RESEARCH METHODOLOGY AND ETHICS

Informed Consent Process

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Objectives

- To describe a topography of informed consent
- To describe relevance in research ethics training
- To have time for discussion

Informed Consent

Most codes dealing with human experimentation start out with the bland assumption that consent is ours for the asking. This is a myth. The reality is that informed consent is often exceedingly difficult to obtain in any complete sense…Nevertheless, it remain a goal toward which one must strive for sociological, ethical, and legal reasons."

Henry Beecher Ethics and Clinical Research, NEJM, 274:1354-60, 1966

Informed consent is the bedrock principle on which most of modern research ethics rest…This was at the heart of the crucial ethical provision stated in the first words of the Nuremberg Code, and it remains equally compelling a half century later.

Menikoff J, Camb Quarterly 2004 p 342

Why do People Participate In Research?

- Altruism
- New options and alternatives
- Free medical care and medications
- Trust
- Self-interest
- Attention
- What is the right reason? Will be dependent on individual?
- Do we want to constrain people if we think they are doing things for the wrong reasons?

- Informed consent process helps provide a structure for providing all individuals with relevant information that allows an informed choice

INFORMED CONSENT
Then and Now

"I don't know what they used us for. I ain't never understood the study."

Survivor of Tuskegee Syphilis Study, 1932-72

"It looked safe. It was presented as safe. I encouraged my son to do this. But I wasn't given all the information. And some of the information I was given was not true…. I have come to the painful conclusion that I was fairly naive to have trusted the investigators."

Paul Gelsinger, father of 18 y.o. subject who died in gene therapy trial, 1999

Article No. 1 of the Nuremberg Code, 1947

"The voluntary consent of the human subject is absolutely essential."

CIOMS*

- For all biomedical research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or, in the case of an individual who is not capable of giving informed consent, the permission of a legally authorized representative in accordance with applicable law. Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee

*Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization

Informed Consent

- Respect for Persons autonomy or for an individual's capacity and right to define own goals and make choices consistent with those goals.
- Well entrenched in societal values, jurisprudence, medical practice, and clinical research.

INFORMED CONSENT: INTERNATIONAL GUIDELINES

- National and international guidelines recognize informed consent is an essential requirement for ethical conduct in scientific research.
- Consensus about core components of informed consent, but application often differs

CHALLENGES: INFORMED CONSENT

- Scientific concepts difficult to communicate.
- Consent forms lengthy, confusing, difficult to understand.
- Translation of consent forms from one language to another problematic.
- IRB requirements for informed consent (e.g., written documentation) do not always mesh with local realities.

Informed Consent as a Social Process

- Higher congruence between researcher/ participant, greater likelihood of consent conditions.
- Greater dissonance, less likely to achieve consent conditions.
- Goal: develop strategies to diminish dissonance.

What is Informed Consent

- Authorization of an activity based on understanding what the activity entails.
- A legal, regulatory, and ethical requirement in health care and in most research with human subjects
- A process of reasoned decision making (not a form or an episode)
- One aspect of conducting ethical clinical research

Informed Consent: More than just a form

- Consent is a PROCESS in which…
  - investigator discloses all relevant information
  - potential subject has opportunity to ask questions
  - investigator answers questions
  - repeat the above, as much and as often as needed
- The consent form is a record of …
  - information conveyed
  - subject's willingness to participate

The Consent Process

- Ensure respect for individuals' values & preferences in decisions about their research participation
- Consent Process is not a single event or signed form - it is an educational process that occurs between the investigator and the subject
- Consists of
  - full disclosure of nature of research and subject's participation
  - adequate comprehension by the potential subjects,
  - the subject's voluntary choice (freedom from coercion)
  - Commitment to provide new information as appropriate

Considerations Consent Process

- Who is being asked to consent?
  - Are they able to decide and communicate a decision (competency)?
  - Who is legally authorized rep?
- Where is consent obtained?
- When is consent obtained?
- Who obtains consent?
- How do we assure a subject understands?

Conditions : Consent process

- Seek consent under circumstances that provide the prospective subject or the representative
  - opportunity to consider whether or not to participate
  - minimize the possibility of coercion or undue influence.
- Coercion: The act of compelling by force of authority
- Undue influence: An unjust, improper, or illegal power affecting a person
- Language understandable to the subject or the representative.

Elements of Consent

- participation is voluntary;
- may refuse/withdraw; no penalty or loss of benefits otherwise be entitled;
- the purpose,
- explanation of how the research differs from routine medical/psychological care; if applicable
- research design (e.g., randomization, double-blinding)
- number, duration of visits, the total time involved, possibility of early termination of the trial and why
- explanation of research procedures
- potential foreseeable risks/harms (pain, discomfort, inconvenience, social or economic)

Elements of Consent (cont)

- potential benefits, (direct to subject/indirect to society) if any
- alternatives if any and applicable
- provisions privacy and confidentiality including limits and risk of breaches
- compensation (money or other goods)
- provisions for research related injuries
- contacts for questions (research and research subject rights)
- what happens when study ends

Other Potential Elements

- Sponsors of the research
- potential for unknown risks
- risk to fetus pregnant or nursing women
- incidental finding : genetics, imaging, depression, suicidality, mandated legal reporting (abuse neglect, communicable diseases)
- tissue issues: secondary use, storage, ability to withdraw, distribution, potential for development of commercial products
- whether the investigator is only investigator or both investigator and the subject`s physician;
- investigator's responsibility to provide medical services to the participant

Who provides consent

- Competent adults consent for themselves
- If not competent ; legally authorized representative
  - for children it is parents
  - mentally incapacitated ; psychiatric, dementia, clinical state
  - ability to consent for clinical care may not translate to consent for research
  - must consider local laws for age of majority etc.

Do you always need written consent?

- Regulations and guidelines allow IRB/REC to waive the requirement for written consent
- CIOMS "*Waiver of informed consent is to be regarded as uncommon and exceptional, and must in all cases be approved by an ethical review committee.*"
- Will not apply to drug/device clinical trials
- Used in survey, observation

Emergency Situations

- Life-threatening situation necessitating test article
- Subject unable to give consent
- No time for authorized representative to consent
- No alternatives
- You need to understand local regulations, laws and guidelines to determine if this is permissible

Vulnerability - Mentally Incapacitated

- Emotional, psychiatric, dementia, clinical state , developmental disabilities
- Consider risk of research: minimal or greater than minimal
- Consider potential for benefit
- Caution against exclusion
- Is research related to their condition or could you use another population?

Extra Protections: Mentally Incapacitated

- Who determines competency? (research or uninvolved individual)
- Use of subject advocate in addition to guardian or caretaker
- Advanced directives when possible
- Assent from the individual, when feasible
- Ensure understanding by the caretaker

Other Vulnerability Categories

- Children-
  - limits on amount of risk after considering potential benefits
  - one or both parents permission
  - assent form those capable
  - what is age they can consent for themselves
- Pregnant women-
  - risk to fetus
  - does father also need to consent?

Other Vulnerability Categories

- Individuals whose rights have been limited (prisoners)
- Economically and socially disadvantaged
- Terminally ill
- Students

- Exercise: Describe why these groups are vulnerable in regards to obtaining consent and what extra steps can be taken protect them

Other Challenging Issues

- Storage of Specimens/Data for Future Unspecified Research
- Ongoing Consent
- Developing Countries
- Cultural Sensitivities
  - Community Consent
  - Oral Traditions
  - Language barriers
- Trust

Storage of Specimens/Data for Future Unspecified Research

- Increasingly common approach
- Challenging for IRB, investigator and subjects
- Points to consider
  - Where will specimens be stored?
  - For how long?
  - Who has access?
  - With or without identifiers?
  - Re-consent for specific use?
  - Re-contact?
  - What if clinically relevant findings?
  - Potential for commercialization?

Ongoing Consent

- New Information: ethical obligation to share with subjects
  - newly identified risks
  - new standards of care may alter risk .benefit
- Re-visiting consent decision
  - long term studies
  - when capacity to consent may change
- Longitudinal studies with children/adolescents
  - mechanism for re-consenting at age of majority

Cultural Sensitivity Community Consent

- May be necessary for research in certain communities (Tribal chiefs, Spiritual leaders)
- Adds an element of security in traditional societies where communal consciousness and living is the norm
- Predicated on the presence of a legitimate political /social system
- Consult with community leaders
- Need opportunities for individuals to seek advice or permission from third person, such as a spouse or head of household, community leaders
- Community consent does not replace the requirement for individual consent

Cultural Sensitivity: Oral Traditions

- Cultural emphasis of oral contracts and importance of the spoken word.
- Researchers need to understand cultural differences and what the community deems appropriate.
- Adapt methodologies to fit the cultural context where study takes place .
- Recognize a fundamental reconsideration of what qualifies as “genuine consent” given the cultural context.

Cultural Sensitivities: Language Barriers & Interpreters

- Interpreters:
  - used for more than obtaining consent
  - have a better understanding of the cultural norms of the community than the researcher.
  - advise the researcher on culturally appropriate ways to initiate contact with participants, interact with participants, or ask questions of participants.
  - avoid family members as interpreters
- Words or concepts in one language may not translate directly to another language.

Literacy

- Participants in developing countries and some in developed countries may not be - literate and cannot give informed consent through signing forms
  - Instead of using written waivers and consent forms, researchers can sign a form indicating that the appropriate information was given to the participant and that verbal consent was received.
  - Both the information communicated to the participant and the participant's verbal consent may be recorded on audio tape and/or may be performed in front of an independent witness.

Developing Countries

- Participants believe that they must participate in the research study in order to receive medical care or treatment.
- The researcher must make sure that it is clear to participants that they may receive medical treatment without automatically having to consent to participating in the study. If this is not made sufficiently clear, participants may feel coerced into participating without the researcher being aware of it.

Developing Countries

- Mechanisms of obtaining informed consent in developed countries evolved in communities that are literate and generally aware of modern health practices. Researchers can therefore engage the potential subjects on the basis of pre-existing scientific knowledge and concepts. These mechanisms are non-functional in non-literate communities and/or communities with different conceptions of health and disease.

- Researchers must carefully redesign their informed consent procedures in a manner that takes into account the characteristics of the community. A one-size-fits-all approach will not satisfy the principle of genuine informed consent.

Trust may play a major role in the informed consent process

"There's not a lot you can control when you're sick, so you have to rely on your doctors…if he suggests you should go into a research project, I think you should really take his advice…they would never steer you wrong."

Patients assumed that they need not pay attention to what was written… or that although the form was not particularly readable, it did not matter. The stories these patient-subjects told about why they decided to participate in research suggest that the current emphasis on… autonomous decision making is insufficient. The paradigm must be [sensitive] to the profound trust participants place in researchers and the research enterprise.

There may also be pockets of mistrust that prevent communities from participating (i.e black community in United States)

From the ACHRE Subjects Interview Study, Kass, Sugarman, Faden, Schoch-Spana, Hastings Center Report, 1996

Group Exercises

- Cases 1- 5
- Discussion on examples of obtaining informed consent for research that present challenging or problematic situations