Promoting Public Trust in Organ Donor Intervention Research

Meeting of the Committee on Issues in Organ Donor Intervention Research
National Academies of Sciences • Engineering • Medicine

December 14, 2016

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Three Keys to Promoting Public Trust in Organ Donor Intervention Research

- Recognize and acknowledge that such research is non-exempt human subjects research under applicable federal regulations
- Obtain the informed consent of the organ recipients, who are the human subjects of the research
- Ensure appropriate and meaningful IRB review of the research

Experiments Involving Manipulation of Donor Organs: Scenario 1 - In Vivo Intervention

Deceased donors randomly assigned

Control Intervention

Experimental Intervention

Remove organs

Implant organs, measure outcome(s) in recipients

Experiments Involving Manipulation of Donor Organs: Scenario 2 – Ex Vivo Intervention

Deceased donors

Removed organs are randomly assigned

Control Intervention

Experimental Intervention

Implant organs, measure outcome(s) in recipients

Definition of Human Subject Under the Common Rule

Human subject **means a living individual about whom an investigator… conducting research obtains**
(1) Data through intervention or interaction with the individual, or
(2) Identifiable private information.

Intervention **includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes…**
Private information **includes …information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record) …**

Experiments Involving Manipulation of Donor Organs: Scenario 1 - In Vivo Intervention

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Control Intervention

Experimental Intervention

Remove organs

Implant organs, measure outcome(s) in recipients

Action by VA's Office of Research Oversight Promotes Public Trust

- It was reassuring to see that the VA's Office of Research Oversight (ORO) promptly reached the same conclusion regarding hypothermia kidney transplant clinical trial published by Neimann et al (*N Engl J Med*. 2015;373:405-414).

Undermining Public Trust in Organ Donor Intervention Research

- **ORO's statement: "[G]iven the widespread uncertainty within the transplant community, ORO acknowledges that other federal agencies may well come to different conclusions regarding application of the Common Rule to their deceased organ donor intervention research."**

- **OHRP's refusal to open a formal investigation into Public Citizen's complaint and its failure to take a leadership role by joining with ORO in declaring what should be obvious to OHRP staff: that the hypothermia kidney transplant trial was human subjects research.**

Undermining Public Trust in Organ Donor Intervention Research

- **ORO also noted:**

  "In the course of its review, ORO identified considerable uncertainty and confusion within the transplant community regarding the application of federal human research protection requirements to deceased organ donor intervention research, …

  "For example, a recent survey of transplant surgeons, OPO professionals, and IRB members [Rodrigue et al, *Am J Transplant*. 2016;16(1):278-286] 'found wide variations in their perceptions about research classification, risk assessment for donors and organ transplant recipients, regulatory oversight requirements, and informed consent in the context of deceased donor intervention research.'"

Not So Much Confusion Among IRB Members and Transplant Surgeons

- Online survey of IRB members (n=317) and transplant surgeons (n=294) at 100 U.S. organ transplant centers.
- One scenario: Randomized, controlled trial in which deceased organ donors would be randomly assigned to receive a new agent shown to improve liver transplants outcomes in animals. Investigators would assess whether the donor livers were transplanted and collect clinical data on liver function from liver transplant recipients.
  - 94 % of IRB members and 93% of transplant surgeons considered the study to be human subjects research.
  - 97 % of IRB members and 93% of transplant surgeons said the study required IRB review.
  - 99% of IRB members and 96% of transplant surgeons said transplant patients who are offered a liver from a study donor should be informed of the study. Of these, 90% of IRB members and 82% of transplant surgeons said the patients' written informed consent should be obtained.

Actions That the Committee Should Take (1)

- The Committee first should declare emphatically that organ donor intervention research like the donor hypothermia kidney transplant clinical trial published by Neimann et al represents human subjects research under federal regulations.

- The Committee then should recommend that OHRP and all other federal agencies responsible for the funding, conduct, or oversight of such research issue unequivocal statements to the same effect to the IRB, research, and organ transplant communities.

Actions That the Committee Should Take (2)

- The Committee should conclude that — consistent with the Common Rule and the Belmont Report's principle of respect for persons — investigators conducting organ donor intervention research must obtain the informed consent of the transplant recipient subjects prior to the subjects' involvement in the research.
- The Committee should develop recommendations for enhancing the consent process for the subjects of such research.

Actions That the Committee Should Take (3)

- The Committee's recommendations regarding informed consent should address the following:
  - Waiver of informed consent: In most, if not all, cases, such research will not be eligible for waiver of informed consent under the Common Rule (particularly given the required finding by the IRB that the research could <u>not</u> practicably be carried out without the waiver).
  - Timing of obtaining informed consent
  - Minimizing the possibility of coercion or undue influence
  - Disclosure that there may be unforeseeable risks

Actions That the Committee Should Take (4)

- The Committee should conclude that — consistent with the Common Rule — organ donor intervention research must be reviewed and approved by an IRB.
- The Committee should develop recommendations for enhancing IRB review of such research:
  - Adequate expertise among members or engage external consultants
  - Understand usual transplant care (donor and recipient) and how research will affect that care
  - Minimization of risks

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