent bone and heart diseases and anaemia.

Kidney transplantation involves implanting a kidney from a donor into the person with ERF. Kidneys for transplantation may come from living donors

(not included in the appraisal) or deceased organ donors. Deceased organ donors may be certified as dead either by brain-stem criteria (deceased heart-beating donors or donation after brain death) or after cardiac arrest (non-heart-beating donors or donation after cardiac death). Kidneys from deceased heart-beating donors have blood flowing to the kidneys up to the point of retrieval. Kidneys from non-heart-beating donors have no blood flowing from the time of cardiac arrest to the time of retrieval. The availability of kidneys from deceased heart-beating donors has decreased by approximately 20% in the last decade, possibly because of a reduction in fatal road traffic accidents and deaths from intracranial haemorrhage. Kidneys from deceased heart-beating donors are allocated nationally; kidneys from non-heart beating donors are allocated only locally.

Kidneys from non-heart-beating donors are categorised according to the Maastricht criteria, and described as controlled (where cardiac death is expected) or uncontrolled (where cardiac death is unexpected). Kidneys from non-heart-beating donors (particularly uncontrolled) may have long periods of warm ischaemic time, that is, the time that the organ spends deprived of oxygen before it is retrieved and cooled. (In some cases a cannula can be placed for perfusion and cooling of the organs before retrieval.) As a result, kidneys from non-heart-beating donors can have higher rates of delayed graft function (the graft does not function immediately) or primary non-function (the graft never functions) than those from heart-beating donors. Kidneys are also affected by cold ischaemic time (the duration of storage in cold conditions between retrieval and transplantation), but cooling the organ reduces the metabolic rate and thereby decreases the rate of damage compared with warm ischaemia.

As well as using kidneys from non-heart-beating donors, to expand the donor pool kidneys from “extended criteria” deceased heart-beating donors may also be used. These are kidneys from donors who are aged over 60 years, or are over 50 years and have two or more of:

- a history of hypertension
- a history of cerebral vascular accident
- terminal creatinine levels greater than 133 micromoles/litre.

Like kidneys from non-heart-beating donors, those from extended criteria donors are also associated with higher levels of delayed graft function and primary non-function than those from non-extended criteria donors.

Successful transplantation removes the need for dialysis, but ongoing medication with immunosuppressant drugs is necessary to prevent rejection of the graft. Complications of immunosuppression include increased risk of infections and an increased risk of malignancy, especially skin cancer and lymphoproliferative disorders. Nephrotoxicity is a particular complication of some immunosuppressive regimens. Post-transplant diabetes mellitus is a potentially serious side-effect of treatment. Other treatment side-effects, depending on the drugs used, may include hirsutism, alopecia, tremors, mood swings or gastrointestinal intolerance.

In 2005, 76% of people accepted for renal replacement therapy started treatment with haemodialysis, and 21% started treatment with peritoneal dialysis. Only 3% of patients received a kidney transplant before they started dialysis. There is increasing demand for kidney transplants, and the waiting list has increased by 48% since 1998. The demand for kidneys currently outstrips the supply. In 2006 1440 kidneys were transplanted (from 765 kidney donors), and 6480 people were on the waiting list. Therefore, there is a need to increase kidney donation and to make those kidneys that are donated function in the best possible way.

# 2 The technologies

It is necessary to preserve kidneys before transplantation to allow time for matching the kidney to the recipient, for transportation and preparation of the recipient and kidney, and for implantation of the kidney. It is important that the kidney is cooled and prepared as quickly as possible to minimise any damage caused by warm ischaemia. There are two established methods of preservation: cold static storage and hypothermic machine perfusion.

**Table 1 Summary description of technologies**

| | | |
|---|---|---|
| **Perfusion systems** | | |
| Name | RM3 renal preservation system | LifePort kidney transporter |
| Manufacturer | Waters Medical Systems | Organ Recovery Systems |
| List price | Unknown | £10,700 per machine[a] |
| **Storage solutions** | | |
| Non-proprietary name | Belzer University of Wisconsin | Marshall's hypertonic citrate |
| Proprietary name | Viaspan | Soltran |
| Manufacturer | Bristol-Myers Squibb | Baxter Healthcare |
| List price | £116[b] for a 1 litre bag | £9.60 for a 1 litre bag |
| [a]machines are usually purchased in pairs (one for each kidney)<br>[b]sold in packs of six 1-litre bags for £696 | | |

### Cold static storage solutions

In cold static storage, the kidney is flushed through with a sterile non-pyrogenic preservation solution after retrieval and kept on ice in a box before transplantation. The assessment report states that approximately 2 litres of preservation solution are used for each kidney. Two preservation solutions are widely used in the NHS for cold storage: Marshall's hypertonic citrate and Belzer University of Wisconsin (Belzer UW). The submission from the British Transplant Society indicates that in the UK from 2000 to 2007 approximately 74% of kidneys from deceased donors were preserved using Marshall's hypertonic citrate solution and most of the remainder with Belzer UW storage solution (23%). For the subset of kidneys from non-heart-beating donors, 48%

were preserved using Marshall's hypertonic citrate solution and 42% with Belzer UW solution.

Marshall's hypertonic citrate solution is categorised as a medicine in the UK and has a marketing authorisation for use in the preservation of the human kidney before transplantation. The submission from the British Transplant Society notes that if organs are perfused in the donor before removal the same solution will perfuse the kidneys, liver, pancreas and intestine. When organs other than the kidneys are being harvested, Marshall's solution is not suitable because it is not considered to be safe for the extended preservation of liver, pancreas or intestine. However, the summary of product characteristics includes indications for the preservation of liver and pancreas.

The manufacturer of Belzer UW storage solution was advised by the Medicines and Healthcare products Regulatory Agency that the product was neither a device nor a medicine and therefore medical devices and medicines legislation does not apply. It does not require a marketing authorisation or CE mark in the UK. The solution does have a marketing authorisation in some European Union markets and is indicated for the preservation of kidney, liver and pancreas. It is not recommended for continuous machine perfusion.

**Machine perfusion systems**

Machine perfusion systems continuously pump cold preservation solution through the kidney. The solution provides nutrients, sometimes provides oxygen, carries away toxic metabolites and buffers the build up of lactic acid. Machine perfusion requires dissection of the artery to attach the kidney to the machine and further dissection of the kidney to make the seal watertight. This preparation process takes longer than cold static storage, but may encourage assessment of the kidney for abnormalities.

The LifePort kidney transporter is a portable machine perfusion system which can perfuse a single kidney and can run without being overseen. The system requires a solution to perfuse the kidney; Belzer UW machine preservation solution (KPS-1) is manufactured by Organ Recovery Systems for use with

the LifePort kidney transporter. The LifePort kidney transporter is CE marked for the continuous hypothermic machine perfusion of kidneys for the preservation, transportation, and eventual transplantation into a recipient.

The RM3 renal preservation system is a non-portable system that can perfuse two kidneys simultaneously under supervision. It is CE marked for the hyperthermic pulsatile perfusion of kidneys. No further information is available.

Of 21 kidney transplant centres in England and Wales, eight use LifePort kidney transporters in addition to cold static storage. These are centres with non-heart-beating donor programmes. The RM3 is not used in any centres in the UK. The submission from the British Transplant Society indicates that in the UK from 2000-2007 approximately 2% of kidneys from deceased donors were stored using machine perfusion (excluding cases where the method of storage was not reported). For the subset of kidneys from non-heart-beating donors 20% of kidneys were stored using machine perfusion (excluding cases where method of storage was not reported). However, the data for the subset might not be accurate since only 50% of records for kidneys from non-heart-beating donors included information on how the kidney was stored.

The use of portable machine perfusion is limited by current transplant arrangements that mean that the devices are the property of individual NHS trusts and have to be returned once transportation of the kidney is complete to the transplant centre that owns the machine. For logistical reasons, this means that they are only used in the local transplant region. Their use solely in the local transplant region is not compatible with the national allocation of kidneys from deceased heart-beating donors. Therefore, they are used mainly to preserve kidneys from non-heart-beating donors. A recent report from the Department of Health's Organ Donation Taskforce has indicated that in future arrangements may less regionally based.

# 3 The evidence

## *3.1 Clinical effectiveness*

The Assessment Group identified studies that compared different methods of kidney storage. They identified 11 studies. Five were randomised controlled trials (RCTs; two ongoing), one was a cohort study and five were retrospective record reviews (two published only as abstracts or posters). Four of these studies (three RCTs, and one retrospective review) compared Belzer UW storage solution with Celsior, a storage solution in development and not included in the appraisal. These four studies are excluded from the summary in this overview. The outcomes reported in this overview are rates of primary non-function, delayed graft function, graft survival and patient survival.

### 3.1.1 RM3 renal preservation system compared with LifePort kidney transporter

Two retrospective record reviews reported as abstracts or posters compared the two machine preservation systems. One study (n = 744 kidneys transplanted) was a review over a 5-year period that included a change in practice from the use of the RM3 renal preservation system to the LifePort kidney transporter. The kidneys included in this study were from extended criteria deceased heart-beating donors (78%) or non-heart-beating donors (22%). The second study (n = 89 kidneys transplanted) reviewed transplant records over a 22-month period and included kidneys mainly from deceased heart-beating donors (98%). Reporting in both studies was insufficient to do a thorough assessment of quality. The relative risks reported below were calculated by the Assessment Group. They differ in some cases from those reported in the study.

Results of the larger study are summarised in table 2. The smaller study reported graft survival. At 30 days graft survival was 97% and 94% in the RM3 and LifePort groups, respectively (relative risk [RR] 0.97, 95% confidence interval [CI] 0.89 to 1.06, p = non significant [ns]), and at 90 days 97% and 90% (RR 0.93, 95% CI 0.83 to 1.04, p = ns).

**Table 2 Clinical effectiveness results: RM3 compared with LifePort**

| | RM3 (%) | LifePort (%) | Relative risk | p value |
|---|---|---|---|---|
| Primary non-function | 3 | 2 | 1.44 (95% CI 0.59 to 3.54) | ns |
| Delayed graft function | 24 | 32 | 0.76 (95% CI 0.62 to 0.94) | 0.01 |
| Patient survival (1 year) | 97 | 93 | 1.05 (95% CI 1.01 to1.08) | 0.01 |
| Graft survival (1 year) | 97 | 93 | 1.05 (95% CI 1.01 to 1.08) | 0.01 |

### 3.1.2 Belzer UW storage solution compared with the Lifeport kidney transporter

Two ongoing RCTs and one retrospective record review compared Belzer UW storage solution with the LifePort kidney transporter. One RCT, (the Machine Preservation Trial (MPT) study; n = [redacted] kidneys retrieved) included kidneys from both deceased heart-beating ([redacted]%) and non-heart-beating donors ([redacted]%). The other (the PPART study; n = [redacted] kidneys retrieved) included kidneys from non-heart-beating donors. The primary outcome in both RCTs was rate of delayed graft function. The RCTs were considered to be of good quality, but the results of the smaller RCT may have been [redacted]. The record review (n = 36 kidneys transplanted) included kidneys from non-heart-beating donors. The primary outcome for this study was immediate graft function.

For the larger RCT (MPT) the overview presents the statistical analysis completed by the manufacturer after receipt of the manufacturer's submission using a two-tailed significance test. One-tailed significance tests were included in the manufacturer's submission. Six-month results for the MPT study are shown in table 3. Results for 12 months were also reported for patient survival and graft survival. The results for 12-month graft survival were [redacted] in the LifePort and Belzer UW groups, respectively (hazard ratio for

graft loss [redacted] The results for patient survival were [redacted]).

**Table 3 Clinical effectiveness results at 6 months: the MPT study**

| | LifePort (%) | Belzer UW (%) | Relative risk | p value |
|---|---|---|---|---|
| Primary non-function | [redacted] | [redacted] | Not reported | [redacted] |
| Delayed graft function | [redacted] | [redacted] | Not reported | [redacted] |
| Patient survival | [redacted] | [redacted] | [redacted] | [redacted] |
| Graft survival | [redacted] | [redacted] | Hazard ratio for graft loss [redacted] | [redacted] |

The smaller RCT (PPART) reported no statistically significant differences between Belzer UW storage solution and the LifePort kidney transporter. The 3-month results are reported in table 4.

**Table 4 Clinical effectiveness results at 3 months: the PPART study**

| | LifePort (%) | Belzer UW (%) | Relative risk | p value |
|---|---|---|---|---|
| Primary non-function | 2 | 0 | 3.00 (95% CI 0.13 to 71.74) | ns |
| Delayed graft function | 58 | 56 | 1.04 (95% CI 0.73 to 1.49) | ns |
| Patient survival | 98 | 100 | 0.98 (95% CI 0.92 to 1.04) | ns |
| Graft survival | 96 | 100 | 0.96 (95% CI 0.89 to 1.03) | ns |

The retrospective record review reported statistically significant results favouring the use of the LifePort kidney transporter in comparison with Belzer UW solution. Delayed graft function is reported as 28% and 89% in the LifePort and Belzer UW solution groups, respectively (RR 0.31, 95% CI 0.15 to 0.67, $p < 0.001$).

### 3.1.3 Marshall's hypertonic citrate compared with LifePort kidney transporter

One sequential cohort study (n = 60 kidneys transplanted) compared Marshall's hypertonic citrate with the LifePort kidney transporter. This study included kidneys from non-heart-beating donors, where death was controlled. All kidneys were stored using the solution for the first 2 years of the study, after when they were stored using the perfusion machine. The results are reported in table 5. The data given for both patient and graft survival were the same. The significance tests reported are those calculated by the Assessment Group.

**Table 5 Clinical effectiveness results: LifePort compared with Marshall's**

| | LifePort (%) | Marshalls (%) | Relative risk | p value |
|---|---|---|---|---|
| Primary non-function | 0 | 0 | NA | NA |
| Delayed graft function | 53 | 87 | 0.64 (95% CI 0.43 to 0.93) | 0.012 |
| Patient/Graft survival (1yr) | 100 | 93 | 1.07 (95% CI 0.96 to 1.20) | ns |
| Patient/Graft survival (2yr) | 97 | 90 | 1.07 (95% CI 0.94 to 1.23) | ns |

### 3.1.4 Belzer UW storage solution compared with Marshall's cold storage solution

One retrospective record review of kidneys from deceased donors (n = 58,607 kidneys transplanted) included in the US Collaborative Transplant Study database included data for kidneys stored using either Belzer UW storage solution (n = 53,560) or Marshall's cold storage solution (n = 5047). This study specifically considers differences in graft survival of kidneys that had been subject to different lengths of cold ischaemia. The analyses and significance tests reported below were completed by the Assessment Group.

The analyses by the Assessment Group show no statistically significant differences between the two solutions. Three-year graft survival among kidneys that had been exposed to 0-18 hours of ischaemic time was 81% and

80% in the Belzer UW and Marshall's storage solution groups, respectively (RR 1.02, 95% CI 0.10 to 1.04, p = ns). Comparable results are reported for cold ischaemic time greater than 36 hours: 75% and 73% in the Belzer UW and Marshall's storage solution groups respectively (RR 1.03, 95% CI 0.96 to 1.11, p = ns). Overall, the data suggest that the incidence of graft failure increases as cold ischaemic time increases, but that this incidence does not differ between the solutions.

### 3.1.5 Summary

Two retrospective reviews comparing the two machine perfusions systems favour the use of the RM3 renal preservation system. However, the differences reach statistical significance in only one study. Both studies may be subject to confounding. Analyses comparing the two cold storage solutions based on data from a retrospective review identified no statistically significant differences between solutions across a range of cold ischaemic times. No studies compared the use of the RM3 renal preservation system with Marshall's cold storage solution.

One sequential cohort study compared the use of the LifePort kidney transporter with Marshall's hypertonic citrate solution. This study reported statistically significant results favouring the use of the LifePort kidney transporter for delayed graft function but not for patient or graft survival.

Three studies compared the LifePort kidney transporter with Belzer UW storage solution. Two of the studies were RCTs, one including kidneys from non-heart-beating donors and one including kidneys from mainly deceased heart-beating donors. The former reported no statistically significant differences, while the latter reported results [redacted]. A third retrospective analysis reported a large statistically significant difference favouring the use of the LifePort kidney transporter for the endpoint of delayed graft function. However, the Assessment Group noted that differences in group characteristics, duration of

cold ischaemia and the potential for bias due to the lack of randomisation mean that the results of this study must be interpreted with great caution.

## *3.2 Cost effectiveness*

The manufacturers of the technologies did not submit economic analyses. The Assessment Group identified two published economic analyses, one from the UK and another from Canada, both using a healthcare system perspective. The UK study reported cost per quality-adjusted life year (QALY), while the Canadian study reported cost per delayed graft function event avoided. Both studies reported that machine perfusion was associated with lower costs and greater benefits than cold static storage. Probabilistic sensitivity analysis in the Canadian study suggested that machine perfusion dominated cold static storage in 99% of simulations. In the UK study kidneys were assessed according to whether they were from deceased heart-beating or non-heart-beating donors. The study reported that machine perfusion dominated cold static storage in 50-60% and 80% of probabilistic sensitivity analysis simulations for kidneys from deceased heart-beating and non-heart-beating donors, respectively. Both economic analyses were completed before the most recent RCT data from the PPART and MPT studies becoming available.

The Assessment Group developed an economic model that made three comparisons.

(1) LifePort machine perfusion was compared with Belzer UW storage solution. This comparison was completed in two different populations: kidneys from non-heart-beating donors using data from the PPART study and kidneys from mainly deceased heart-beating donors ([redacted]) using data from the MPT study.

(2) LifePort machine perfusion was compared with Marshall's hypertonic citrate solution using data from a cohort study.

(3) Belzer UW solution was compared with Marshall's hypertonic citrate using data from a retrospective record review.

The Assessment Group was unable to do any cost-effectiveness analyses that included the RM3 machine perfusion system because cost data, although requested, were not made available.

The model was a Markov state transition model that included the health states immediate graft function, delayed graft function, transplant failure, explantation and a return to dialysis, and subsequent transplant. The characteristics of the cohort modelled were chosen to be consistent with data obtained from the UK transplant and renal registry. The cohort was followed up until almost all (97%) had died. The Assessment Group developed a standard data set for use in the model which was modified to reflect the comparisons described above.

Cost data for machine perfusion were annualised and it was assumed that perfusion machines were used for 10 years with no resale value afterwards. The estimated number of kidneys stored by each machine each year was calculated based on the total number of transplantations per year divided by the number of transplant centres. It was estimated that each machine stored 61 kidneys (in the analyses using data from the MPT study) and 16 kidneys (in the analyses using data from the PPART study) per year. The costs for machine perfusion also included an annual maintenance contract and the costs of the perfusion kit and solution used in the machine. This resulted in a cost per kidney stored of £544 for the analyses using data from MPT and £737 for the analyses using data from PPART. The costs of storing a kidney using cold static storage included the costs of the solution and the box required to store the kidney. This was calculated to be £262.53 per kidney with Belzer UW solution and £49.73 per kidney with Marshall's solution.

Utility data were derived from published literature. The utility of living with a transplant varied according to age and was 0.83 for people aged 18 to 34 reducing to 0.66 for people aged over 65. The utility decrement of living with dialysis was 0.12. Therefore, a person aged 18 to 34 on dialysis had a utility of 0.71 and a person aged over 65 had a utility of 0.54. Renal registry data

were used to model patient survival while on dialysis and with a transplant, this was also varied according to age.

### 3.2.1 LifePort compared with Belzer UW storage solution – non-heart-beating donors

Data for delayed graft function, primary non-function and graft survival from the PPART study were used to model the cost effectiveness of LifePort compared with Belzer UW storage solution (shown in table 4). Because only 3-month data were available from the PPART study 5-year graft survival data from UK transplants were used to estimate survival curves.

**Table 6 Estimates of cost effectiveness: LifePort compared with Belzer UW using PPART study data**

| | Discounted costs (£) | Discounted QALYs | ICER |
|---|---|---|---|
| Belzer UW storage solution | 139,205 | 9.19 | |
| LifePort | 141,319 | 9.13 | Was dominated |
| differences | 2114 | -0.066 | |

The results of the deterministic analyses are shown in table 6. One-way sensitivity analyses suggested that differential delayed graft function and graft survival rates between the two groups had the greatest impact on the net benefit outputs. Probabilistic sensitivity analyses predicted that over a range (£0-£100,000) of willingness to pay levels the probability of LifePort being cost effective was approximately 40%.

### 3.2.2 LifePort compared with Belzer UW storage solution – deceased heart-beating and non-heart-beating donors

Data for delayed graft function, primary non-function and graft survival from the MPT study were used to model the cost effectiveness of LifePort compared with Belzer UW storage solution (described in table 3). Because only 1-year data were available from the MPT study, 5-year graft survival data from UK transplants were used to extrapolate beyond the 1-year data.

**Table 7 Estimates of cost effectiveness LifePort compared with Belzer UW solution using MPT study data**

| | Discounted costs (£) | Discounted QALYs | ICER |
|---|---|---|---|
| Belzer UW solution | 142,805 | 9.58 | Was dominated |
| LifePort | 139,100 | 9.79 | |
| differences | -3,695 | 0.218 | |

The results of the deterministic analyses are shown in table 7. One-way sensitivity analyses suggested that differential effectiveness levels and dialysis costs had the greatest impact on the net benefit outputs. The Assessment Report notes that the sensitivity to dialysis costs is because the differential effectiveness levels lead to dialysis cost savings being a major factor in the incremental cost, which in turn affects net benefit. Probabilistic sensitivity analyses predicted that over a range (£0-£100,000) of willingness to pay levels the probability of LifePort being cost effective was 80%.

### 3.2.3 LifePort compared with Marshall's hypertonic citrate – non-heart-beating donors (controlled)

Data for delayed graft function, primary non-function and graft survival from a cohort study (described in section 3.1.3) were used to model the cost effectiveness of LifePort compared with Marshall's hypertonic citrate. Because only 2-year data were available, 5-year graft survival data from UK transplants were used to extrapolate beyond the 2-year data.

**Table 8 Estimates of cost effectiveness: LifePort compared with Marshall's hypertonic citrate**

| | Discounted costs (£) | Discounted QALYs | ICER |
|---|---|---|---|
| Marshall's hypertonic citrate solution | 144,332 | 8.55 | Was dominated |
| LifePort | 132,953 | 9.54 | |
| differences | -11,379 | 0.993 | |

The results of the deterministic analyses are shown in table 8. One-way sensitivity analyses suggested that differential effectiveness levels and

dialysis costs had the greatest impact on the net benefit outputs. This is explained by the high levels of delayed graft function reported in this study meaning that differential graft failure after delayed graft function has a strong impact on the net benefit output. Probabilistic sensitivity analyses predicted that over a range (£0-£100,000) of willingness to pay levels the probability of LifePort being cost effective was 95%.

### 3.2.4 Marshall's hypertonic citrate in comparison with Belzer UW storage solution – deceased donors

Data for graft survival from a retrospective record review (described in section 3.1.4) were used to model the cost effectiveness of Marshall's hypertonic citrate compared with Belzer UW storage solution. This study analysed kidneys by the length of cold ischaemic time. The cost-effectiveness analyses are based on kidneys that endured 19-24 hours of cold ischaemic time. For these kidneys graft survival at 3 years was reported as 79.5% and 77.7% in the Belzer UW and Marshall's hypertonic citrate solution groups, respectively.

**Table 9 Estimates of cost effectiveness: Marshall's hypertonic citrate compared with Belzer UW solution**

| | Discounted costs (£) | Discounted QALYs | ICER |
|---|---|---|---|
| Belzer UW solution | 151,001 | 8.62 | |
| Marshall's storage solution | 151,826 | 8.57 | Was dominated |
| differences | 825 | -0.049 | |

The results of the deterministic analyses are shown in table 9. One-way sensitivity analyses suggested that differential graft failure rate for patients in the model who experienced immediate graft function had the greatest impact on the net benefit outputs. Probabilistic sensitivity analyses predicted that over a range (£0-£100,000) of willingness to pay levels the probability of Marshall's storage solution being cost effective was 40%.

# 4 Issues for consideration

The RM3 renal preservation system is included in the scope of the appraisal, but it was not possible to include it in the cost-effectiveness analyses. It is also a non-portable system and therefore is not used for kidney transportation.

If organs are perfused in the donor before removal the same solution will perfuse the kidneys, liver, pancreas and intestine. Although the summary of product characteristics for Marshall's hypertonic citrate solution includes indications for the preservation of liver and pancreas. The submission from the British Transplant Society noted that in this situation the use of Marshall's solution is not suitable because the solution is not considered to be safe for the extended preservation of liver, pancreas or intestine.

The Assessment Report notes that definitive data that showed an advantage in graft survival of one kidney storage method compared with another would provide clear evidence for choosing that method as the most cost-effective option. Given the uncertainties that the Assessment Group identified in the available clinical effectiveness evidence, is it possible to distinguish between methods of kidney storage on the basis of clinical and cost effectiveness?

The scope for this appraisal includes kidneys from deceased heart-beating and non-heart-beating donors. Specific consideration is also given to extended criteria heart-beating donors and kidneys from controlled and uncontrolled non-heart-beating donors. Does the Committee consider that it is able to distinguish between different methods of kidney storage for kidneys from different types of donors?

In the UK, kidneys from deceased heart-beating donors are allocated on a national basis, but ownership of machine perfusion systems is local. Logistical issues around returning machines to transplant centres militate against the use of machines for transporting kidneys from deceased heart-beating donors. The clinical trial data from MPT is based mainly on kidneys from deceased heart beating donors, and the cost-effectiveness analyses using MPT data are

based on the use of the machines to preserve this type of kidney. Given current UK methods for transplant allocation, if machine perfusion were considered cost effective, would it be possible to implement the use of the machines for national allocation of kidneys from deceased heart-beating donors?

The costs of machine perfusion and results of the cost-effectiveness analyses are dependent on the number of kidneys per year that each machine perfuses. The number of kidneys perfused by a single machine will be dependent on machines being ready in the correct location as kidneys become available.

Kidney perfusion systems may facilitate testing for viability of organs before transplant. This is not included in the cost-effectiveness analyses.

# 5 Ongoing research

The PPART trial is ongoing with follow-up planned over a 5-year period. The PPART trial is also collecting resource data. Economic analyses are planned as part of the MPT trial but these have not yet been completed.

# 6 Authors

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# Appendix A: Sources of evidence considered in the preparation of the overview

A The assessment report for this appraisal was prepared by Penninsula Technology Assessment Group.

- Bond M, Pitt M, Akoh J et al. The effectiveness and cost effectiveness of methods of storing donaed kidneys from deceased donors; a systematic review and economic model (June 2008).

B Submissions or statements from the following organisations:

I Manufacturer/sponsor

- Organ Recovery Systems
- Bristol Myers Squibb

II Professional/specialist, patient/carer and other groups:

- British Transplant Society
- Royal College of Nursing