Optimizing Inclusion and Exclusion Criteria in Clinical Research

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Inclusion/Exclusion Criteria

• Inclusion/Exclusion Criteria should have clear scientific or clinical rationale, and may differ depending on the study design (ex. observational vs. interventional):
  – Balance of scientific ideals and the real world
  – Balance of essential and trivial details
  – Balance of structure and flexibility
Inclusion/Exclusion Criteria

• Gender
  – Need compelling reason to only include one gender (ex. prostate cancer, menopause)
  – May need increased sample size if gender differences expected

• Age range
  – Consider pubertal and developmental changes (ex. brain development)
  – Don’t exclude older subjects just on age
  – For pediatric studies, tailor criteria to disease biology, scientific objective, existing data regarding safety
Inclusion/Exclusion Criteria

• **Weight and Diet**
  – Does the study design require a certain BMI range?
  – Do the subjects need to be consuming a stable diet?
  – Do you need to exclude certain diets or foods?

• **Smoking etc**
  – Do the subjects need to be nonsmokers?
  – What about marijuana, other recreational drugs?

• **Physical activity**
  – Do the subjects need to be sedentary, or avoid extremes in physical activity?
Inclusion/Exclusion Criteria

• Medical conditions
  – Are there medical conditions that would compromise patient safety or data fidelity?

• Medications
  – Are there medications that would interfere with or increase the risk of the experimental therapy?
  – Are there medications that would compromise data fidelity?
  – Are contraceptives OK?
  – What about any OTC products?
Inclusion/Exclusion Criteria

• Laboratory abnormalities
  – Are there laboratory abnormalities that need to be excluded due to safety issues (ex. GFR for reduced renal function, ECG for underlying cardiac disease)?
  – Are there laboratory abnormalities that need to be excluded due to interference with your study aims, aside from safety issues?
• **Practical/logistical issues**
  – Do the subjects need to reside within a certain distance of Portland due to transportation issues?
  – Are there exclusions due to language barriers (ex. surveys only validated in English)?
  – Are there cognitive or cultural barriers to consent?
Inclusion/Exclusion Criteria

• Consider broad exclusion statements
  – like “other medical conditions/medications that would interfere with subject safety or data collection in the opinion of the PI,” rather than trying to think of everything.

• **Consider broad statements** like “clinically relevant laboratory abnormalities” or cut-off levels, rather than any laboratory abnormalities, to avoid excluding subjects for trivial laboratory findings.

• **Consider dosing adjustments for mild renal insufficiency** rather than outright exclusion.

• **Consider dose adjustments for BMI ranges**, if BMI extremes are a problem, rather than excluding BMIs at upper or lower extremes.
Example: Enrollment Criteria too Broad

Study: Blood samples for new lab assay

- **Inclusion Criteria**
  - Healthy Subjects

- **Exclusion Criteria**
  - Evidence of infection
  - On medication
  - Medical conditions that may compromise the quality of cells
  - Disorders that may cause problems for the subject
Example: Enrollment Criteria Too Narrow

Study: The relationship between hormone levels and PMS symptoms

- **Inclusion Criteria**
  - Women between 18 and 30
  - PMS symptoms every cycle for at least 1 year
  - Normal pap smear within last year
  - Regular Menstrual cycles >26 and <32 days

- **Exclusion Criteria**
  - Hysterectomy
  - Hormonal contraceptives in last 3 months
  - History of smoking
  - History of psychiatric disorder
  - History of alcohol/drug abuse
  - Use of medications that could affect mood or sleeping
  - Abnormal screening blood tests (TSH, LFT, HGB)
  - Pregnancy within last year or plan to get pregnant during study
  - Use of medications/alternative treatments for PMS within last 60 days
  - History of insomnia
  - History of migraines
Example: Enrollment Criteria Just Right

Study: Any Clinical Research Study

- **Inclusion Criteria**
  - Characteristics that are relevant to the research question
  - Demographic characteristics (e.g. age)
  - Clinical characteristics (e.g. diagnosis)
  - Geographic characteristics (e.g. Clinic Patients)
  - Vulnerable Populations (if applicable)

- **Exclusion Criteria**
  - Describe subset of population that won’t be studied
  - Characteristics that make it unethical to withhold treatment
  - Subjects at high risk of side effects
  - High likelihood of lost to follow-up
  - Characteristics that might interfere with the quality of the data
Pragmatic Vs. Explanatory Trials

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Pragmatic vs. Explanatory Trials

• **Pragmatic trials**
  – seek to answer the question “Does an intervention work under usual conditions?”

• **Explanatory trials**
  – seek to answer the question “Can an intervention work under ideal conditions?” Can help to explain the mechanism...the why.
Pragmatic trials determine...

- Does it work?
- For whom does it work?
- How much does it cost?
- Is the new treatment better than existing care?
  - Does not determine if the new treatment is better than no treatment or placebo.
- Pragmatic trials sacrifice internal validity for generalizability
Why are pragmatic trials important?

Relevance.....We are

• Not reaching patients with complex, comorbid conditions
• Not testing in conditions and with staff most similar to clinical situations
• Not addressing issues most important to clinicians, policy makers, patients
• Some evidence-based interventions are not feasible in real world
Key features of pragmatic trials

- Broad eligibility
- Recruit from a variety of settings to increase generalizability
- Usually head-to-head comparison of two active drugs
- Medical management consistent with clinical care
- Often omits study procedures that alter ecology of care
- Outcomes of importance to the patient
- Duration to examine benefits, risk
- Large enough sample size to examine benefits, risks
- Objective and subjective measures
Thank You