Research Involving Adults with Decisional Impairment: Ethical Guidance in a Regulatory Void

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Objectives

- Discuss the current regulatory milieu involving subjects with decisional impairment, with a focus on current OHRP interpretations of existing regulations concerning vulnerable subjects
- Review practices which may be employed to provide additional safeguards for human research subjects with decisional impairment
- Explore opportunities for further clarity/enhancement of human subjects protections for these populations

Background

- NBAC (National Bioethics Advisory Commission, December 1998)
- NHRPAC (National Human Research Protections Advisory Committee, July 2002)
- OHRP request for comments (2007-2008)
- SACHRP SIIIDR (Subcommittee on Inclusion of Individuals with Impaired Decision-Making in Research (March 2009)

Background

"Confluence of several considerations, including ***perceived gaps*** in the federal system for the protection of human subjects; historical and contemporary cases in which the protection of human subjects appears to be ***inadequate***; and the need to ensure that research designed to develop ***better treatments for mental disorders*** can proceed with full public confidence in its ethical framework. The continuing vitality of the research enterprise ultimately depends on the public's ***trust*** that appropriate ***ethical constraints*** are in place and will be followed."

http://govinfo.library.unt.edu/nbac/capacity/TOC.htm

Background

- Regulatory citation:

  'When some or all of the subjects are likely to be ***vulnerable*** to coercion or undue influence, including those with cognitive limitations, the IRB must be sure that ***additional safeguards*** have been included in the study to protect the rights and welfare of these subjects {45 CFR 46.111 (b)}

Belmont Principles

- Respect for Persons
  - Autonomy, and special protections if diminished autonomy
- Beneficence
  - Risk:Benefit assessment
- Justice
  - Fair distribution of burdens and benefits

- Difference between medical PRACTICE (benefit to patient) and medical RESEARCH (benefit to research)

- Tread carefully in applying techniques from the practice world to the research realm

Definitions

- Adults with decisional impairment:

‘Limited decision making capacity covers a ***broad spectrum***. A healthy person in shock may be temporarily decisionally impaired. Another may have been severely mentally retarded since birth, while yet a third who has schizophrenia may have fluctuating capacity. Researchers should be sensitive to the differing levels of capacity and use assessment methods tailored to the specific situation. Further, researchers should carefully consider the timing of assessment to avoid periods of heightened vulnerability when individuals may not be able to provide valid informed consent.’

http://grants.nih.gov/grants/policy/questionablecapacity.htm

Definitions

- Persons with mental disorders are not, of course, unique in being at risk for loss of decisionmaking capacity. Accident and trauma victims, highly medicated patients, and many people who are severely ill may be significantly impaired in making autonomous and self-protective decisions. Indeed, ***a comprehensive list*** of individuals whose decision making might be compromised includes, in addition to persons with certain mental disorders, children, comatose patients, critically ill patients, institutionalized individuals, prisoners, people lacking certain language skills, and others

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Definitions

- Intent is not to label persons, but rather to describe and explain appropriate concerns and to propose ways to ensure adequate protections while promoting important research

Definitions

- ...'legally effective informed consent of the subject or the subject's ***legally authorized representative*** 45CFR46.116

- LAR means an individual or judicial or other body authorized ***under applicable law*** to consent ***on behalf of*** a prospective subject to the subject's participation in the procedures involved in the research 45CFR46.102

Issues to explore

1) Surrogate consent issues
2) Capacity assessment
3) Advance Directives
4) Need for assent
5) Risk:Benefit assessment
6) IRB expertise
7) Researcher investment

1) Surrogate Consent

- DPOA (appointed while subject retains capacity) vs court appointed LAR (appointed after capacity is lost)

- LAR/NOK/Applicable law

Surrogate Judgment

- …'on behalf of…' (part of LAR definition, 45CFR46.102)
- Best Interest standard?

or

- Substituted Judgment standard?

Wendler: Am J Psych 2002;159:585-591

ATS: Am J Resp Crit Care Med 2004;170:1375-1384

2) Assessment of Capacity

- Society has not decided what degree of impairment counts as a lack of capacity
- Case by case basis
- Protocol-specified method
- Quizzes, consent monitor, formal assessment via Mc-CAT, etc

NBAC re: Capacity

- At least four types of limitations in decisionmaking ability should be considered when planning and conducting research with this population: fluctuating, prospective, limited, and complete.

Transitional capacity

- Fluctuating: consider delaying consent process, or re-consenting
- Progressive: consider using advance directives while capacity is retained

3) Advance Directives

- With capacity: name a surrogate
- Healthcare proxy type
- What judgment is used?

4) Assent

- Regardless of surrogate permission issue, solicit subject assent in all cases where possible
- Respect participant dissent (both verbal and non-verbal)
- Assent gives a voice to whatever degree of autonomy is retained

Assent

- Consent process methodology: consider small sessions, repetitions
- Simple form: KISS
- Quiz
- Verbal and non-verbal cues

5) Risk:Benefit Assessment Approach

- In the absence of a regulatory framework, many people will adopt a model that incorporates aspects of an existing regulatory framework, such as Subpart D, Children

- “The core ethical challenge is to define the ***limits on the kinds of research*** risks that the proxy can accept on behalf of a noncompetent subject”

Karlawish,JH: NEJM 2003; 348:1389-1392

Proposed Risk:Benefit Assessment Approach

- Minimal risk
- Greater than minimal risk with potential for direct benefit
- Greater than minimal risk without potential for direct benefit: set parameters for level of risk and societal benefit
- Not otherwise approvable: set parameters for alternate review mechanism

6) Necessity for IRB Expertise

- Members
- Consultants
- Collaborations

7) Researcher Investment

- Justification for inclusion of vulnerable subjects must be rigorous and defensible

- Cannot target vulnerable population if you can achieve the research objective through enrollment of others (Relevant principle of distributive justice)

Researcher Investment

- Points to Consider: additional safeguards
  - Consent monitors
  - Subject advocates
  - Family education/consultation
  - Consent process waiting period
  - Use of a DSMB

Trust in researchers

"No matter how many regulations are put in place or guidelines are written, and no matter how intense the scrutiny by IRBs or other authorities, there can be no substitute for the ***ongoing commitment*** by researchers and the institutions in which they work to ethically appropriate behavior throughout the research process."

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Conclusions

- Careful attention to surrogate consent issues, capacity assessment, risk:benefit assessment, and assent and advance directives issues
- Continue the HIC/Researcher collaborations on these issues
- Stay tuned!