

Research Involving Humans

Dr. Michael McDonald and
Nina Preto, Doctoral Student
W. Maurice Young Centre for Applied Ethics, UBC
Responsible Conduct of Research Course
December 3rd, 2008

So far in this course

- Discussed
 - Use of data
 - Publication
 - Conflict of interest
- Now a brief look at the large and complex area of research involving humans

Road map

- What are we talking about and why?
- 7 requirements for ethical clinical research;
- Specific issues:
 - Data collection;
 - Use of human tissue;
- General remarks about RIHS;
- Some current research initiatives in research ethics;
- Concluding comments.

RCR Dec/08

3

3 cases: questions

1. Using excess clinical samples of human tissue for stem cell research
2. Pathology research on knee joints using materials from cadavers
3. Epidemiology research based on patient chart review

Do these raise any special ethical issues? What sort?

RCR Dec/08

4

Tempting answers

- As long as the science is good, we should be able to use the tissue or data
- The results will likely contribute to better health outcomes on a societal scale
- “Donors” won’t likely know or care much
- These uses would not really harm donors – they are dead, unaware, or anesthetised

RCR Dec/08

5

Rejoinders

- What gives scientists the right to use data or tissue contributed and collected for non-research (especially clinical) reasons?
- Why should donors be “conscripts” for science rather than informed volunteers?
- What donors don’t know can hurt them
- Many harms are social and psychological, not just physical; privacy and dignity matter

RCR Dec/08

6

Answers

- Three cases count as research involving humans
- Raise important ethical issues in regard to donors of tissue or data
 - Was their donation informed and voluntary?
 - How might their donation affect their interests?
 - Did their donation contribute to valid & beneficial science?
- Cases come under special rules & processes

RCR Dec/08

7

Complicating factors

- Research involving human subjects, and the ethics thereof, would be much easier if we accepted that the end justifies the means
 - Simple cost-benefit analysis
- But other factors need to be considered
 - Human dignity & autonomy
 - Subject expertise: subjects are experts on their own lives

RCR Dec/08

8

7 Requirements

- For determining if clinical research is ethical
 - Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701-2711.
- Based on analysis of key guidelines, regulations and professional norms
 - History of ethically problematic “cutting edge” research
- Addresses research from conception to formulation and through implementation;
- For each requirement, ask about criteria, decision-maker(s), means of implementation

RCR Dec/08

9

1. Value:

Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701

- Does the research have social, scientific or clinical value?
 - Do total potential gains outweigh potential costs?
- Who decides this?
 - Research sponsors?
 - Research institutions?
 - Researchers?
 - Public?
- Caution: be alert to distorting influences of fame, fortune, & complacency

RCR Dec/08

10

2. Validity

Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701

Is the research “scientifically” sound?

- Bad science → Bad ethics; But good science ≠ good ethics—lots of other considerations;
- Is it appropriate to move to human subjects?
 - What can't we learn through *in vitro* and animal studies that we can learn with humans?
- Choice of the right type of methodology and research design

RCR Dec/08

11

3. Subject Selection

Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701

Fair subject selection

- Based on scientific reasons not convenience, vulnerability, etc.
- Not excluding groups without good reason—eg—scientific reason or susceptibility to risk
- Promote a just distribution of the benefits of research
- Draw subjects from the class of patients likely to benefit

RCR Dec/08

12

4. Risk-Benefit

Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701

- Three conditions
 - Risks to subjects minimised
 - Benefits to subjects maximised
 - Benefits to society and subjects are proportionate to and outweigh risks

RCR Dec/08

13

5. Independent Review

Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701

- Review of full protocol by an independent REB following appropriate standards
 - TCPS, ICH-GCP, professional standards, law
 - Counter self-interest, blind spots, etc.
- BUT major shortcomings with current ethics review
 - Lack of evidence base, quality assurance, and sufficient subject input; excessive reliance on REBs
 - See special issue of Health Law Review (2005) 13, 2-3 on problem areas

RCR Dec/08

14

6. Informed Consent

Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701

- Intended to allow individuals to control their research participation & exercise autonomy;
- Is a process, not a piece of paper
 - Communication/information issues
 - Choice issues
 - Free of controlling influences & manipulation?
 - Lack of competence & diminished capacity
 - Assent/dissent, representation
 - Best interests or substituted judgement?

RCR Dec/08

15

7. Respect For

Emmanuel, Wendler, & Grady, (2000) JAMA (283) 2701

- Potential and enrolled subjects
 - Respect for confidentiality
 - Withdrawal at any time without penalty
 - New information provided
 - Monitoring welfare (e.g., necessary treatment provided; removal/stopping rules)
 - Information about research results and acknowledgement of subjects' contributions

RCR Dec/08

16

Data collection

- See TCPS Section 3 Privacy & Confidentiality
- Exceptions or limitations
 - Public records
 - Mandatory reporting, public health, cancer registries, etc.
- Importance of data protection & stewardship
- More difficult areas
 - Secondary uses of data
 - Biobanks and tissue repositories

RCR Dec/08

17

Tissues

- See TCPS Section 10 Human Tissue
 - A historical reflection: more than just ownership and privacy at stake
- What is at risk?
 - Potential harm to individual (& community)
 - Harms to the research enterprise if there is a perceived breach of trust

RCR Dec/08

18

Mitigating strategies

[TCPS section 10]

General: risk assessment & informed consent

1. Identifiable tissue
 - Can be immediately linked to a particular individual
 - Professional confidentiality & security safeguards
2. Traceable tissue
 - Is potentially traceable to a specific donor provided there is access to additional information-patient record; database
 - Data steward; security
3. Anonymized
 - While tissue was originally collected with identifiers, these have been permanently stripped from the data
4. Anonymous
 - Not linkable to donor—ie identifiers were never collected;

RCR Dec/08

19

But...

- Linkage has potential advantages
 - For present and future research
 - For the subject's present and future health
- Developing ethical protocols for re-linking to health records and recontacting subjects and their physicians

RCR Dec/08

20

General remarks

- Crucial to look at the research through the eyes of research subjects
 - What do they hope or fear, know or don't know?
 - Talk to subjects; research their perspectives
- To become aware of one's own professional and cultural biases and blind spots
 - E.g., role of researchers in therapeutic misconception

Building effective ethics

- Knowledge components
 - Before, during and after research
 - Develop virtuous learning loops
- Volitional aspects
 - Recognise and overcome likely impediments to ethical choice, e.g., conflicts of interest
 - Reinforce good choices
 - Create & sustain an ethical ethos on the research team

Ethics research

- Centring the human subject in health research - Understanding the meaning and experience of research participation
 - Cox, McDonald, J. Kaufert, P. Kaufert
 - CIHR
- Canadian Network for the Governance of Ethical Health Research Involving Humans: Evidence, Accountability and Practice
 - McDonald & 19 others
 - CIHR

RCR Dec/08

23

Concluding comments

- Ethics is NOT just an REB responsibility!!!
- Avoid bureaucratic reductionism in research ethics
 - Ethics = REB approval + signed “consents”
 - Consent forms & REBs are only forms of social control
- Cannot have ethical research without ethical researchers!

RCR Dec/08

24

Useful sources

■ Research ethics

- Weijer, Dickens, Meslin, “Bioethics for clinicians: 10. Research ethics” CMAJ 1997
- Emmanuel, Wendler, Grady What makes clinical research ethical, JAMA (2000) (283) 2701-2711.
- Tri-Council Policy Statement on the Ethical Conduct of Research involving Humans
<http://www.pre.ethics.gc.ca/english/policystatement/policystatement.cfm>
- UBC Research Ethics, Office of research services
- Useful general source: www.ethics.ubc.ca