PATIENT ADVOCATES IN CLINICAL RESEARCH: SCIENTIFIC, ETHICAL, AND PRACTICAL CONSIDERATIONS

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History

- "Research is all too often done on participants, rather than with or by them." Cornwall, 1996
- HIV/AIDS Activists
- Breast Cancer Advocacy Groups
- Participatory Research
- Increased involvement in research planning, conducting, and interpreting research

Scientific Value of Inclusion

- Increase public health value of research
- Information on which health problems should be studied
- Information relevant to optimal study approach
- Potential problems with study plan

Ethical Reasons for Inclusion

- Improve content and methods designed to promote informed choice about research participation
- Decisions about whether research benefits justify risks to participants
- Awareness of risks to participants that might otherwise be overlooked
- General knowledge about research from prospective subject's perspective

Practical Considerations & Inclusion

- Possible increase in patients' willingness to join studies
- Possible increase in research participants' cooperation with study requirements
- Possible increase in research participants' willingness to complete studies
- Subjects and their advocates know what matters to patients and participants, e.g., high-quality research staff, reasonable study requirements

Research Design → Risk-Expected Benefit Questions

- **US Belmont Report: Maximize benefits of research to subjects and society, minimize risks to subjects; Reduce risks to those necessary to achieve the research objective**
- **US Common Rule: IRBs must ensure that:**

"risks to subjects are minimized … by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk"

"risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result"

Risk-Expected Benefit, cont'd

- Emanuel, Wendler, Grady, What Makes Clinical Research Ethical? (JAMA, 2000)

Favorable risk-benefit ratio is required: "risks must be minimized, potential benefits enhanced, and the potential benefits to individuals and knowledge gained for society must outweigh the risks"

Helsinki Declaration (2013) "Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects."

Surrogate Endpoints & Ethics

- FDA Accelerated Approval Policy
- Problems with clinical endpoints
- FDA accepts surrogate endpoints reasonably related to clinical benefits
- Insufficient follow-up research to verify clinical value of surrogate measures
- Potential problems with surrogate endpoints: undiscovered risks; ineffective drugs

Adaptive Trials and Ethics

- Allow more participants to be assigned to interventions with better expected results, based on accumulating data
- Do adaptive trials produce good data?
- Early enrollment / no advantage
- Are early enrollers aware of this?
- Is subject selection fair?

Other Design Issues

Mandatory vs. voluntary tissue submission:

Is tissue essential to achieve research objective?

Are there ways to reduce risk to subjects while obtaining "good enough" data?

Eligibility requirements for drug "holidays"

Is no-drug period essential to achieve research objective?

- **Helsinki: No intervention acceptable if no proven intervention exists OR**
- **"For compelling and scientifically sound methodological reasons," no intervention is "necessary to determine the efficacy or safety of an intervention"**
- **Patients who receive no intervention "will not be subject to additional risks of serious or irreversible harm as a result"**

Return of Results in Genetic Research

- **Survey and focus groups – vast majority of subjects and prospective subjects wanted to know about individual results, including health risks "even if there was nothing they could do about them"**
- **Also information relevant to family risk, reproductive decisions, environmental risks, life & financial planning, & potential future research participation**
- **But not everyone wants to know – let subjects decide**
- **Researchers providing individual research results must set aside money to cover high-quality genetic testing and professional time devoted to the discussion of results.**

Challenges & Strategies

- Training for advocates and researchers
- Need to explain & justify legitimate design constraints to constituents
- Just ask, "why?"
- Personal knowledge is as valuable as scientific knowledge