

Access to “Standard Alternative Therapies”

Ethical Analysis

Issues raised by case

- Alternatives to participation in research
 - When no realistic alternatives exist, is voluntariness of participation severely compromised?
- “Therapeutic misconception”
 - How to avoid?
- “Free” clinical care at NIH
 - An undue inducement to participate in research?

Alternatives to participation

- Reasons for inclusion in informed consent process
 - To remind (inform?) potential subjects that other options exist
 - To enable subjects to compare risks and potential benefits of experimental treatment with those of standard therapy, and choose accordingly

When is standard therapy unavailable?

- No standard therapy exists anywhere
 - Early years of HIV/AIDS epidemic
- Patient (or family) living in US has no medical insurance and does not qualify for Medicaid
- Standard therapy is not provided by the public health system in resource-poor country where patient lives
 - How does this situation differ from preceding one?

When standard therapy is unavailable

- Should participation in clinical trials be denied to individuals who lack access?
- No, because
 - Denial of participation would close off the only prospect of benefit to patients
 - A case of “double denial”
 - It would constitute an unacceptable “social” exclusion criterion

When standard therapy is unavailable

- Should the NIH provide alternative therapies?
 - Presumably, NIH does in clinical trials designed to compare experimental intervention with standard therapies
 - However, as a research institution, NIH has no obligation to provide standard therapies to patients outside clinical trials

Therapeutic misconception

- The mistaken belief that the *purpose* of clinical trials is to provide beneficial medical treatment to patients who are research subjects
 - This is consistent with the fact that clinical trials often do provide direct benefit to subjects
 - Research may fail to provide benefits
 - Harms may outweigh benefits

Therapeutic misconception

- Risks of holding this misconception are greatest when
 - Individuals lack access to standard treatment outside a clinical trial
 - Individuals have failed all standard treatments
 - Study design provides standard therapy in one arm

Therapeutic misconception

- Very hard to dispel
 - Research subjects maintain belief despite what researchers may emphasize and despite what consent document says
 - Researchers themselves may encourage the misconception by over-emphasizing the potential benefits of experimental treatments
 - Occurs in some phase I cancer trials

Risk-benefit analysis

- Potential therapeutic benefit is an element in the risk-benefit analysis
 - It is necessary to contrast research that holds out the prospect of direct benefit to subjects from other types of research where there is no such prospect
 - There may be evidence of potential benefit from earlier phases in clinical trials

Risk-benefit analysis

- Potential therapeutic benefit is especially important in more-than-minimal-risk studies in children
 - Federal regulations contain stringent requirements for research involving children that is more than minimal risk but does *not* have the prospect of direct benefit
 - IRBs must determine that risks are reasonable in light of potential benefits

Free clinical care at NIH

- Does it constitute an “undue inducement” to participate?
 - Free care may be an inducement to participate in research
 - But not “undue”
 - It is not an enticement for people to engage in an undesirable activity they would otherwise choose to avoid

Free clinical care at NIH

- A far greater inducement is the prospect of cure or improvement in medical condition resulting from the research itself
 - But if this were considered “undue,” no clinical trials could ever be conducted

Free clinical care at NIH

- How should this be handled in the consent process?
 - “Free care” should *not* be stated as a “benefit” of participation in research
 - Subjects may perceive it as a benefit, but free care is not one of the benefits that IRBs should take into account in making their risk-benefit assessments

Research subjects from developing countries

- What are the obligations of NIH?
 - Obligations to these subjects are the same as what is owed to US subjects during the conduct and follow-up of clinical trials in both intramural and extramural research
 - After the trial is concluded, what if research subjects still need the intervention that benefited them during the trial?

Declaration of Helsinki

- “At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.”
 - Controversial paragraph 30

Helsinki paragraph 30

- Does not specify *who* has the obligation to ensure access by subjects who still need a therapeutic method proven by the study
 - Sponsors of the study?
 - NIH
 - Commercial sponsor
 - Public health system of country where study is conducted?

NBAC Recommendation

- Researchers and sponsors in clinical trials should make reasonable, good faith efforts before the initiation of a trial to secure, at its conclusion, continued access for all participants to needed experimental interventions that have been proven effective for the participants. Although the details of the arrangements will depend on a number of factors (including but not limited to the results of a trial), research protocols should typically describe the duration, extent, and financing of such continued access. When no arrangements have been negotiated, the researcher should justify to the ethics review committee why this is the case.

Conclusions

- Lack of access to standard therapy may lead people to seek enrollment in research
- That situation itself is not unethical, as long as researchers take steps to prevent the therapeutic misconception

Conclusions

- The NIH is *not* obligated to provide standard therapy as an alternative for subjects who otherwise lack access
- The NIH *is* obligated to arrange for proper follow-up for research subjects who return to a resource-poor country where they lack access to high quality medical treatment