The NIH Clinical Center Department of Bioethics: clinical care and clinical research

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Outline

The NIH CC Department of Bioethics

Tension between clinical research and clinical care

Examples from the CC Bioethics Consultation Service and other activities
CC Department of Bioethics Mission

Address ethical issues in clinical care, clinical research, and public health

Support and complement the CC and NIH mission of improving human health through scientifically and ethically rigorous research, training, and patient care.
To fulfill Dept. Bioethics mission and contribute to the CC and NIH mission:

Provide high quality consultation to CC and NIH research participants and clinical, research, and administrative staff

Educate the NIH community and others about bioethics

Conduct research on important and timely bioethical issues

Train the next generation of bioethics scholars, educators, and consultants
Clinical Research and Clinical Care
<table>
<thead>
<tr>
<th>Differences</th>
<th>Clinical Research</th>
<th>Clinical Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goals</td>
<td>Answer valuable questions to science, clinical practice, or public health</td>
<td>Benefit the patient</td>
</tr>
<tr>
<td>Methods</td>
<td>Utilize methods such as randomization, double-blinding, dose-escalation, strict schedules of tests/interventions</td>
<td>Utilize standard methods for diagnosis, prevention, &amp; treatment tailored to patient circumstances</td>
</tr>
<tr>
<td>Justification for risks</td>
<td>Risks (of extra scan or blood draw, for e.g.) justified by importance of knowledge to be generated</td>
<td>Risks justified by potential benefit to patient</td>
</tr>
<tr>
<td>Uncertainty</td>
<td>Uncertainty about outcomes is starting point</td>
<td>Interventions chosen based on evidence and experience</td>
</tr>
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</table>

**Ethically salient differences between clinical research and clinical care**
Tension can manifest in decisions about:

- Study design
- Recruitment and eligibility
- Informed consent
- Procedures and monitoring
- Dose or intervention modifications
- Withdrawal and study termination
Overlap between clinical research and clinical care

Clinical research often includes persons with illnesses who are seeking care and treatment. Research aims can include therapeutic benefit for participants. Quality clinical care is provided to research participants by physicians, nurses, and other health care providers in hospital settings.
Active protocols, first 2 quarters 2017

- Screening
- Training
- Natural history
- Sample Data Analysis
- PD/PK
- Clinical Trials

Courtesy of Kim Mitchell, Office of Protocol Services
Clinical Research Spectrum

Clinical research with little clinical care:
- PET, MRI, or other imaging studies, Phase 1 vaccine safety testing in healthy volunteers

Clinical care is the focus of clinical research:
- Randomized, double-blind, placebo controlled crossover trial for a major disease
- Natural history study...
  “All procedures and tests done in this study are part of standard medical care. No experimental drugs or treatments will be used.”
Ethical relevance - clinical research and clinical care

Clarity about how clinical research differs from clinical care facilitates:

1. Negotiating tensions between rigorous science, the protection of research participants, and good clinical care.

2. Negotiating role tensions of clinician/investigators

3. Assuring that participants are well informed
How does CC Bioethics play a role?
Clinical research raises challenging questions about how to collect useful data while respecting participants’ rights and providing good care.

Multidisciplinary professionals trained in ethics help researchers and others answer these questions.

Ethics professionals are integrated at NIH from helping to develop and implement policies, design and approval of studies (IRBs), study conduct and patient care (rounds and consultation), discharge and reporting results.

Provide consultation and subject matter expertise in complex situations.
CC Department of Bioethics

Participation on IRBs, DSMBs, NIH Committees, Study sections, etc.

NIH Ability to Consent Assessment Team (ACAT)

Bioethics Consultation Service
Participation on IRBs

12 NIH Intramural IRBs*

Each IRB has a ‘bioethicist’ as a primary voting member
“An ethicist or individual who has expertise in the ethics of human subjects protection.” SOP#2, OHSRP

Bioethics fellows as observers
Research Ethics Education

Ethics Grand Rounds

Ethical and Regulatory Aspects of Clinical Research

Other (e.g. clinical fellows, psychiatric fellows, nurse interns, pastoral interns, FIC international trainees, Bioethics Interest Group, etc.)
Bioethics consultation service

Clinical ethics consultation

Research ethics consultation

Lead consultant and fellow from Bioethics, members of the CCEC.
Bioethics consultation service

24/7/365 service

Requests from anyone at NIH

Written reports- analysis and recommendations

Consult database

301-496-2429, page operator, or through CRIS
CC Bioethics Consultations by Year

Total Consultations Called

Year
88 212 171 112 131 137 148 146

Courtesy of Akilah Jefferson, Sophie Gibert, Marion Danis
Consult requests 2016
Bioethics Consultation Service Consult Issues (2016)

- Consent: 51 consultations
- Recruitment/Enrollment: 44 consultations
- Research Involving Children: 21 consultations
- Decision-Making Conflict: 17 consultations
- End of Life: 14 consultations
- Confidentiality: 10 consultations
- Advanced Directive/DPA: 9 consultations
- Treatment Off Protocol: 8 consultations
- Communication Problem: 7 consultations
- Transplant Question: 6 consultations
- Truth Telling: 5 consultations

N= 270

Courtesy of Akilah Jefferson, Sophie Gibert, Marion Danis
Clinical care and clinical research
Ability to consent assessment team (ACAT)

- Voluntary informed consent - important protection for participants of research.
- Some important studies involve persons with questionable capacity or without capacity to provide their own consent because of cognitive impairment or other factors that reduce their capacity to understand or make decisions, e.g. Alzheimer’s study, alcohol studies, studies of rare genetic diseases, neurological diseases, others.

- ACAT (Bioethics and NIMH Human Subjects Protection Unit) offers an important service to safeguard research participants.
- Protocol-related and unplanned, examples.
Ability to consent assessment team (ACAT)

ACAT offers:
- Independent assessment of consent capacity,
- Assistance in identifying and assessing an appropriate surrogate when indicated,
- Assessment of capacity to appoint a surrogate,
- Assent and dissent monitoring

Policy and SOP

Assessment Tools

Process

Outcomes
Consultation example: study planning

Background: NIMH proposing a study of the Neurobiology of suicide. Goal to evaluate neurobiological risk factors for suicide. Enroll several cohorts of individuals from emergency rooms, local psychiatrists, or inpatient psych units, including those with recent suicidal ideation or attempt.

Consult request- advice regarding enrollment and consent from actively suicidal patients
Consultation example: neurobiology of suicide

Ethical significance: Ethical clinical research requires protecting rights and welfare of research participants and obtaining their voluntary informed consent. Persons who are actively suicidal are at particular risk of harm (pose a risk of harm to themselves), may have compromised capacity to protect their own interests (e.g. may readily accept risk because they disvalue their lives and may be pessimistic about future), and may have reduced consent capacity.

Recommendations: Informed consent- ACAT to assess consent capacity and monitor consent. Participants well informed that treatment may be delayed, that they may be discontinued from or withdraw from the research but may not be able to leave without special arrangements. Research team needed plans for participants who changed their minds, are not eligible, or are at significant risk of harm. Plans for mitigating risk and post-study continuity of care.
Consultation example: study design issue

Request from a research participant about the design of oncology studies, especially eligibility criteria for cancers with poor prognosis.

Ethical issue: Regular practice, based on protection of participants, to require completion of standard chemotherapy before enrollment in investigational cancer protocol. Patient argued that for certain aggressive cancers, in which very few respond to standard chemotherapy, this practice does not protect the patient or serve his interests. He suggested an alternative design which would allow some patients to enroll without standard chemo.

Bioethics consultation service discussed issue with the patient and his wife on multiple occasions, brought his concerns, ideas, and rationale to the study team and the IRB chair. Case was presented at Ethics Grand Rounds and to a national collaborative on research ethics. Commentary in a bioethics journal
Consultation examples: study participation

The appropriateness of particular persons as research participants? Tension between concern about the integrity of the science, risk to the participant, patient’s clinical needs, and the complexity of patient circumstances

Examples:

◦ A potential research participant recruited for a study of a new chemotherapeutic agent who lived in a rural area without a phone, limited social support, and little money.
◦ A potential research participant with a history of mental illness and substance use which may make it difficult to follow an intense inpatient protocol regimen
◦ A participant who is non-adherent to her primary care treatments, but expresses a wish to continue in research
◦ A participant who is abusive to staff and resistant to procedures, but who has few other options for treating his disease
Consultation examples: study participation

Ethical considerations:
1. Fairness
2. Risks to the research participant
3. Integrity of the study data
4. Exploitation or discrimination of persons in certain circumstances
5. Non-adherence or difficult behavior could signal lack of capacity
6. Interference with research or care of others
Consultation example: clinical discharge

Young boy (11yo) experienced multiple complications after peripheral stem cell transplant for leukemia. He is here with his mother and his family lives in another country.

He expressed a desire to go home.

Research team very concerned about their obligations to him, and especially worried whether comparable or adequate care could be arranged or whether discharge would hasten his death.
Consultation example: clinical discharge

Ethical considerations- what is in the best medical interests of the child, what other interests are at stake, what are the responsibilities of the NIH researchers and care team? How should this decision be made?

Bioethics Consultation- Helped clarify goals, options, expectations, and implications with research and clinical team, and independently with patient and his mother
## Evaluation Responses 2016

<table>
<thead>
<tr>
<th>Overall satisfaction with the consult</th>
<th>Very Satisfied</th>
<th>Satisfied</th>
<th>Neutral</th>
<th>Dissatisfied</th>
<th>Very Dissatisfied</th>
<th>N/A or blank</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>90%</td>
<td>10%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

In 2015, **81%** of responders were “Very Satisfied”, and **19%** were “Satisfied.”

<table>
<thead>
<tr>
<th>Would you recommend the service to co-workers?</th>
<th>Absolutely</th>
<th>Probably</th>
<th>Neutral</th>
<th>Likely Not</th>
<th>No</th>
<th>N/A or blank</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>95%</td>
<td>5%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

In 2015, **93%** marked “Absolutely,” and **7%** marked “Probably.”
Selected evaluation responses 2016: What was most helpful?

“Rapid response; same day resolution. Written consult note within 2 days. Very impressive. Provision of relevant literature.”

“The team was very helpful, responsive and respectful. We were blown away by their sincere effort to help us.”

“Open discussion allow for airing of relevant information and expression of multiple viewpoints. Consideration of the issue from a specific ethical framework.”

“The opportunity to review this difficult case with the ethics team and discuss different approaches to the same situation.”
Summary

Ethical clarity can help mitigate possible tensions between rigorous clinical research, protection of research participants, and good clinical care.

Bioethics consultation helps to address such tensions, analyze ethical quandaries in clinical care and research, and work with researcher and clinical teams and others to identify best paths forward.

The NIH CC Bioethics Department offers a valuable resource for the CC and the NIH.

Thank you.