NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

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

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)

Definitions:

Consultees – Organisations that accept an invitation to participate in the appraisal including the manufacturer or sponsor of the technology, national professional organisations, national patient organisations, the Department of Health and the Welsh Assembly Government and relevant NHS organisations in England. Consultee organisations are invited to submit evidence and/or statements and respond to consultations. They are also have right to appeal against the Final Appraisal Determination (FAD). Consultee organisations representing patient/carers and professionals can nominate clinical specialists and patient experts to present their personal views to the Appraisal Committee. Where clinical specialists and patient experts make comments on the ACD separately from the organisations that nominated them, these are presented alongside the consultee comments in the tables below.

Commentators – Organisations that engage in the appraisal process but that are not asked to prepare an evidence submission or statement. They are invited to respond to consultations but, unlike consultees, they do not have the right of appeal against the FAD. These organisations include manufacturers of comparator technologies, NHS Quality Improvement Scotland, the relevant National Collaborating Centre (a group commissioned by the Institute to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups (for example, the NHS Confederation, NHS Information Authority and NHS Purchasing and Supplies Agency, and the *British National Formulary*).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but may be summarised by the Institute secretariat – for example when many letters, emails and web site comments are received and recurring themes can be identified.

Comments received from consultees

Consultee	Comment	Response
Organ recovery systems	Thank you for the opportunity to provide comments on the Appraisal Consultation Document (ACD) for the above appraisal. Organ Recovery Systems is supportive of the recommendations contained within the ACD. In particular we are encouraged by the decision to recommend both cold storage and machine perfusion options while directing 'The choice of storage method should take into account clinical and logistical factors within both the retrieval teams and transplant centres'. While we consider that all the currently available and relevant information has been taken into account we have the following clarification points	Comments noted, see responses below.
Organ recovery systems	Section 4.1.6 This section is currently incorrect referring to the Machine Preservation Trial but then presenting, within the same paragraph the results of a separate retrospective record review published by Moustafellos et al. For accuracy this section should be divided into two separate points as follows: '4.1.6 The results of the Machine Preservation Trial study were provided as academic-in-confidence and are not included in this document '4.1.7 A retrospective review reported……..'	The sentence stating that the results of the Machine Preservation Trial were provided academic in confidence has a separate section in the FAD section 4.1.5 to separate it from the results of the retrospective record review.
Organ recovery systems	Section 4.3.6 Within this section we have three points we would like to comment on: The current statement on the Machine Preservation Trial 'The Committee was aware that this study included mainly kidneys from deceased heart beating donors….' excludes the information which is available on kidneys on DCD donors which demonstrates the effectiveness of LifePort over static storage in preserving these kidneys.	The Committees consideration of kidneys from non heart beating donors is reflected in section 4.3.7. Section 4.3.7 includes a statement about the results of the Machine Preservation Trial in this group of kidneys. No changes made to the FAD.

Consultee	Comment	Response
Organ recovery systems	The statement; 'The Committee considered that this study suggested a small benefit in terms of graft survival favouring the use of machine perfusion' is misleading and does not highlight to the reader the statistically significant results observed at 12-months post transplantation. In the first year post transplantation compared with cold static storage machine perfusion significantly: • ***AIC information removed*** • ***AIC information removed*** We would recommend that the Committee consider revising the current text as follows; 'The Committee considered that this study suggested a statistically significant benefit in terms of graft survival favouring the use of machine perfusion'	In the absence of data values in the FAD document, it is necessary to provide some qualitative consideration of the difference. The FAD has been amended to state a small statistically significant difference. See FAD section 4.3.6. This text has also been included in the FAD evidence section 4.1.5.
Organ recovery systems	The ACD makes the statement; 'The Committee heard clinical specialists express concern about the exclusion of a large number of kidneys from the statistical analysis in the Machine Preservation Trial, and the effect that these exclusions may have had on results'. While we agree that the number of exclusions may seem rather large this is primarily due to the requirement for achieving successful randomisation. Within the trial the acceptance criteria used required randomisation to be performed at an early stage when there was merely the possibility of a potential kidney donor. Only after both kidneys had actually been transplanted could it be determined whether this kidney pair would meet the inclusion criteria. In addition all combined organ transplants were excluded according to the study protocol.	Comments noted, this statement reflects concerns of the clinical specialists present at the Committee meeting and also a comment received as part of the ACD consultation. No changes made to the FAD.
Organ recovery systems	4.3.4. In order to reflect the pending Machine Preservation Trial data on viability testing we would suggest the following underlined text is added: '….The Committee concluded that although viability testing is potentially important, there was insufficient evidence at this point in time to make this a deciding factor in choice of storage methods.'	This has been amended in the FAD.
Organ recovery systems	4.3.7. Again to reflect pending results from the Machine Preservation Trial we would recommend the addition of the following sentence to the end of this recommendation: 'Additional 12-month outcomes data will be available from the Machine Preservation Trial'	The FAD clearly states that the analyses for the kidneys from non heart beating donors are preliminary. No changes made to the FAD.
Organ recovery systems	Appendix B Ken Tupling, nominated by BODY is a transplant recipient and Secretary of British Organ Donor Society not a clinical specialist	This has been amended in the FAD.

Consultee	Comment	Response
British Transplantation Society	The British Transplantation Society welcomes the NICE appraisal of different methods to preserve kidneys prior to transplantation and would like to congratulate the Institute on the report given the paucity of data upon which to base a recommendation. Moreover we welcome the Institute's decision to perform an early review of its appraisal to assess data from the two ongoing studies of machine preservation.	Comments noted, no changes to the FAD required.
British Transplantation Society	One area that the Institute has not stressed is the deleterious effect of cold ischaemia that the preservation solutions and techniques are designed to ameliorate. It would be helpful to clinicians were the Institute to recommend that kidneys be transplanted with the shortest ischaemic times possible, and that transplant units need to have improved access to the appropriate facilities including operating theatre time to facilitate this.	The NICE technology appraisals programme issues guidance on clinical and cost effectiveness. It is beyond the remit of this appraisal to issue guidance on the appropriateness of facilities and length of ischaemic time. The Committee was aware of the importance of ischaemic time. See FAD section 4.3.2.
British Transplantation Society	Paragraph 1.1. Belzer produced two solutions that are referred to as Belzer University of Wisconsin solution. For the purposes of the ACD we recommend that NICE always refers to it as University of Wisconsin (ViaSpan) solution when referring to the solution made for static cold storage in order to remove any ambiguity.	Guidance documents do not refer to product brand names except in section 3 of the document. Viaspan has been referred to as Belzer UW storage solution throughout the document, to differentiate it from UW machine perfusion solution.
British Transplantation Society	Paragraph 2.2 The BTS suggest replacing the word nauseous with nauseated: "Patients with established renal failure can become tired and **nauseated**…". The word nauseous may be taken to mean either they feel sick or they make someone else feel sick.	This has been amended in the FAD
British Transplantation Society	Paragraph 2.4 "Kidney transplant**ation**, which involves implanting a kidney from a donor, is the preferred therapeutic option where it is possible. Kidneys for transplant**ation** may…" We suggest that NICE use the word transplantation, rather than transplant, for the act of implanting the kidney.	This has been amended in the FAD.

Consultee	Comment	Response
British Transplantation Society	Paragraph 2.5 " … the time that the organ spends deprived of oxygen before it is **cooled and retrieved**…." The kidney is first cooled then retrieved. We suggest the word order is reversed as above.	This has been amended in the FAD.
British Transplantation Society	Paragraph 2.7 "Successful **kidney** transplant**ation** removes the need for dialysis …"	This has been amended in the FAD.
British Transplantation Society	Paragraph 2.8 This paragraph needs to be changed such that it clearly refers to deceased donor kidneys and not all kidneys. The data are not the same as those recorded by UK Transplant (the official body recording these data) and it is not clear where the Institute has obtained them. The UK Transplant website includes an official datafile which I suggest should be the source of your data: (http://www.uktransplant.org.uk/ukt/statistics/calendar_year_statistics/pdf/yearly_statistics_2006.pdf). The paragraph could thus be rewritten: "In the UK 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; the waiting list has increased by 48% since 1998. Demand for kidneys outstrips supply. In the UK in 2006, **1403 deceased donor** kidneys were transplanted (from 765 **deceased kidney** donors); **6384** people were **active** on the **kidney** waiting list. Therefore, there is a need to increase kidney donation and to make donated kidneys function in the best possible way."	This has been amended in the FAD.
British Transplantation Society	Paragraph 4.1.9 "One retrospective record review (58,607 kidneys transplanted) of kidneys from deceased donors included in the ~~US~~ Collaborative Transplant Study…" The Collaborative Transplant Study is an international registry based in Heidelberg, Germany. It is not a US registry; indeed it is much more European than US.	This has been amended in the FAD.

Consultee	Comment	Response
British Transplantation Society	Paragraph 4.1.10 The BTS remains uncertain as to the accuracy of the PenTAG data here. The original paper clearly shows a difference at longer ischaemic times. Were the authors consulted regarding the reworking of their data? This is important as it is the only piece of evidence concerning the effects of different solutions at longer ischaemic times.	The percentage figures used in the analyses and reported in the Assessment Report, guidance documents and published paper are the same. These figures show a small benefit for UW storage solution. The statistical analysis in the published paper considers the differences in the rate of increase in risk over time between the different solutions, the Assessment Group compared the different solutions at single time points (up to 18 hours, 19-24, 25-35 and greater than 36 hours). The FAD section 4.3 summarises the Committee's consideration of the issue, FAD section 4.3.5 notes that Belzer UW storage solution may be more appropriate if there is a longer cold ischaemic time. No changes made to the FAD.
British Transplantation Society	Paragraph 4.2.4 The registries quoted in this paragraph have not been accurately cited. It should read: "… The characteristics of the cohort modelled were chosen to be consistent with data obtained from **UK Transplant** and **The Renal Registry …**"	This has been amended in the FAD.
British Transplantation Society	Paragraph 4.2.8 The institute should be mindful that the control group in the Machine Preservation Trial received either UW solution or HTK (Custodiol) solution, the latter being a different preservation solution and one that has not been appraised by NICE. The Institute might wish to consider how this affects the cost analysis which has been done assuming that all the controls received UW solution, which they did not. However the BTS acknowledge that this is another reason why definitive conclusions based on this study cannot be made pending formal publication of its results.	The Assessment Report notes that both UW solution and HTK solution were included in the MPT study. The Assessment Group identified evidence that suggested no difference in outcomes between the two solutions (See page 50 of the Assessment Report). The Committee did not preferentially recommend LifePort over other forms of storage, because it was mindful of the limitations in the evidence base. No changes made to the FAD.

Consultee	Comment	Response
British Transplantation Society	Paragraph 4.3.2 Early graft failure or non-function is also associated with a significantly increased risk of death in the ensuing months[1], something that the Institute might wish to mention in this paragraph.	This has been included in the background section of the FAD. See FAD section 2.5.
British Transplantation Society	Paragraph 4.3.6 The BTS is uncertain how the Institute could conclude that "machine perfusion may be marginally more clinically effective than Belzer UW solution for the storage of kidneys from deceased non-heart-beating donors" based upon evidence from two properly powered, randomised controlled trials that gave opposite results. It suggests a bias by the Institute. The BTS recommends that the Institute reconsiders this statement in favour of one which concurs with the statement at the foot of paragraph 4.3.7 in which the Institute states "The Committee concluded that the clinical effectiveness evidence did not allow it to distinguish between the LifePort kidney transporter and cold static storage for the storage of kidneys from non-heart-beating donors."	Paragraph 4.3.6 refers to the Committee's consideration of kidneys from deceased heart beating donors. Paragraph 4.3.7 refers to non-heart beating donors. This has been amended in the FAD.
British Transplantation Society	Appendix B. The penultimate line of this section spells Donor as Doner. It should be changed to: "Mr Tom Fearon, Chairman of and nominated by the British Organ Donor Society – patient expert"	This has been amended in the FAD.
Department of Health	I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Comments noted, no changes to the FAD required.
Royal College of Nursing	The Royal College of Nursing welcomes the opportunity to review the Appraisal Consultation Document (ACD) of the technology appraisal of machine perfusion systems and solutions for cold (static) storage of donated kidneys. Nurses working in this area of health have reviewed the ACD. They consider the document comprehensive and have no further comments to make on it. The RCN would welcome guidance to the NHS on the use of this health technology.	Comments noted, no changes to the FAD required.
Welsh Assembly Government	Thank you for giving the Welsh Assembly Government the opportunity to comment on the above appraisal. We have no further comments to make at this stage	Comments noted, no changes to the FAD required.
Clinical expert 1	See comment from NHS QIS (reviewer 1)	See response below.

Comments received from commentators

Commentator	Comment	Response
Kidney Research UK	**Do you consider that all the relevant evidence has been taken into account?** There is a paucity of published evidence and it is unfortunate that the final results of two randomised clinical trials (PPART and Machine Preservation Trial studies) are not yet available for consideration. However the early review of this NICE guidance in 2010 is welcomed and we would hope that this would take into account the evidence upon their completion and follow-up studies.	Comments noted, no changes to the FAD required.
Kidney Research UK	Initial results from the PPART study, taking place in the UK, involved non-heart beating donor kidneys and showed no benefit for machine perfusion over static cold storage using delayed graft function as the primary outcome measure. In contrast, the European Machine Perfusion Trial study concentrated largely on kidney from heart-beating donors and did not show a statistically significant advantage for machine perfusion over static storage, in terms of better initial graft function. Therefore the main difficulty for NICE and the transplant community is basing clinical practice on this relatively limited evidence and unfortunately, both these trials have limitations, which have been pointed out by some of the experts giving evidence to NICE.	Comments noted. The Committee considered this evidence. See FAD sections 4.1.5, 4.1.6, 4.3.6, 4.3.7, 4.3.11.
Kidney Research UK	Some of the specific limitations of these two studies are as follows: The PPART study is relatively small with 90 patients randomised, largely studying non-heart-beating kidneys from controlled donors (i.e. where cardiac death was predictable and thus in which warm ischaemic time can be limited to only a few minutes) More marginal donors are obtained from uncontrolled NHBDs in which cardiac death is sudden and therefore warm time suffered by these kidneys tends to be prolonged and in the region of 30-60 minutes. Therefore more evidence is needed for the effects of machine perfusion in these particular marginal kidneys. Another concern with this study is that it used a rather unusual cumulative statistical analysis, which was used to stop the trial when it was clear that there was not going to be any benefits from using machine perfusion which seems completely opposite to the usual situation where power calculations are performed and interim analysis of data is not allowed. Finally, concern over the reproducibility of the way in which the machine perfusion was used as some kidneys were perfused for very short periods and others much longer periods which makes any comparisons of outcomes more difficult.	Comments noted. The Committee was mindful of the limitations of the evidence base as it considered the evidence. See FAD section 4.3.7.

Commentator	Comment	Response
Kidney Research UK	Although the European Machine Preservation Trial study was much larger involving 600 kidneys, there are two worrying aspects to the study, as approximately half the numbers of kidneys considered for entry into the study were excluded for one reason or another which seems excessive, even unprecedented, for a clinical trial. The trial also placed kidneys with multiple vessels which were considered too difficult to store using the machine perfusion into the cold storage group, therefore making 'randomisation' questionable. It is known that kidneys with multiple vessels have a higher incidence of a poorer outcome and in particular a higher incidence of delayed graft function, therefore this is likely to have skewed the results against cold storage. We are aware that the study group are using further statistical analysis to address this issue and these results are not yet available.	Comments noted. The Committee was mindful of the number of kidneys considered for entry but subsequently excluded from this study. See FAD section 4.3.6.
Kidney Research UK	**Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?** The summary of the clinical effectiveness is a reasonable interpretation of the available evidence, however it is noted that the full data of the Machine Perfusion Trial study is not available but the DGF rates of 89% (4.1.6) are higher than anticipated, particularly when compared with the 56% rate in the PPART study for UW preservation (4.1.5).	The DGF rate of 89% is from the retrospective record review and is not the outcome of the MPT study. The outcomes of the MPT study were provided as academic in confidence and are not included in the FAD. See FAD sections 4.1.5, 4.1.7.
Kidney Research UK	Although detailed economic modelling was used there are some assumptions that have been made and the limited data makes accurate interpretation difficult. In sections 4.2.7 and 4.2.8 in the comparisons between Belzer UW Solution and the Lifeport the cost differences are not that different, but the findings are opposite presumably because of the marked different rates of DGF as highlighted above. Furthermore in section 4.2.10 in the comparison between Marshalls and Belzer UW preservation solutions there were slightly higher costs for the former, although numbers were much smaller and may have been from an earlier time cohort which may have affected graft survival. The document summaries have recognised that the cost effectiveness data is limited by the evidence available and as a result recommendations based on cost-effectiveness have not been made.	Comments noted. The Committee recognised that the incremental differences in the costs and QALYs were very small. See FAD sections 4.3.10, 4.3.11.
Kidney Research UK	**Do you consider the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for preparation of guidance to the NHS?** In view of the evidence available these provisional recommendations are realistic in that any of the interventions under consideration are permitted under appropriate circumstances. **Are there any equally related issues that may need special consideration?** We are not aware of any. **Other comments** Kidney Research UK seems to be excluded from Appendix B under point B. II	Comments noted, no changes to the FAD required. Kidney Research UK is classified as a research organisation and is included as a commentator in this appraisal. The FAD has been amended to include Kidney Research UK in Appendix B point IV.

Commentator	Comment	Response
NHS QIS Reviewer 1	I commend the committee on this document and appreciate the deliberations undertaken in considering technologies where the quality of evidence is so poor but where the clinical issues are varied, complicated and vitally important.	Comments noted, no changes to the FAD required.
NHS QIS Reviewer 1	Before addressing the questions asked I would like to draw attention to the fact that in Appendix B of the ACD, NHS Quality Improvement Scotland is placed in B IV "Commentator organisations (did not provide written evidence and without the right of appeal)". NHS QIS asked [redacted], Consultant Transplant Surgeon, Royal Infirmary, Edinburgh to produce a written report on its behalf and this statement was available to the Appraisal Committee and the invited clinical specialists and patient advocates at the meeting on 13th August.	Comment noted, the clinical specialist commented on the draft Assessment Report on behalf of NHS QIS. They did not provide written evidence at the start of the appraisal. NHS QIS is included as a commentator in this appraisal.
NHS QIS Reviewer 1	Specific headings i) Yes. The relevant evidence for these technologies is sparse and I consider that all the relevant evidence was presented very clearly in the written documentation prepared prior to the Appraisal Committee meeting in August, presented and discussed at the Committee meeting and summarized in the ACD. I know of no other published reports which are relevant. There has been a presentation at the Transplantation Society meeting in Australia last month when further data from the Machine Perfusion Trial showed that in the subgroup of kidneys from non heart beating donors the kidneys which did develop delayed graft function experienced this for a shorter period of time (mean 3 days less) in the machine perfused group compared to the kidneys which were preserved with static cold storage. This data is as yet unpublished.	Comments noted, no changes to the FAD required.
NHS QIS Reviewer 1	Specific headings (continued) ii) Yes. Within the restraints of the paucity of good quality evidence I consider that the summaries of the clinical and cost effectiveness are reasonable interpretations of the available evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate. iii) Yes. I consider that the provisional recommendations of the Appraisal Committee are sound and are a suitable basis for guidance to the NHS. iv) No. I do not see any equality related issues that may need special consideration.	Comments noted, no changes to the FAD required.

Commentator	Comment	Response
NHS QIS Reviewer 1	General Comment This is a very well thought out report which takes into account the general lack of quality evidence relating to machine perfusion systems and solutions for cold storage of donated kidneys. The committee has appreciated and given heed to all the additional information and concerns expressed by the organisations and the individuals active in the clinical field and produced a document that presents the facts and makes recommendations that are safe for the viability of the kidneys within a cost awareness environment without unduly restricting responsible clinical practice. The recommendations for further research are appropriate in that further data is awaited from the 2 RCTs relating to machine perfusion and it is important for individual transplant units to record and audit the outcomes of their preservation practice(s). The review date in 2 years appears appropriate to allow reassessment after further evidence is available from the as yet incompletely analysed RCTs and their follow up data but may be too soon to have reported data on the impact of the implementation of the recommendations of the organ donor task force report. It is unlikely that the recommendations of the organ donor task force report will be fully implemented before about this time next year. If then we require at least a year to see what changes this produces and then to analyse the data it will not be available for consideration before the proposed August 2010 review. The task force recommendations should increase the numbers of donors and of transplants but may have little effect on the methods or quality of kidney preservation.	Comments noted. A decision to review the guidance will only be made following consultation. Consultees will have the opportunity to comment on the timeliness of a review of the guidance. No changes made to the review date.
NHS QIS Reviewer 2	Section 1, 1.1 recommends LifePort transporter or cold storage with UW or cold storage with Marshall's as the three options for storage of kidneys. I am confused by the next paragraph (1.2) which states that "when different storage methods are considered equally appropriate, the least costly should be used". Are they talking about methods different to the three mentioned in 1.1 or do they mean the choice between LifePort & the two different cold storage methods? I imagined that the purpose of the NICE review was to comment on the most appropriate method, rather than stating that when there are different methods which are considered equally appropriate, choose the cheapest.	A NICE technology appraisal considers the clinical and cost effectiveness of technologies. The appraisal makes recommendations about 3 technologies LifePort kidney transporter, Belzer UW storage solution and Marshall's hypertonic citrate solution. The Committee considered that there was insufficient evidence to distinguish between the technologies in terms of clinical effectiveness. The Committee therefore recommended all the technologies be options for the storage of donated kidneys, but that where more than one of the three technologies was considered equally appropriate, the cheapest be used.

Commentator	Comment	Response
NHS QIS Reviewer 2	A fundamental shortcoming with this document is that it considers storage of kidney allografts in isolation from organ retrieval and it focuses solely on storage of kidneys rather than retrieval/storage/transplantation of all organs that are transplanted Organs for transplantation from deceased donors are perfused with cold preservation solution prior to retrieval. The vast majority of deceased organ donors contribute other organs in addition to kidneys for transplantation. UW solution was primarily developed as a pancreatic perfusion/preservation solution. Its superiority over Marshall's solution for pancreas and for liver perfusion and preservation has been proven beyond any doubt. No multi-organ retrieval procedure will use Marshall's as the only perfusion solution. Organ retrieval procedures where only kidneys are retrieved constitute a small proportion (certainly less than 10%, probably less than 5% of all retrievals) of all retrievals. In multi-organ retrieval UW is the standard perfusion solution in the UK. Having perfused the organs with UW, it seems illogical to then store the kidneys in Marshall's solution. I don't know how to interpret the information in paragraph 3.5 which states that in the UK in 2000-2007 74% of deceased donor kidneys were preserved with Marshall's solution. It seems that the appraisers do not have a complete understanding of how organ retrieval is performed and have not considered the needs of other organs (primarily liver and pancreas, less commonly small bowel).	The remit of the appraisal was to consider the clinical and cost effectiveness of different methods of storing of kidneys from deceased donors. Consideration of the complete process from retrieval to transplantation for kidneys and other organs goes beyond the remit of a technology appraisal. The Committee heard from clinical specialists about the use of different solutions in multi-organ donation. See FAD section 4.3.5. The information in section 3.5 is data from UK Transplant and was provided in the submission from the British Transplantation Society.
NHS QIS Reviewer 2	LifePort transporter can indeed run without supervision (3.7) but in practice most transplant units who store kidneys in LifePort machines do make provision for an additional member of staff to check the machine regularly during the time that kidneys are perfused in it. This clearly adds a significant amount of extra work and cost which has not been considered in any of the analyses.	The Committee considered the potential for additional costs associated with the use of the LifePort kidney transporter. The cost effectiveness analyses are sensitive to the costs of dialysis that arise from graft failure rather than the upfront costs associated with any one of the technologies. The Committee therefore did not consider that upfront costs should be a deciding factor in their decision making. See FAD section 4.3.8.

Commentator	Comment	Response
NHS QIS Reviewer 2	Attachment of kidneys to the LifePort transporter requires a complete and appropriate sized patch of aorta around each renal artery. This is not always available. No published data exists but from my experience of several hundred organ retrieval procedures, I estimate that in approximately one fifth of organ retrieval procedures at least one of the kidneys can not be attached to the LifePort device because of the presence of multiple renal arteries, atherosclerotic disease of the aorta, inadequate patch size on one side…etc. This will only be evident at the end of the organ retrieval operation, after the kidneys are removed from the body. At that stage all the disposable (and expensive) consumables for the LifePort device will have been opened. Hence these costs will be incurred even if the kidney(s) can not be attached to the device. Again none of the analyses take this into account.	The Committee considered the potential for additional costs associated with the use of the LifePort kidney transporter. The cost effectiveness analyses are sensitive to the costs of dialysis that arise from graft failure rather than the upfront costs associated with any one of the technologies. The Committee therefore did not consider that upfront costs should be a deciding factor in their decision making. See FAD section 4.3.8.
NHS QIS Reviewer 2	Secure attachment of the renal artery to the LifePort device is a critical requirement for successful pulsatile preservation of kidneys. This can be an intricate and exacting surgical manoeuvre. If it fails, the worst possible outcome may be inadequate preservation (and discard) of the kidneys. Published data regarding discard of kidneys before transplantation is scarce (paragraph 4.3.6). Whilst discard because of inadequate cold preservation rarely occurs, if it does it must be more common in machine preserved (rather than cold stored) kidneys.	The Committee was aware of the importance of discard rates. See FAD section 4.3.6.
NHS QIS Reviewer 2	As discussed above, the vast majority of deceased donor kidneys that are transplanted are retrieved as part of a multi-organ retrieval. Multi-organ retrievals are performed by liver transplant teams (sometimes one liver team and a separate pancreas transplant team). In Scotland all multi-organ retrievals are performed by the Edinburgh transplant team. It is uncommon for additional surgeons from the “kidney only” transplant unit to be present at the retrieval procedure (it never happens in Scotland). Hence, if LifePort devices are used, the attachment of kidneys to LifePort devices need to be performed by the liver transplant team at the end of the retrieval procedure. This inevitably delays the departure of the liver transplant team by approximately 45-60 minutes. This delay can translate into increased cold ischaemia time for the liver transplant procedure. The outcome of liver transplant operations, in particular when livers from non-heart beating donors are used, can critically depend on cold ischaemia time and in this context an additional 45-60 minutes delay can be clinically significant.	The Committee was aware of the need to use different solutions depending on the organs being retrieved. See FAD section 4.3.5. The Committee recognised that there may be clinical considerations that could affect whether machine perfusion or cold static storage was used. See FAD section 4.3.6.
NHS QIS Reviewer 2	The committee states that “the results of the PPART study were not consistent with clinical opinion or practice for storing this type of kidney” (paragraph 4.3.7). PPART study is the first (and the most reliable and virtually the only) prospective randomized study comparing LifePort transporter and simple cold storage for NHBD kidneys. Until this study was conducted, there were no clinical experts nor an accepted expert clinical opinion on this issue. The results certainly did not come as a surprise to me. I agree with the final sentence of paragraph 4.3.7	The Committee heard from clinical specialists present at the Committee meeting that the results of the PPART study were not necessarily what they had expected based on their experience of storing kidneys from non heart beating donors. No changes made to the FAD.

Commentator	Comment	Response
NHS QIS Reviewer 2	The economic modelling is based on small numbers, some assumptions are made not all of which are justified and it doesn't take into account other important aspects of the process such as potential discard rates, influence on other organs to be transplanted and other hidden costs associated with LifePort (costs of the supervision of the machines, expensive disposables opened but not used..). Importantly it also misses the fundamental point of the difference between organ perfusion during the retrieval operation and organ storage. The storage costs are part of the total cost of perfusing kidneys and other organs during the retrieval process and subsequently storing them until transplantation takes place. As stated above, this latter point is of central importance to the whole analysis, not only the economic modelling.	The cost effectiveness analyses are sensitive to the costs of dialysis that arise from graft failure rather than the upfront costs associated with any one of the technologies. The Committee therefore did not consider that upfront costs should be a deciding factor in their decision making. See FAD section 4.3.8. The remit of the appraisal was to consider the clinical and cost effectiveness of different methods of storing of kidneys from deceased donors. Consideration of the complete process from retrieval to transplantation for kidneys and other organs goes beyond the remit of a technology appraisal.
NHS QIS Reviewer 2	Another relevant issue, mentioned in the appraisal document (4.3.2) is the need to consider NHBD and heart-beating deceased donor kidneys separately. These two types of allografts are not only different in their potential to be influenced by the storage method but they are currently subject to different rules for allocation. It is likely that in the future NHBD kidneys will be allocated nationally (similar to heart-beating donor kidneys). This will increase travelling of allografts throughout the UK and will have implications for the storage method.	Comments noted, no changes to the FAD required. Consultees may request an early review if there is evidence or a change in the clinical context which may change the guidance recommendations.
NHS QIS Reviewer 2	Ultimately, I agree with the conclusion of the appraisers that there is no evidence to support the use of LifePort kidney transporter system in preference to simple cold storage (4.3.11). Given the additional concerns about the LifePort system discussed above, it is debatable whether LifePort system can be considered as an alternative or whether it should only be used as part of clinical studies. My personal prejudice and preference would be the latter.	Comments noted, no changes to the FAD required.

Commentator	Comment	Response
NHS QIS Reviewer 3	1. Whether you consider that all the relevant evidence has been taken into account. *As far as I can tell, all relevant information provided has been taken into account.* 2. Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence. *Yes* 3. Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS. *Yes as long as acceptable to the clinical community*	Comments noted, no changes to the FAD required.

Comments received from members of the public

Role*	Section	Comment	Response
None received			

* When comments are submitted via the Institute's web site, individuals are asked to identify their role by choosing from a list as follows: 'patent', 'carer', 'general public', 'health professional (within NHS)', 'health professional (private sector)', 'healthcare industry (pharmaceutical)', 'healthcare industry'(other)', 'local government professional' or, if none of these categories apply, 'other' with a separate box to enter a description.