ITHS
Institute of Translational Health Sciences

Resolving Ethical Dilemmas in Clinical Research Studies

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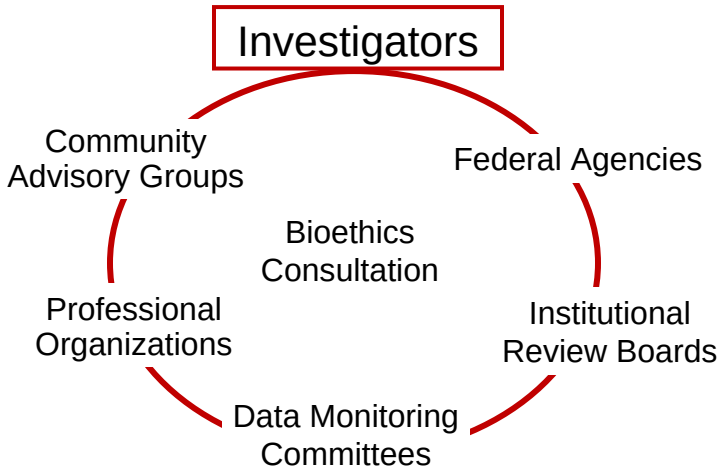
UW Bioethics & Humanities

Regulatory Support & Bioethics Cores

Ethical Dilemmas Can Arise Mid-Study

- What should I do if a participant doesn't have the capacity for consent?
- Can I withdraw a participant against his/her wishes?
- What must I do if my participants need medical care or other help?
- Should I tell participants about their research findings?
- What if a participant requests their data be withdrawn?
- How should I share the research data with the community?
- How should I negotiate disagreements with community stakeholders?

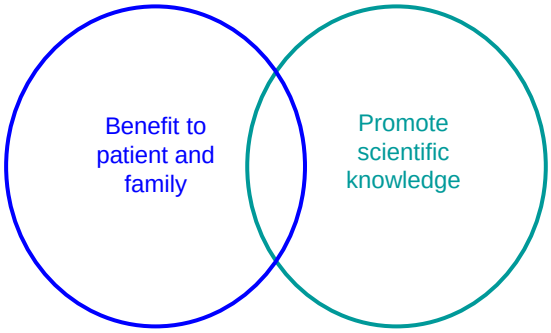
Ethical and Regulatory Engagement and Oversight



Framing Questions

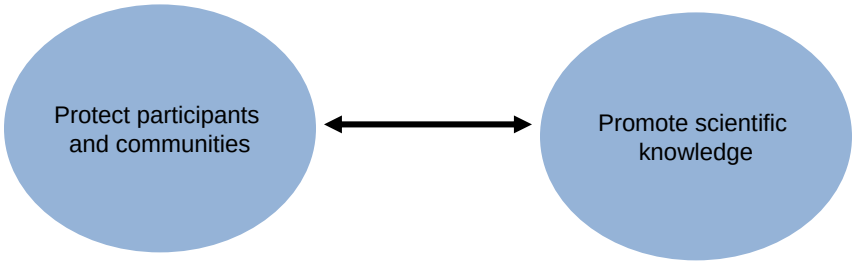
- How is the goal of research different from clinical care?
- What is the mission of research oversight?

Goals are Constrained by Ethical Obligations



Joffe and Miller. Hastings Center Report 2008

Why Research Oversight?



Especially Challenging Concerns Surround *Disclosing Research Information* to:

- Research participants
- Family members
- Communities

Research Participants

- When is it appropriate to provide new information about the efficacy or safety of approved medications provided during a study?
- What overall (*aggregate*) findings from the study should be shared and how might such sharing influence on-going research participation?
- Is there an obligation to disclose *individual* research findings, and does it matter if such findings were discovered incidental to the primary study aims?
- Is disclosure of prior findings required if investigators want to recruit study participants for follow-up research?

Family Members

- When the provision of research findings to one research participant will indirectly reveal information about close family members, must all agree to the disclosure?
- Should investigators disclose to a "healthy" adolescent that he should not be a stem cell donor to his adult sister because he may carry the same genetic defect, even though he expressed wishes to not know if he is a carrier?
- To what degree are investigators responsible for ensuring that health risks revealed by research participation (e.g. a hereditary genetic condition) are conveyed to potentially affected family members?

Communities

- What aggregate study findings are most appropriate to share with the broader community and how is such sharing best accomplished?
- How should result disclosure/dissemination proceed when there are concerns that research findings could paint a specific community in a poor light?

The best approach to resolve these questions?

- See what the consent form says
- Ask a colleague what they would do
- Ask the IRB what to do
- Decide based on what is ethically appropriate to protect the rights and welfare of participants
- Ask for a Research Bioethics Consult

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Consent versus Consent Form

- Consent is not always ethically justified (Voluntary vs. Mandatory participation)
  - Influenza vaccine trial vs. Reporting influenza to CDC
- Must distinguish between consent and "documentation"
  - A *signed* consent *form* is neither necessary or sufficient for valid *consent*

Forms May Not Provide Good Guidance

- May not address the issue at all
- May state the opposite of what is in research protocol
- May state the opposite what would otherwise be appropriate
- Multiple consent forms may provide conflicting solutions
- Some may include multiple choice check box responses that are inconsistently completed

Consent Form Should Not Be Regarded as a Contract

- Cannot be negotiated like many other contracts
- Does not typically provide guidance for addressing contract breaches
- May not be read by many participants
- May not be understood by many participants
- May further reduce effectiveness of consent forms as a communication tool in promoting understanding

Another Take on Consent Forms?

- Consent forms can *guide* others to interpret decisions *about future use*
  - Like advance directives in clinical medicine
- Consent forms can be important to help participants *decide to join* a study

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Federal Policy for the Protection of Human Subjects

- "Common Rule"
- 45 Code of Federal Regulations (CFR) Part 46, Dept Health & Human Services
- http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

Human Subjects Protections

Belmont Report, 1979

- **Respect for Persons**: protecting the autonomy of all people and treating them with courtesy and respect;
- **Beneficence**: maximizing good outcomes for humanity and research subject, while minimizing or avoiding risks or harm; and
- **Justice**: ensuring reasonable, non-exploitative, and well-considered procedures are administered fairly (the fair distribution of costs and benefits).

http://ohsr.od.nih.gov/guidelines/belmont.html

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When Should We Return Results?

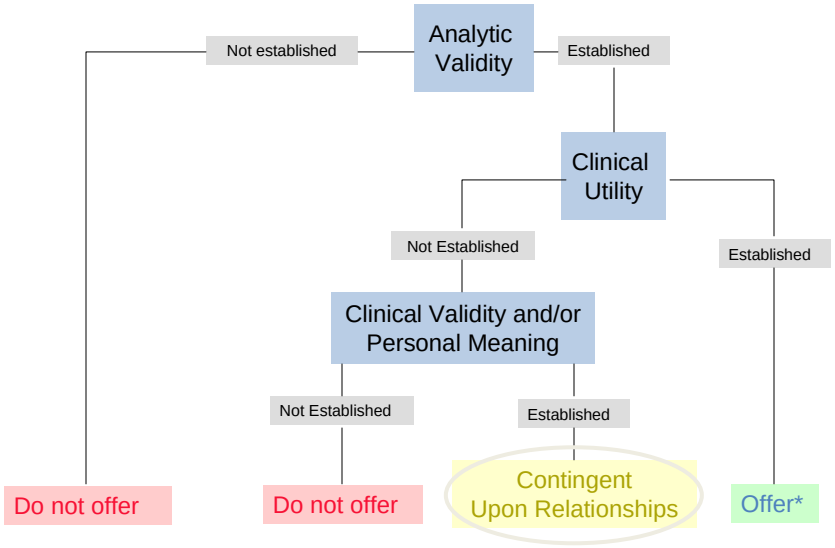
Research focused approach
Limited obligations, unless clear benefit

Autonomy focused approach
Broad obligations, unless clear harm

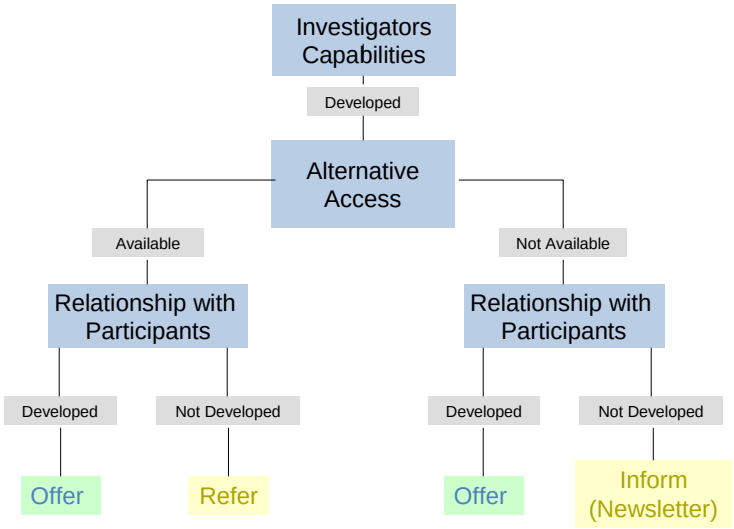
Result evaluation approach
Informational considerations
Relational considerations (contextual)

Ravitsky and Wilfond. AJOB 2006

Informational Considerations



Relational Considerations



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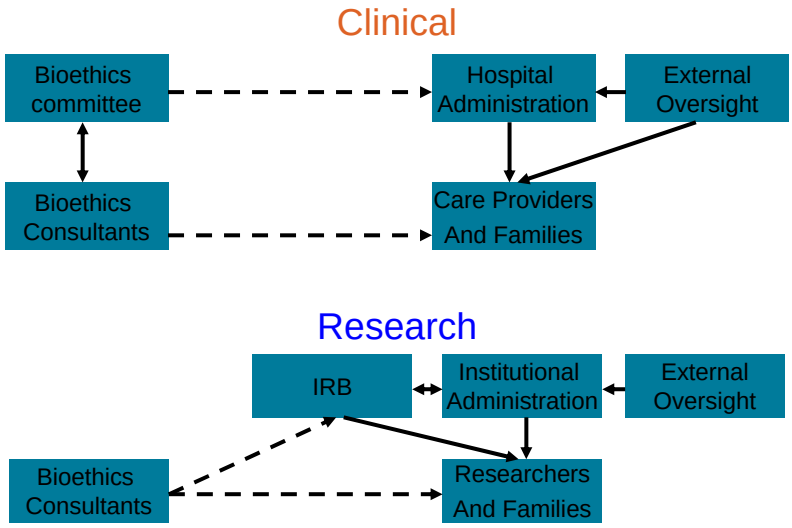
ITHS Bioethics Consultations

- Providing a forum for discussion and analysis of ethical issues in clinical and translational research
- For researchers, research staff and trainees, IRBs, research participants and their families, and communities
- Advisory to requestor
- Supplemental to IRB or DMC oversight
- Conducted via phone, email or in person
- Written report can be provided

Bioethics Consultation and Oversight



Research Bioethics Consult Questions

- **Community engagement:**
  - How can I establish sustainable relationships with communities?
  - How should I negotiate disagreements with community stakeholders?
  - How should I share the research data with the community?
- **Study Development:**
  - Should I provide incentives for participation?
  - What if informed consent isn't practical for my study?
  - When is a placebo-control ethically appropriate?
- **Study Implementation:**
  - What should I do if a participant doesn't have the capacity for consent?
  - Can I withdraw a participant against his/her wishes?
  - What must I do if my participants need medical care or other help?
- **Study Analysis:**
  - Should I tell participants about their research findings?
  - What if a participant requests their data be withdrawn?
  - Who should be an author on the publication of my study?

All in the Family:
Disclosure of "Unwanted" Information to an Adolescent to Benefit a Relative

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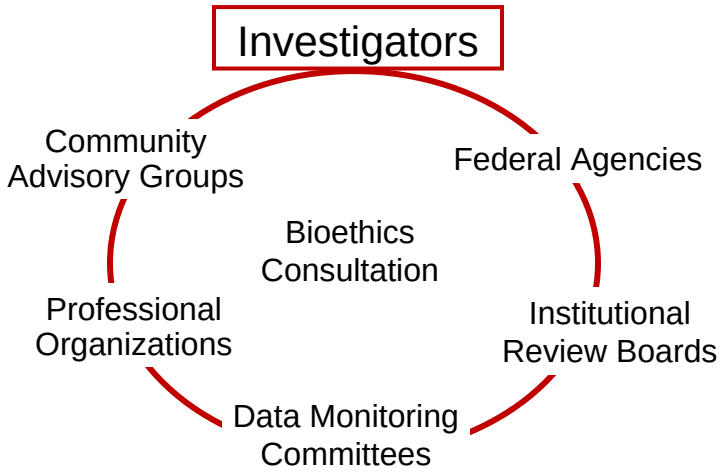
Ethical assessments of clinical decisions are typically based on the preferences and interests of the individual patient. However, some clinical interventions, such as genetic testing or organ donation, may involve multiple family members. In these cases, one family member may have the potential to benefit, while another family member is exposed to potential physical or psychological risk. In the research setting, the balancing of benefits and risks between family members may be further complicated by uncertainty about their magnitude and likelihood. In addition, when the individual facing these apparently uncompensated risks is a child, the situation becomes particularly ethically complicated, as we appreciated in a recent case. Investigators at the National Cancer Institute were faced with a decision about whether it would be appropriate to disclose apparently "unwanted" research test results (length of telomeres in leukocyte subsets) to an adolescent about risk of future disease (dyskeratosis congenita), possibly causing psychological harm and an ethical wrong. These issues were not expected at the outset of the family's study participation but rather emerged with new data about the research tests. Disclosure of the research finding was an important consideration in order to avoid using the adolescent as a stem-cell donor for his sister. Disclosure to the adolescent could not be justified by merely considering the immediate interests and preferences of the adolescent. However, an expanded ethical analysis that considers the adolescent's familial context offers a more complete picture of the adolescent's interests and preferences which provides justification for disclosure.

Key words: ethics; genetic disclosure; minor children; dyskeratosis congenita; research results

Consult Recommendations

- "All in the family"- Disclose results to adolescent
  - Not clear how much weight to place in initial decision to not know results
    - Not aware of implications for sister
    - Has expressed interest in helping sister
  - Disclose results and implications in person

Ethical and Regulatory Engagement and Oversight



Beyond Consultation: Governance of Research-Related Decisions

- Partnerships between investigators, participants, communities, sponsors, data monitoring committees, community advisory boards and IRBs
- Some projects may benefit from explicit committees with ongoing engagement and oversight
  - National Children's Study
  - Electronic MEdical Records & GEnomics Network
- Developing, implementing and modifying plans for
  - Community engagement
  - Communication of findings with participants and communities
  - Returning results to participants
  - Consent form interpretation

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