Resolving ethical dilemmas that emerge during a research study

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Ethical and regulatory engagement and oversight

Investigators
Institutional Review Boards

Federal Agencies
Professional Organizations

Bioethics Consultation

Data Monitoring Committees
Community Advisory Groups
Ethical issues can arise during a study that are related to disclosing research information to:

- Research participants
- Family members
- Communities

Dilemmas about contacting research participants

- To Provide Information
  - New information about efficacy or safety of approved medications provided during a study
  - Aggregate Results Disclosure
    - May be relevant to continued participation in current study
  - Individual Results Disclosure
    - MRI findings suggestive of a mass
    - Unusual genetic finding
    - Pregnancy in an adolescent

- For Recruitment
  - To permit further research on collected data and samples
  - To permit recruitment for further research studies
Implications of research findings for family members

• Should investigators disclose information to an adult daughter about BRCA status, against the wishes of the father?

• 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 carries that defect?

• How should investigators advise a father in research study who learns that his lung disease is hereditary about contacting his adult daughter whom he gave up for adoption and who recently requested no further contact with her father?
What is the best approach for investigators to resolve these questions?

• A. Decide based on what is ethically appropriate to protect the rights and welfare of participants

• B. Decide based on what will facilitate further research

• C. See what the consent form says

• D. Ask the IRB what to do

• E. Ask for a Research Bioethics Consult
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

- Benefit to patient and family
- Promote scientific knowledge

Clinical Care  Research

Joffe and Miller. Hastings Center Report 2008
What is our mission?

- Protect participants and communities
- Promote scientific knowledge

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Consent vs 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

Consent forms may not provide good guidance

• May not address the issue at all

• May state the opposite 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
Why we should not think of the consent form as a contract

- Can not 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

A kinder and gentler approach to 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*
Consent forms: helping participants to decide to join a study

- Keep information focused and brief to promote understanding
- Keep options open
  - “We may contact you for lots of reasons”
  - “We will do lots of stuff with your information”
- “Supplemental information” available about
  - What all participants should know before they decide about any study
  - What some participants might want to know to decide about this study
  - What all participants need to know once they join this study
  - What a lawyer might want to know

Our initial dilemma: When should we return results?

<table>
<thead>
<tr>
<th>Research focused approach</th>
<th>Autonomy focused approach</th>
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<tbody>
<tr>
<td>Limited obligations, unless clear benefit</td>
<td>Broad obligations, unless clear harm</td>
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Result evaluation approach
- Informational considerations
- Relational considerations (contextual)

Ravitsky and Wilfond. AJOB 2006
Informational Considerations

- **Analytic Validity**
  - Not established
  - Established

- **Clinical Utility**
  - Not established
  - Established

- **Clinical Validity and/or Personal Meaning**
  - Not established
  - Established

- **Contingent Upon Relationships**
  - Offer

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Relational considerations for results with *personal meaning but without established clinical utility*

- **Investigators Capabilities**
  - Developed

- **Alternative Access**
  - Available
  - Not Available

- **Relationship with Participants**
  - Developed
  - Not Developed

- **Offer**
  - Refer
  - Inform (Newsletter)
Consult recommendations

• "Deliberate deceit" - Do not disclose results to daughter
  • We don’t really know that the father has not told his daughter
  • Maintaining an alliance with the father may be instrumental to the parent later deciding to inform the daughter
  • Continue to engage with father

• “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

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

Clinical

- Bioethics committee
- Hospital Administration
- External Oversight
- Bioethics Consultants
- Care Providers And Families

Research

- IRB
- Institutional Administration
- External Oversight
- Bioethics Consultants
- Researchers And Families

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?
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Research governance

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

• Developing, implementing and modifying plans for
  • Community engagement
  • Communication of findings with participants and communities
  • Returning results to participants
  • Consent form interpretation