Ethical issues of Observational Studies and Clinical Trials In Pregnant and Lactating Women

Task Force on Research Specific to Pregnant Women and Lactating Women

Jeanne S. Sheffield, MD
Maternal-Fetal Medicine
Johns Hopkins Medicine

Study Designs
Observational Studies

- Cohort study: following groups of subjects over time
  - Descriptive e.g. incidence of outcomes over time
  - Analytic e.g analyze associations between predictors and outcomes
  - Prospective or retrospective
  - Nested Case control design within a cohort trial

Study Designs
Observational Studies

- Cross-sectional study: all observations are made on a single occasion
- Case-control study: Investigators work backwards. Chose the cases (outcome of interest) and then pick controls from the population without the outcome

Study Designs
Clinical Trials

- Clinical Trial: Apply an intervention and prospectively observe the effect on the outcome
  - Randomized blinded trials

Comparison of Study Types

Observational Trials

- Pros
  - Less resources needed
  - Often less time consuming
  - Background data generation
- Cons
  - Causal inferences
  - Inability to define outcomes up front

Randomized Trials

- Pros
  - Ability to demonstrate causality
    - Randomization
    - Blinding
- Cons
  - Time consuming
  - Expensive
  - Often requires a larger number of subjects
  - Exposure to potential risks

Ethical Issues of Human Subjects Research

- Previously Collected Data and Specimens
  - No physical risks
  - Informed consent is often a general consent
    - Not specific to the current project
    - Feasibility of going back to obtain consent
  - Breaches of confidentiality
  - Participants may object to their data/specimens being used for certain research
    - Religious objections

Designing Clinical Research. 2001 Hulley SB et al.

Ethical Issues of Human Subjects Research

- Randomized Clinical Trials
  - Treatment is determined by chance
    - Judgement that both arms of the protocol are in equipoise
      - Current evidence does not support either arm as being superior
  - Intervention for control subjects
    - Principle of nonmaleficence
      - Cannot withhold therapies known to be effective
      - Placebo: still may be used if no serious risk to withholding
        - » Thorough discussion of other effective interventions

Designing Clinical Research. 2001 Hulley SB et al.

Ethical Issues of Human Subjects Research

- Randomized Clinical Trials
  - Intervention for control subjects – other considerations
    - Ability to access health care outside of the trial
      - "Undue inducement"
      - Avoid vulnerable populations if possible unless that is the population being studied
  - Continuation of a trial if early benefit noticed or if anticipated to go on longer
    - DSMB – not the investigators

Designing Clinical Research. 2001 Hulley SB et al.

Ethical Issues of Human Subjects Research

- Genetic Research
  - Significant confidentiality concerns
    - ? Disclosure
    - Genetic counseling
- PK/PD studies

Designing Clinical Research. 2001 Hulley SB et al.

Ethics of Study Design

Pregnancy Considerations

- Clinical Trials
  - 2 subjects – mother and fetus
    - Short term and long term consequences
  - Importance of nonpregnant preclinical and clinical studies
  - Designing trials with no direct benefit to the pregnant woman or her fetus is acceptable
    - Definitions of minimal risk
  - Risk discussion: risk in a specific situation, not general pregnant population

Ethics of Study Design

Pregnancy Considerations

- Clinical Trials
  - Consent issues
    - mother, father or both
    - Timing
    - What happens when the interests of the fetus conflict with interests of the pregnant woman
  - Risk of inaction: what are the risks if we exclude the mother and/or fetus?