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

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

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

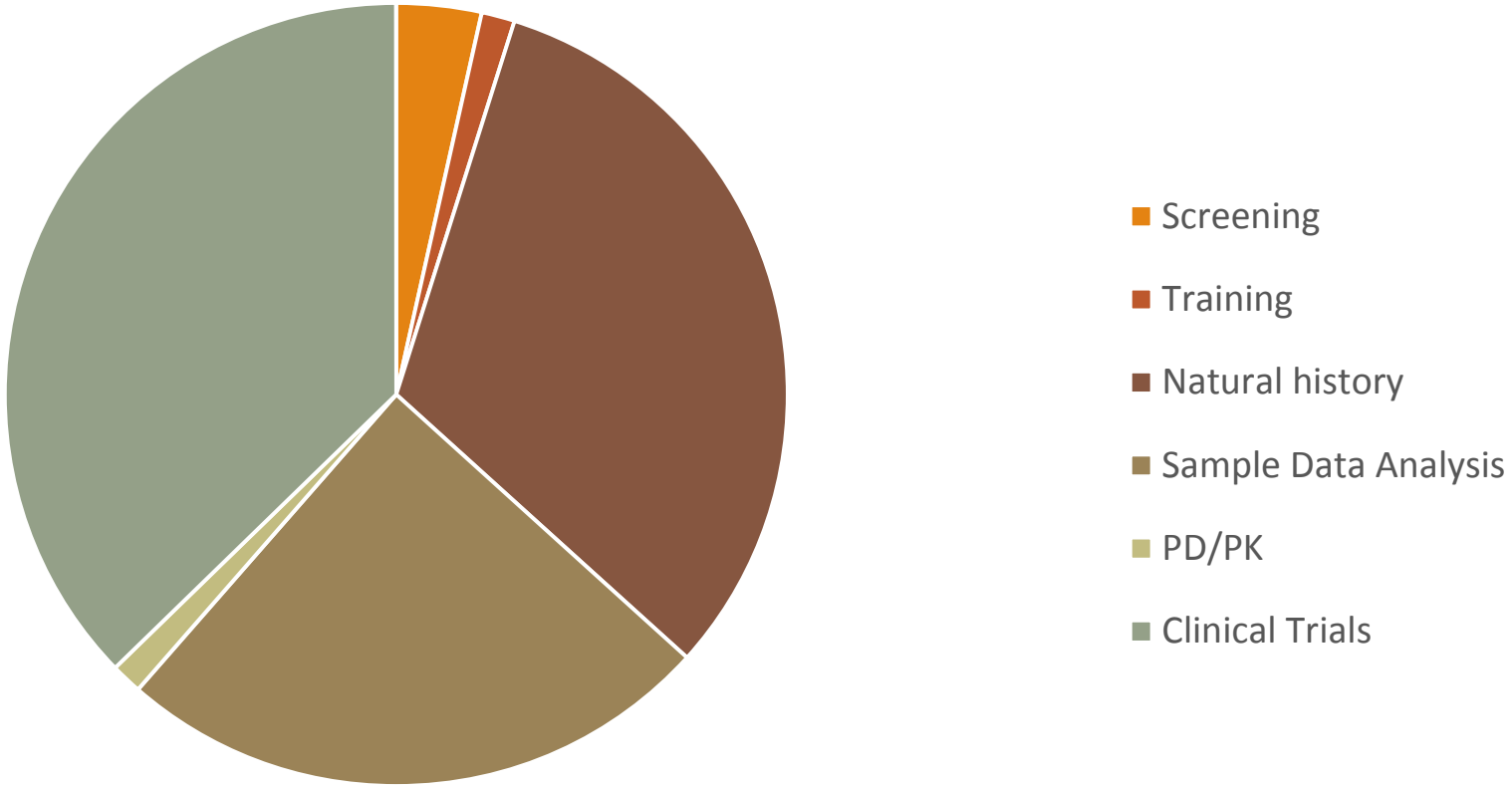
Overlap between clinical research and clinical care

Clinical research often includes persons with illnesses who are seeking care and treatment

Research aims can included 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

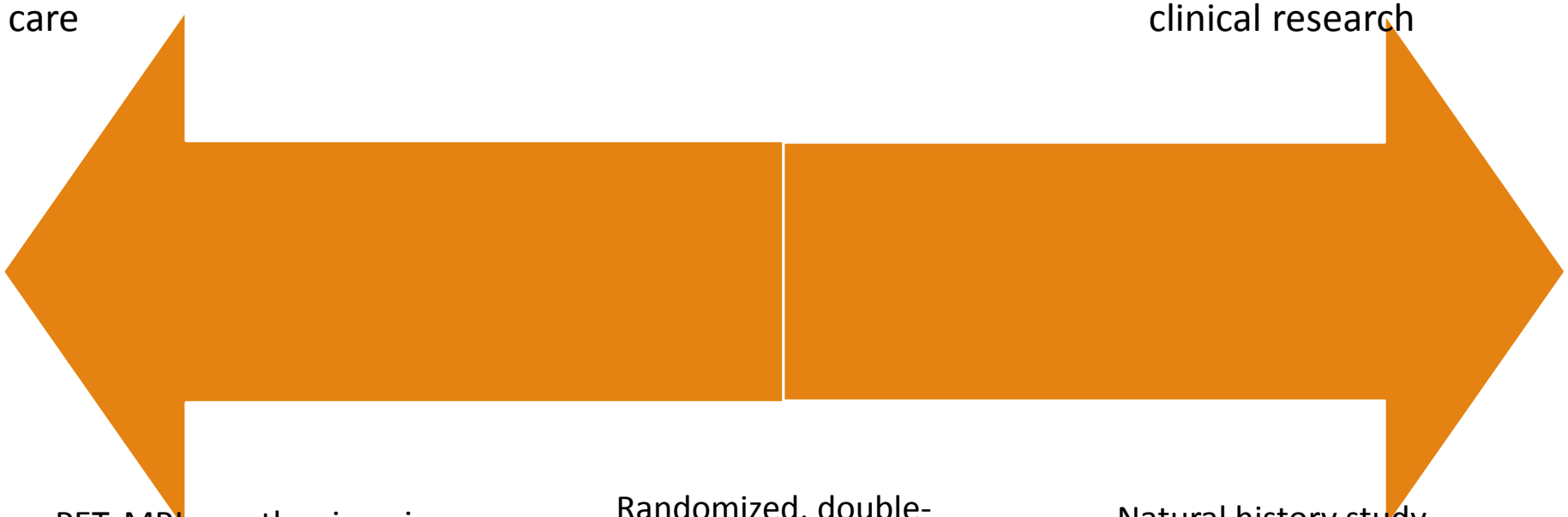


Courtesy of Kim Mitchell, Office of Protocol Services

Clinical Research Spectrum

Clinical research with little clinical care

Clinical care is the focus of clinical research



PET, MRI, or other imaging studies, Phase 1 vaccine safety testing in healthy volunteers

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?

CC Department of Bioethics

NOT

Rather-

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

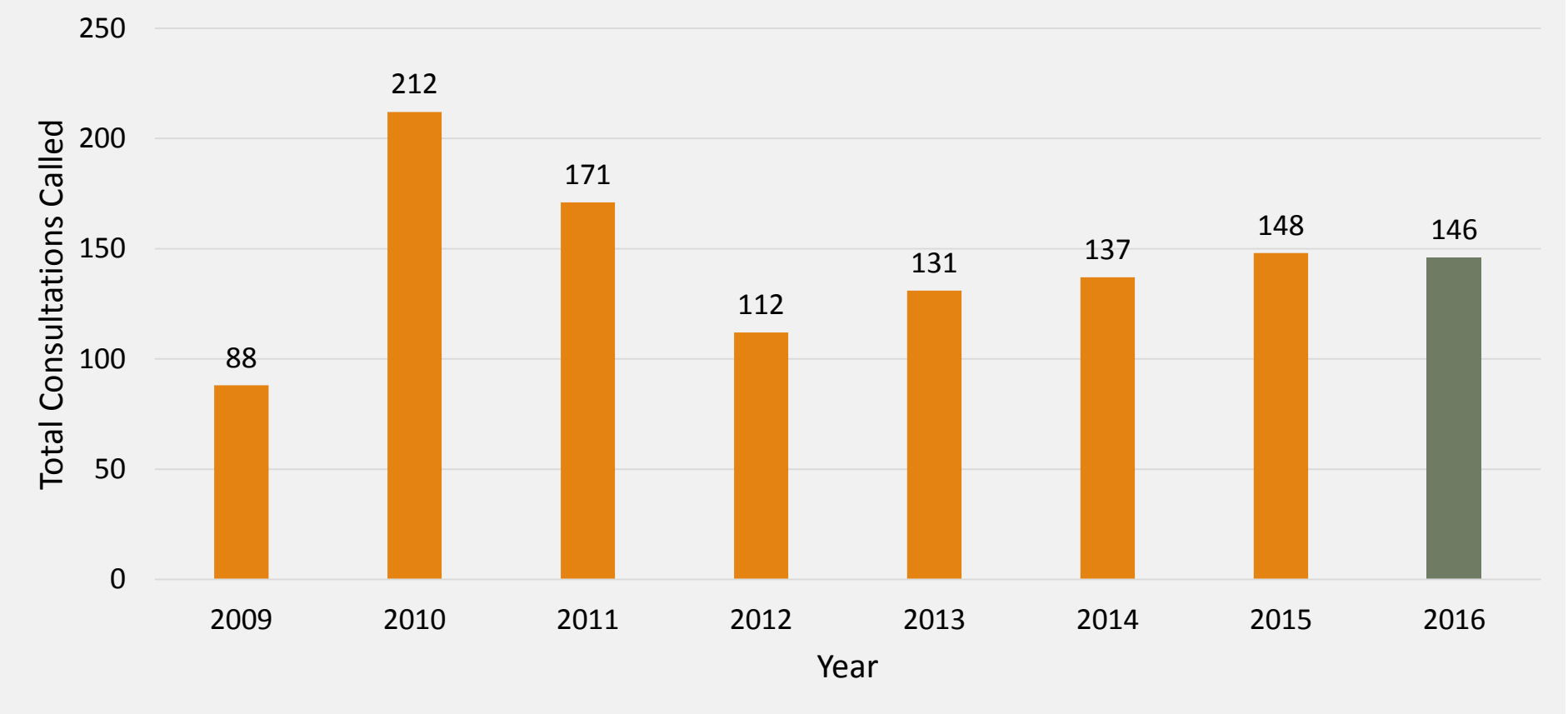
Requests from anyone at NIH

Written reports- analysis and recommendations

Consult database

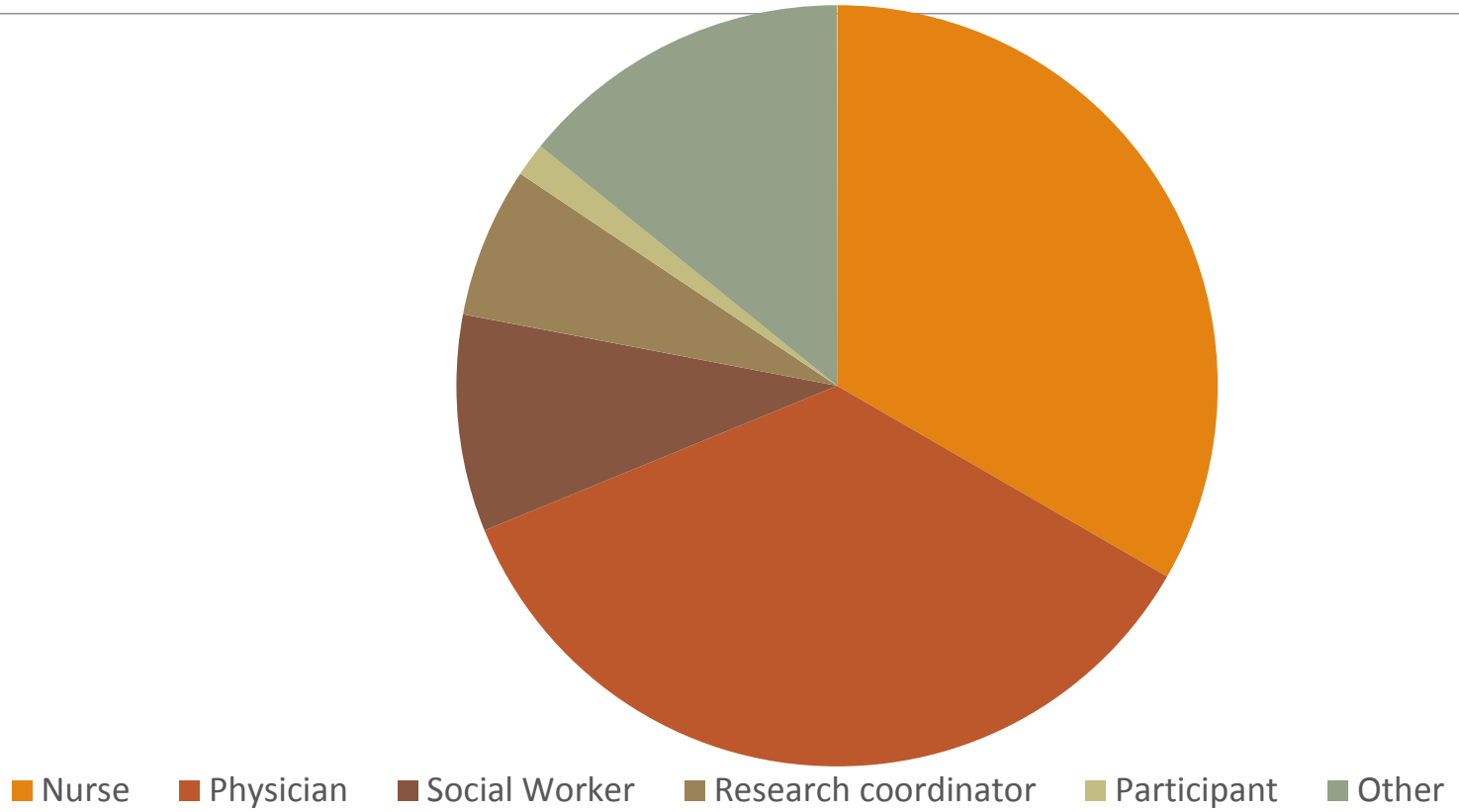
301-496-2429, page operator, or through CRIS

CC Bioethics Consultations by Year

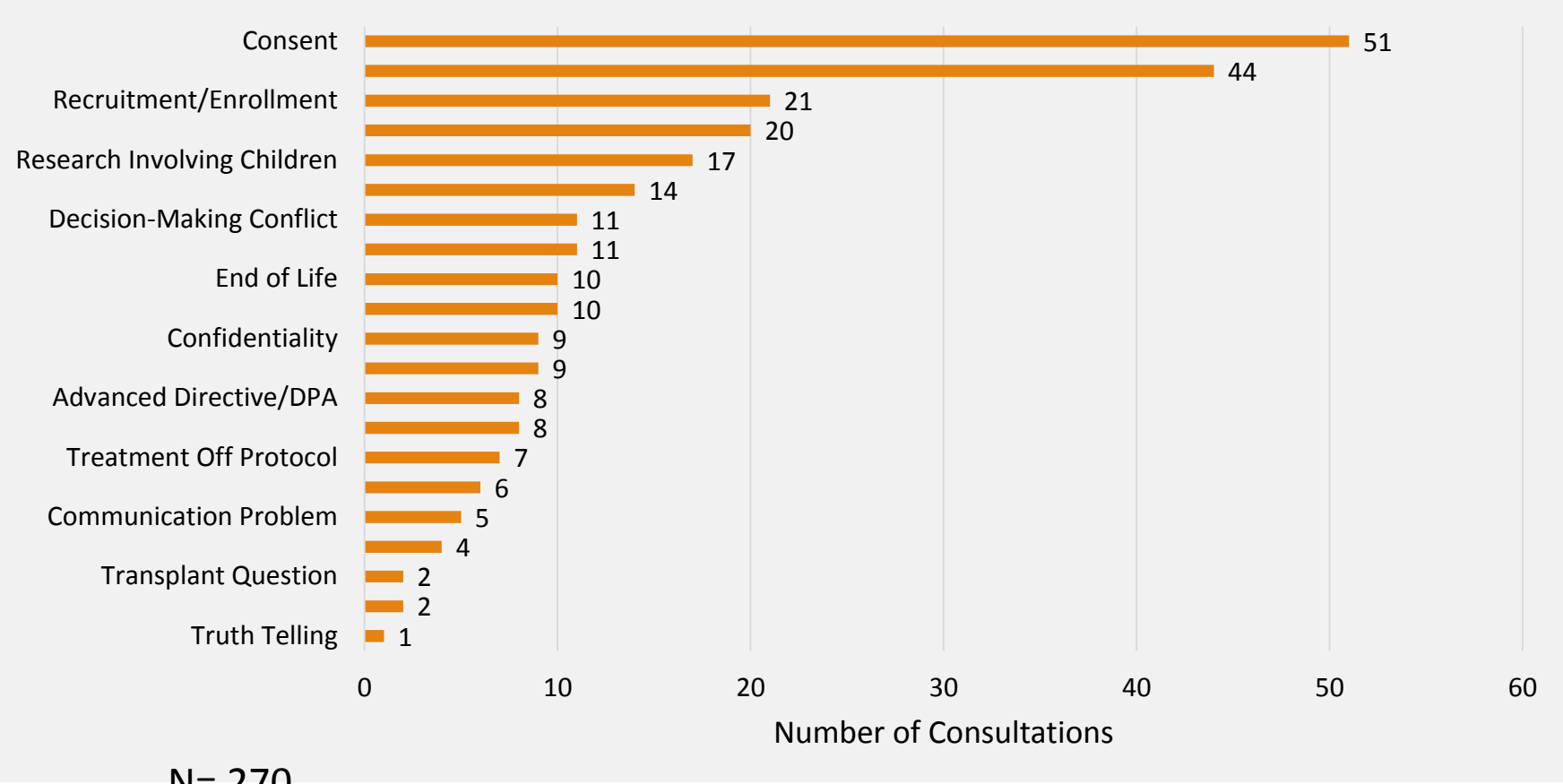


Courtesy of Akilah Jefferson, Sophie Gibert, Marion Danis

Consult requests 2016



Bioethics Consultation Service Consult Issues (2016)



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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

	Very Satisfied	Satisfied	Neutral	Dissatisfied	Very Dissatisfied	N/A or blank
Overall satisfaction with the consult	**90%**	**10%**	0%	0%	0%	0%

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

	Absolutely	Probably	Neutral	Likely Not	No	N/A or blank
Would you recommend the service to co-workers?	**95%**	**5%**	0%	0%	0%	0%

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.