UKDEC
UK Donation Ethics Committee

Research in Transplantation

A UKDEC position statement donor and recipient consent to research.

Introduction

The UKDEC/NRES workshop on ethics of transplantation research, held on 10 November 2010, made a number of recommendations relating to consent procedures for both donor and recipient consent for participation in transplantation research. UKDEC has considered these recommendations, and after further deliberation has developed this position statement. The relevant extract from the workshop report can be found at Annex 2.

1. Donor Consent

1.1. The Human Tissue Act sets out a legal requirement for consent to be sought from the donor (or their family) for any research intervention on an organ (or tissue sample). This requirement only ceases when the organ or tissue has been transplanted into the recipient. Discussion at the workshop indicated that this requirement is not well understood, with some transplant surgeons regarding any interventions as requiring the consent of the recipient only if they happen after the organ has arrived at the transplanting centre, for example.

1.2. A further complication that has arisen is that numerous samples, originally taken for cross-matching purposes, are kept in transplant centres and could now be a very valuable research resource. However, no consent for research was sought at the time of the retrieval, which means that research on these samples is unlawful unless the donor families were contacted again and consent sought. An exception is made for anonymised samples, but the extensive record keeping and tracking of organs between donor and recipients are what make this such a potentially valuable resource.

1.3. UKDEC considers that the interpretation of the legal requirements are very important to ensure that donor families are adequately informed, but not over-burdened with lengthy consent procedures. The context of seeking consent to research from donor families is very different to other research consent situations. The family is in extreme circumstances, having to come to terms with what is likely to have been the unexpected death of a loved one. They will already have spent a considerable amount of time with the Specialist Nurse for Organ Donation, working through the consent to donate process and the donor's medical history.

1.4. Under current arrangements, the consent procedure for donation includes brief discussion of use of material not suitable for

transplantation in research and other processes, but does not address the research question when material is intended for transplantation.

1.5. **UKDEC recommends that the consent procedure for donation is amended to incorporate the following issues**:

(1) Consent to research on the organ or tissue whilst it is still in the donor, where the intention is for transplantation. (Note: The donor will have been diagnosed as dead when the research intervention is carried out. Research on a potential donor, who is alive but incapacitated, for any purpose other than to investigate the condition that has caused their incapacity is unlawful under the Mental Capacity Act. This means that it is not lawful to conduct research on, for example, a potential DCD donor to determine whether particular interventions after the withdrawal of life-sustaining treatment may improve the outcome of the transplant).

(2) Consent to research on the organ or tissue after it has been retrieved from the donor, where the intention is for transplantation

(3) Consent to research on the organ or tissue when it will not be transplanted.

1.6. At a minimum a straightforward blanket consent, not defining the particular research project, should be sought. Families should also be offered the opportunity to find out more about research projects that may have been undertaken at a later date when they feel ready.

1.7. There will be circumstances when a more detailed consent process will be appropriate. This is most likely to apply to research in category (1), where sensitivity will be needed if research interventions are more invasive than the usual retrieval operation. [Or are particularly sensitive, such as re-starting a heart after death has been diagnosed by cardiorespiratory criteria].

1.8. For research in category (2), it is arguable that the donor (or their next of kin), having given their consent to transplantation, has no further interest in the detail of what happens to the organs on their way to the recipient. It is the consent of the recipient which carries greater moral weight. For that reason UKDEC expects that a simple blanket consent satisfying the legal requirements under the Human Tissue Act, would be the norm in this category.

1.9. Research in category (3) may include both immediate research on organs that are not suitable for transplantation, and future research, as yet undefined, on stored samples. A consent to future, undefined, research can only be a simple blanket agreement. Immediate research may need a more detailed process, depending on the nature of the project.

1.10. Research Ethics Committees, considering individual research projects, will need to consider how to balance the need for families to be properly informed with the reality of their extreme situation at the time consent is sought, and advise on the level of detail required for the consent process accordingly. UKDEC recommends that, in all circumstances, donor families are offered the opportunity to find out more detail at a later date should they wish to do so.

2. Recipient Consent

2.1. UKDEC believes that society has an interest in pursuing transplantation research in order to benefit future recipients. In an area such as transplantation, where organs are a scarce resource, the challenge is to seek consent from recipients without coercion – either in real or perceived terms.

2.2. Good ethical governance, including consideration by a Research Ethics Committee, should mean that potential research participants are not asked to do anything unreasonable. Indeed it can be argued that research participants are potentially receiving a benefit, as the research is aimed at improving transplantation (although benefit cannot be guaranteed – the purpose of research is to determine whether a benefit can be achieved).

2.3. Some recipient consent issues arise from the belief that there is a choice to be made between accepting an organ now that is modified and part of a trial or waiting for an organ that is unmodified and not part of a trial. This will not always be the case: an unmodified organ may not become available in time to benefit the recipient. In reality, all recipients have to decide between accepting the organ they are being offered – whether or not it has been modified at the time of the offer - and waiting for another organ that may or may not become available in the future. Recipients being offered a modified organ should, however, be assured that a decision not to participate in a specific research project does not mean they will go to the bottom of the waiting list for non-researched organs because they do not wish to participate nor because they are perceived as being ‘difficult’ by refusing.

2.4. For recipient to exercise genuine choice, information about the potential and realistic benefit of the modification or treatment must be made available as part of the consent process, alongside information about the risks of waiting for an unmodified organ. The follow-up protocol, (which may include treatments or assessments in addition to the usual post-transplant arrangements) must be included in this information.

2.5. In additional, recipients should be given a clear explanation of their obligations to comply with the follow-up protocol if they accept a modified organ. For the benefits of an intervention to be properly assessed, the performance of the organs has to be followed up. If patients withdraw from the research this follow-up will not happen and the results of the trial will be less reliable. In other areas of clinical research such as drug trials, new interventions are only made available as part of the trial. If a patient withdraws from the trial they cannot continue to take the new drug. In transplantation research the intervention may be a modified organ, which cannot be removed if the patient exercises the right to withdraw from the trial. This suggests that patients who accept modified organs have a greater than usual obligation not to withdraw. This does not remove the right to withdraw but is a consideration that should be explained to recipients at the time they consent to receive modified organs.

2.6. On the other hand, participation and ongoing compliance in research is always entirely dependent on the participants' goodwill, and their social and moral conscience. Ideally, patients accept this and willingly comply with the research protocol. The offer of an organ should not, however, be conditional on such compliance. The logical consequence of this is that, if a recipient is offered an organ that has been modified, which they wish to accept but without being involved in follow-up research, then they should still receive the organ. This is less than ideal from the perspective of furthering knowledge, but more importantly safeguards patients from being coerced into participation in research. It also recognises that any individual's moral conscience will have to take their specific circumstances into account when making decisions. Thus people of 'good' conscience may well arrive at different decisions.

2.7. **Specific recommendations are as follows**:

The consent process needs to start at the time potential recipients go on the waiting list. General information about the possibility of participating in research and the implications of accepting and refusing a modified organ should be given alongside other information provided when the patient consents to join the waiting list., This gives plenty of time for discussion about what issues this might raise and enabling the recipient to form a general view about the burdens and benefits research participation in advance of having to make a decision about a specific piece of research. This discussion will have to be reviewed regularly. The health status of the recipient will also change over time and this may lead them to change their perceptions about the balance of burdens and benefits.

If an organ is modified before allocation, it should be offered using standard allocation schemes on a 'take it or leave it' basis.

Even if a potential recipient has previously stated they do not wish to participate in research, if standard allocation protocols identify them as the best match for a modified organ then they should be given the opportunity to make the final decision, irrespective of whether they simultaneously agree to participate in the research project.

If it is intended that an organ will be modified after allocation, then it should be offered to the potential recipient identified using standard allocation schemes, with the research intervention taking place only if that recipient consents. This keeps control with the recipient, giving someone who has previously consented to research a final opportunity to withdraw that consent if they have changed their mind.

If an organ that would otherwise be unsuitable for transplantation is likely to be suitable only following a research intervention, then it should be offered to the individual identified as the best recipient using standard allocation schemes, with transplantation taking place only if the recipient consents to the research. This operates on the same principle as the recommendation above. The potential recipient, who may or may not have indicated they are willing to participate in research, is given a final opportunity to confirm or withdraw their consent.

Conclusion

In making these recommendations UKDEC recognises that donor families are being asked to make decisions about consent to research in circumstances that are extremely difficult. Equally, for recipients, although discussion about research may begin at a time when they are able to make a sound and rational judgement, the final decision point will be very sudden with very limited time for reflection. The challenge for all concerned is to balance these difficult circumstances with the need for those giving consent to be properly informed, and the wider societal need to pursue research in this field to the ultimate benefit of all those who may need a transplant in the future.

UKDEC, March 2011.

ANNEX 1

UKDEC Membership 2010-2012

Sir Peter Simpson (Chair)	Past President, Royal College of Anaesthetists
Paula Aubrey	Regional Manager, NHS Blood and Transplant
Keshwar Baboolal	Consultant Physician and Nephrologist, University Hospital of Wales, Cardiff
Joe Brierley	Consultant Paediatrician, Paediatric and Neonatal Intensive Care Unit, Great Ormond St Hospital, London
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Stephen Cole	Consultant in Anaesthesia and Intensive Care Medicine, Ninewells Hospital, Dundee
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Bobbie Farsides	Professor of Clinical and Biomedical Ethics, Brighton and Sussex Medical School
Leslie Hamilton	Consultant Cardiac Surgeon, Freeman Hospital, Newcastle Upon Tyne
Penney Lewis	Professor of Law, School of Law and Centre of Medical Law and Ethics, King's College London
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Anthony Warrens	Honorary Consultant Physician and Dean for Education, Barts and The London School of Medicine & Dentistry
Eleanor Updale	Writer
Helen Lovell	Secretary to UKDEC
Observers from the Department of Health and Devolved Administrations, the Academy of Medical Royal Colleges, NHS Blood and Transplant and the Human Tissue Authority may also be in attendance.	

EXTRACT FROM THE REPORT OF THE UKDEC TRANSPLANT RESEARCH ETHICS WORKSHOP HELD ON 10 NOVEMBER 2010

7. Donor Consent

7.1. Technical points:

- The Human Tissue Act requires that consent be sought for use of donor tissue for research. Responsibility for giving consent remains with the donor until the tissue or organ has been transplanted into the recipient.
- Research Ethics Committees (RECs) consider what is ethically appropriate in the given context. In some circumstances a REC may advise that requiring detailed consent from donor families would cause them undue distress. (The legal requirement for consent in some form remains, and this can lead to confusion.)
- The organ donation consent process in England includes a general question asking whether, if organs are found to be unsuitable for transplantation, they could be used for research. This does not include consenting to research being performed on organs that are to be transplanted.
- The authorisation process in Scotland has a simpler formulation for consent for research.

Comment:

7.2. A number of researchers were unaware that the requirement for consent from the donor remained until the point of transplantation. A number of participants described a model of assuming that the organ became the recipient's once it was in the recipient's hospital or theatre, and at that point they regarded the need to obtain consent as having moved from donor to recipient. There was agreement that the continuing requirement for donor consent not only complicated the research process, but also risked placing donor families under considerable additional stress, and adding extra time to the process. A number of ideas were discussed, including considering whether there might be an alternative legal custodian of the organ in the time from retrieval to transplantation. (Human Tissue Authority or coroner).

7.3. There was a clear consensus that the standard consent for donation documentation should have a general consent to research section, with more detailed information available if families requested it. There was some discussion about whether more detailed consent might be appropriate in some circumstances, such as if the research procedure would be happening while the organs where still in situ. After retrieval a more detailed consent process was thought unlikely to be required. Participants reported that talking to patients reveals that, when being asked to consent for 'research', many relatives do not appreciate that the purpose of the research is to improve transplant outcome; they think the research has nothing to do with transplantation. Any addition

to the organ consent form about research must emphasise that it is transplant related research approved by an ethical committee.

7.4. In discussion there had been at least one experience of a REC advising that seeking consent from relatives to take more samples for research could be distressing, and the general consent for research element of the form should be the source of consent for that research project. However the REC did not understand that the general consent clause is to seek permission to use tissues and organs that *cannot be used for transplantation* in research.

7.5. It was noted that respect for the donor is independent of consideration of their family. It was thought it might be useful to have more information about protocols for handling material during research, to consider whether there were appropriate safeguards for preserving dignity and respect for the donor.

7.6. When working with donor families it is important to ensure they understand that using an organ for research may mean an organ that would otherwise have been considered unsuitable for donation is now transplanted, or contributes to the longer term success of the transplantation programme. Careful consideration needs to be given to the language used, which can be off putting for a lay person. A leaflet explaining how donated organs are used might be useful. Information for donor families on outcomes should be considered –results of the research programme, or perhaps why organs might not have been used. This should be incorporated into the usual follow-up arrangements so information remains available if and when donor families wish to have it.

7.7. Donor families should still feel they have the right to refuse to give permission for research, and should have this decision respected.

7.8. Recommendations for action:

- A general clause in the consent forms, asking for permission to undertake transplant related research, should be incorporated, with a view to this being the main source of consent for research on retrieved organs prior to transplantation. This will need to encompass organs that will be transplanted, and those that are unsuitable for transplantation, and blood and tissue samples. It should include an assurance that all research will be approved by a REC.
- Every case is different and researchers and those working with donor families need to tailor discussions to the needs of the donor family, but a general guideline for donor consent might be:
    - If the research intervention is to happen while the organs are still in the donor (such as use of ECMO), or where organs are to be used solely for research, then specific consent should be sought.
    - If the intervention is to happen after retrieval, then the general clause on research would normally suffice.

- Investigate use of the Organ Donor Register to capture more detailed information about a person's wishes during life. A required response to a yes/no type question would be preferable.
- Investigate current practice and follow-up options for follow-up information to be offered to families.

8. Recipient consent

8.1. Technical points

- Once the organ has been transplanted into the recipient, it becomes part of their body and all consent requirements from the donor family cease.
- After retrieval but before transplantation, consent to research on the organ is required from the donor family.

Comment

8.2. The consent process for recipients needs to start at the time they go onto the waiting list, and time should be taken over the process. Information overload is a significant risk, especially for heart, lung and liver patients. If patients refuse initially, they should be followed up as they may change their minds over time. [Post-meeting note: This implies that the opposite should also be true – patients who have given consent for research should be followed up from time to time in case they have also changed their minds].

8.3. From the recipient perspective, recipients need to be aware of the medical and emotional risks of participating in research. Patient interest groups are a useful source of advice but are not necessarily representative of individual patients on a transplant list. Participating in research can also lead to closer monitoring or seeing more senior members of the team than might otherwise be the case, which some find beneficial.

8.4. It was recognised that this is a very difficult area, and recipients may well feel pressurised to agree, but research is vital if transplantation is to improve. It is important to put the risks of research into context with other equally relevant issues. These include being offered organs from donors who do not meet the ideal criteria. Currently recipients are not always given a right to choose whether or not to accept an 'extended criteria' organ, although new guidelines are being produced to address this.

8.5. Recommendations for action

Proposals for best practice –

- If the organ is modified before allocation, then it should be offered using standard allocation schemes on a 'take it or leave it' basis.
- If the organ will be modified after allocation, then it should be offered to the individual identified as the recipient using standard allocation schemes, with the research intervention not taking place if that recipient does not consent.

- If an organ which would otherwise be unsuitable for transplantation is suitable following the research intervention, then the potential recipient identified using standard allocation schemes should be consulted. If that recipient does not consent, it should be offered to successive individuals identified through the standard allocation schemes.

10 November UKDEC/NRES Workshop Delegate List (65 Attendees)

Kosh Agarwal	**Institute of Liver Studies, Kings College Hospital**
Paula Aubrey	**(UKDEC) London OD Services Team Manager NHSBT**
Natalie Akenzua	**Specialist Nurse-Organ Donation NHSBT**
Leslie Brent	**Emeritus Professor**
Joe Brierley	**(UKDEC) – Paediatric & Neonatal Intensive Care GOSH**
Graham Brushett	**(UKDEC) – Transplant Recipient**
Michael B Buck	**Lay Member Herts REC**
Rachel Burman	**Institute of Liver Studies, Kings College Hospital**
Barbara Canning	**Coventry & Warwickshire REC**
Martina Conlon	**Specialist Nurse Organ Donation - NHSBT – Northern Ireland Team**
Nicky Connor	**Consultant Epidemiologists HPA**
Antonia Cronin	**Clinical Research Consultant Nephrologist, MRC Centre for Transplantation, Kings College London**
John Dark	**Lung & Heart Transplant Surgeon, Newcastle upon Tyne**
Hugh Davies	**(UKDEC – Research Subgroup) NRES**
James Douglas	**Clinical Pharmacology & Medical Ethics Queen's University Belfast**
Heather Draper	**(UKDEC) Professor of Biomedical Ethics & Director of the Centre for Biomedical Ethics**
Phil Dyer	**Consultant Clinical Scientist, Director of SNBTS Histocompatibility & Immunogenetics Services**
Peter Friend	**(UKDEC – Research Subgroup) Professor of Transplantation Honary Consultant, Oxford**
Susan Fuggle	**Oxford Transplant Centre**
Barry Fuller	**University Dept of Surgery, Royal Free & UCL Medical School**
Alison Galloway Turner	**Specialist Nurse-Organ Donation NHSBT**
Kate Haire	**National Commissioning Group**
Rachel Hilton	**Consultant Nephrologist, Renal, Urology & Transplantation Directorate, Guys**
Catherine Hutchinson	**Specialist Nurse-Organ Donation** **South East Donation Service**
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Helen Lovell	**(UKDEC Secretary)**
Helen Lucas	**GP & Member of South West London REC**
Liz McAnulty	**HTA**

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David Parkes	**Cambridgeshire REC**
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Gurch Randhawa	**(UKDEC) Professor of Diversity in Public Health**
Karen Redmond	**Surgeon, Harefield Hospital**
John Richardson	**Chair REC Cambridgeshire 3**
Marlene Rose	**Professor of Transplant Immunology Harefield**
Sally Ruse	**Transplant Research Nurse**
Michael Simmonds	**Cambridgeshire 1 REC**
Peter Simpson	**(UKDEC Chair)**
Becky Smith	**NHSBT Yorkshire Organ Donation Services Team**
Magi Sque	**Chair in Clinical Practice & Innovation University of Wolverhampton & Royal Wolverhampton Hosptials**
Susan Tonks	**Research Support Associate, Clinical Trials & Research Governance**
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Katharine Wright	**Nuffield Council on Bioethics**
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