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

Task Force on Research Specific to Pregnant Women and Lactating Women

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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

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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
Ethical Issues of Human Subjects Research

• Genetic Research
  – Significant confidentiality concerns
    • ? Disclosure
    • Genetic counseling

• PK/PD studies
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?