Responsible Conduct of Research: Human Subjects, Part 2

Describe the Informed Consent process for a study in which you have been involved?

Objectives

- Define informed consent
- Review privacy and confidentiality in research
- Evaluate methods of subject recruitment
- Discuss international human subjects research

What is it Informed consent?

"Informed consent is a decision to participate in research, taken by a competent individual who has received the necessary information; who has adequately understood the information; and who, after considering the information, has arrived at a decision without having been subjected to coercion, undue influence or inducement, or intimidation." CIOMS 2002

http://www.cioms.ch/frame_guidelines_nov_2002.htm Accessed on March 15, 2013

Still on consent

Informed consent is the knowledgeable authorization by a patient (in the case of clinical practice or study) to authorize medical intervention, and one that is in accord with the patient's values and preferences; or in biomedical research, a process by which a prospective participant indicates his or her willingness to be part of a research or study

Purpose of informed consent

Emanuel et al. (2000: 2706) identify a 2-fold purpose of I/C as follows:

"to ensure that individuals control whether or not they enroll in clinical research and participate only when the research is consistent with their values, interests, and preferences."

Still on purpose

- To protect patients/research participants from exploitation by investigators
- To protect researchers/sponsors/institutions from unnecessary litigations arising from research
- To ensure that research is conducted according to accepted ethical norms or principles
- Serves as a statement of contract between researchers and participants

Grounds for informed consent

Robert Levine argues thus:

"the firmest grounding for the requirement to seek consent is the ethical principle 'respect for persons'- a principle which, when interpreted in a Kantian sense stipulates that research subjects will be treated as an end and not merely as a means to another's end"

Informed Consent

- Major component of Declaration of Helsinki, Belmont Report, U.S. Food and Drug Administration and U.S. Department of Health and Human Services Regulations, and Good Clinical Practice guidelines
- **Process**, not a form
- Key element of research involving human subjects

Informed Consent

- Trial involves research, purpose of trial, trial treatment, probability of assignment to each group
- Procedures to be followed, subject's responsibilities, aspects of trial that are experimental
- Foreseeable risks/inconveniences, benefits, alternatives
- Compensation/treatment in event of injury

Informed Consent

- Anticipated payment for participation
- Anticipated expenses
- Participation is voluntary, may refuse to participate or withdraw without penalty or loss of benefits
- Monitor, auditor, IRB, and regulatory authorities have access to medical records for verification, without violating confidentiality
- Records identifying the subject will be kept confidential

Informed Consent

- Subject will be informed in a timely fashion about new information relevant to continued participation
- Person to contact for further information and for trial-related injury
- When participation may be terminated
- Expected duration of the trial
- Approximate number of subjects to be studied

Informed Consent

- Subject should receive copy of informed consent before starting study, and updates as appropriate

5 minute conversation

- How can a non-scientist, non-clinician evaluate what 'risk' means in a clinical study?
  - Would they know the difference between a 2% risk and a 5% risk?
  - Would they know the difference between a "very small risk" and a "slight risk" or a "small risk"?
- How much should they be told about details that they can't really understand but might scare them off?

Objectives

- Define informed consent
- Review privacy and confidentiality in research
- Evaluate methods of subject recruitment
- Discuss international human subjects research

Privacy and Confidentiality

- Procedures must be developed to protect the privacy of subjects and the confidentiality of their medical/research data.
- Research subjects must be informed about the extent to which records will be kept confidential, including a description of who may have access to the research records.

Privacy and Confidentiality

- HIPAA (Health Insurance Portability and Accountability Act)
  - US law to protect privacy of health information
- Genetic information
  - NIH requirement to contribute DNA and other research participant information to central repository for Genome-wide Association Studies (GWAS)

Stored Samples

Tissue, blood or DNA

- Was consent obtained for future research?
- If not:
  - Were samples collected in distant past?
  - Are they anonymous/de-identified?
  - Is someone who has identifying information removing the identifiers and providing de-identified data?
- Was consent obtained only for specific uses?
- Was consent time-limited (e.g., 10 years)?

Stored Samples

- If consent was not obtained for future research, samples can only be used if:
  - Research involves no more than minimal risk;
  - Waiver/alteration of consent will not adversely affect the rights and welfare of the subjects;
  - Research could not be practicably carried out without the waiver or alteration; and
  - Whenever appropriate, subjects will be provided with additional information after participation

Objectives

- Define informed consent
- Review privacy and confidentiality in research
- Evaluate methods of subject recruitment
- Discuss international human subjects research

Subject Recruitment

- Media advertising (e.g., print, radio, TV)
- Posters
- Physician-to-physician letters
- Direct to patient letters/phone calls

Issues in Recruiting Human Subjects

- Recruitment incentives (“bonuses”)
- Dual Investigator-physician role
  - What is best for the subject vs. what is best for the protocol
- Confidentiality of medical records
- Financial disclosure – to subjects, regulators
- Subject compensation

Objectives

- Define informed consent
- Review privacy and confidentiality in research
- Evaluate methods of subject recruitment
- Discuss international human subjects research

Why International Research?

- Economic, epidemic, and regulatory contributions to the "fluid map" of clinical trials (Petryna 2006)
  - Economic: recruitment costs, background costs
  - Epidemic: numbers of patients, lack of access to care
  - Regulatory: 1994 change in NIH rules, many countries have loose research oversight

Whose Standards Apply?

- Lurie & Wolfe 1997
- How do we resolve issues of context when considering the ethics of research?
  - Context and the experiment-therapy dilemma
  - Context and clinical equipoise
- What should be considered the standard of care?

Providing Care through Clinical Research: Incentive, Exploitation, or Benefit?

Some of our patients cannot pay for antiretrovirals, "not even one baht" (THAIDS pediatrician)

- When can the export of clinical research reflect principles of justice – both risks and benefits?
- When can a person be considered vulnerable to a potentially exploitative clinical trial?

Post-study Care

"Although we stated clearly in our consent forms that we could not promise post-trial drug supply, we were compelled to take action when faced with the tragic prospect of watching patients reversing their excellent quality of life gained while on antiretrovirals"

"During the first few years at THAIDS…we not strong enough" to require post trial drug support for former study subjects, because companies "just go to some other site"

- How do we account for post-study care within current ethical structures?
- How can we balance public health impact of clinical trials with individual impact for participants?

What is Owed Local Medical Systems?

For example, right now, we are going to do a nutritional trial using some biscuits from [Europe]. To be given to people who still don't need the antiretrovirals, to see the immune response, something like that, as compared to placebo. Just look at the CD4+ count, viral load, and the clinical manifestations. We proposed that we should do a good nutritional assessments. Anthropometrics…biochemical assessment, and nutrition (macronutrients, micronutrients, and so on). Although this was not initially put in as one, in the protocol. So we try to submit as a sub-study. We don't know how, how lucky we will be able to convince the sponsor to do that. But this is something we think,…**because as I always think, if we are going to do research for this types of study, for biscuits, instead of being beneficial for the biscuit producer we should have some benefit for our own**, in terms of our own interest in nutrition, in some…so we can do some of our own research.

(HIV research clinic director, Thailand)

Context and Informed Consent

- Age of majority for women: 16 or at marriage
- Married women have no recognized autonomy from their husbands
- Consequences of divorce include loss of property, severing of rights to children, and no mechanism for alimony
- When does a participant need parental consent?
- Can a woman give independent consent?
- What if a woman wishes to participate, but the husband disagrees?
- What if a woman does not wish to participate, but the husband disagrees?

Logistics of Clinical Trials

- What are the consequences of the form of clinical trials, and how do these forms interact with patient vulnerability?
  - Parachute research
  - Annexed sites
- IRBs, Ethical Boards, local oversight: Do they work?
  - Documentary compliance vs. deep compliance

Philosophical basis of I/C

- Based on several lines of philosophical reasoning: the need to protect and maintain human dignity
- Based on the Hippocratic admonition "to help, or at least, to do no harm"- a way to promote patient or subjects' benefit and welfare

Philosophical basis of I/C

- I/C can be justified on the grounds of social benefit: producing the "greatest good for the greatest number" (utilitarianism)
- Based on the ethical norm of "respect for persons"- not to treat persons as means but as ends (Kantianism)

Religious basis for I/C

Some basic tenets of religions provide a basis for informed consent, e.g., the teaching that each individual's life is a gift from God and is of infinite worth (the "sanctity of life")

Legal basis

The Nuremberg trials and sentencing of Nazi physicians after WW II and some other cases of litigation arising almost exclusively in the context of medical practice provide legal grounding for informed consent, e.g., a 1914 legal judgment in America: *Schloendorff v. Society of New York Hospital*

This is a case about court findings that surgery ought not to have been performed on a patient who had agreed to an abdominal examination under anaesthesia but had declined an operation

The legal basis (2)

The *Schloendorff v. Society of New York Hospital* case is one about court findings that surgery ought not to have been performed on a patient who had agreed to an abdominal examination under anaesthesia but had declined an operation

The legal basis (3)

In the famous statement which eloquently expressed the view of the right of competent people to self-determination, the Judge demurred, saying:

> Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault.

- What are some Informed Consent issues you think need to be addressed to responsibly conduct research?

University Policies and Procedures

Questions & Discussion