



Ethical Differences between Research and Therapy

*Howard Brody, MD, PhD
Institute for the Medical Humanities
UTMB-Galveston
habrody@utmb.edu*



Recent Example of Confusion



- **David Wendler, “Must Research Participants Understand Randomization?”**
 - *American Journal of Bioethics* 9(2):3-8, February 2009

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***
 - **Fox et al., *Am J Bioethics* 9(2): 13-14, 2009**

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



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*
 - Miller & Brody, *Hastings Cen Rep* 33(3):19, 2003



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)?**



Freedman's Answer: Equipoise



- **An RCT is ethical *only* when there is genuine uncertainty, within the relevant medical community, which of the two treatment arms is superior**

- Freedman, *N Engl J Med* 317:141, 1987

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**
 - Appelbaum, *Am J Bioethics* 2(2):22, 2002

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**

