Ethical Differences between Research and Therapy

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Recent Example of Confusion

• David Wendler, “Must Research Participants Understand Randomization?”
Wendler’s Claim

- Research subjects *must* understand “negative aspects” of randomization, especially that research does not = therapy
- Subjects *need not* understand “positive aspects” such as how randomization is actually carried out
Commentaries (Wendler)

- 8 commentaries
- One invoked clinical equipoise as ethical principle “trumping” randomization
- Writers did not perceive a fundamental conflict between Wendler’s viewpoint and that suggested by equipoise
Take Home Message

• There continues to be a lack of appreciation of a basic controversy about the origin and nature of research ethics
• Failure to perceive this controversy can only sow further confusion
The Controversy

Ethics of therapy

Ethics of research

Ethics of research

Ethics of therapy
The Controversy

• Is it best to view research ethics as a subclassification of (therapeutic) medical ethics?
  – “Majority view”

• Or are research ethics and the ethics of therapeutic medicine best seen as distinct?
  – “Minority view” (but correct)
Importance of Controversy

- Major international documents such as Helsinki reflect majority view
- Documents that form basis of research ethics regulation in US (Belmont Report) grounded in minority view
- Argue: majority view fuels therapeutic misconception
**Major Test Case**

- *Clinical equipoise*
- According to majority view, a critical principle of research ethics
- According to minority view, can be dismissed as irrelevant
  - though lack of equipoise may be an indirect signal that other ethical problems exist
The RCT Dilemma

- The physician has an obligation to the patient to administer the best known treatment.
- In an RCT, treatment will be determined by a coin toss.
- How could a conscientious physician participate in an RCT (or refer her patient to one)?
An RCT is ethical *only* when there is genuine uncertainty, within the relevant medical community, which of the two treatment arms is superior.

Equipoise—Success?

- Majority seem to view clinical equipoise as an accepted and central principle of research ethics…
- …despite some counterintuitive implications
  - Such as rendering most placebo-controlled trials unethical
- …thereby accepting without careful scrutiny the view that ethics of research = ethics of therapy
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Another Response

• The dilemma is a dilemma only if we assume that the ethical obligations of the research investigator to subject are *the same as* those of physician to patient

• If not, no dilemma exists

• *How plausible is the equivalence hypothesis?*
Equivalence Hypothesis

• Plausible if medical research and medical therapy are similar activities that share the same goals
• If not, implausible
Medical Therapy

- **Primary** goal is to do the best one can to promote the health of the individual patient
- Gaining new knowledge, if it occurs at all, is a secondary goal
Medical Research

• *Primary* goal is the discovery of valid, new scientific knowledge
• Providing health benefits for the individual subject is a *secondary* goal (if at all)
Need for Ethical Protection

- Both patients and subjects have vital rights and interests that need protection
- Majority view: this is done through equipoise and other principles grounded in therapy
- Minority view: this must be done by somewhat different sets of ethical rules/principles appropriate to different goals and types of activity
Non-Exploitation Guidelines

- Social or scientific value
- Scientific validity
- Fair subject selection
- Favorable risk-benefit ratio
- Independent review
- Informed consent
- Respect for enrolled & potential subjects

  - Emanuel et al., *JAMA* 283:2701-2711, 2000
Why Non-Exploitation?

- Recognizes that research subjects used as a means to an end (new knowledge)
- Therefore, at risk for exploitation (taking unfair advantage of vulnerability)
- Rules required to protect against unfair use
- *This does not confuse research with therapy*
Therapeutic Misconception

• Despite best efforts at informed consent, research subject believes he is receiving treatment
  – Efficacy already proven
  – Personally chosen by physician

• Data shows persistence of substantial level of misunderstanding
Whose Misconception?

• If *investigators themselves* confuse the ethical bases of research and therapy…

• How can they effectively explain to subjects that research and therapy are distinct activities?

• Therefore, majority view represents a *basic* hindrance to informed consent
Aerospace Research

• Compared to (e.g.) cancer research, much harder for a subject to misperceive a therapeutic intent
• Aerospace scientists therefore in an excellent position to remind their colleagues in other fields of the defects of the majority position
• History of military research in US—exploitation common
Conclusions

• Even if you are not persuaded by arguments for minority view...
• You should be aware that controversy exists...
• ...And that concepts like clinical equipoise cannot be accepted at face value without further analysis and defense