Overview of Study Designs in Clinical Research

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Hierarchy of Evidence: Strength of Study Design for Evidence Based Clinical Decision Making

- Evidence-based Systems Literature
  1a Systematic Reviews (SR), Meta-Analysis
  1b Randomized, controlled trials (RCT)
  2a Clinical trials, Cohort Studies
  3a Case Control Case series
  4 Case study / case report
  5 Animal studies, in vitro studies
  6 Expert opinions, editorials

University of Health Sciences
Hierarchy of Evidence: strength of study design

- Systematic Reviews (SR), meta-analysis
- Best Evidence / Evidence Guidelines (AHRQ, CEBM, etc.), Evidence Summaries
- Randomized, controlled trials (RCT)
- Clinical trials, Cohort Studies, Case Control
- Case series
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Hierarchy of Evidence for Clinical Decision Making

- Summarized & synthesized by experts
  - “systems research”
- Usually extremely reliable & high quality (authoritative)
- Useful for quick reads and sound decisions
- “Remove the practitioner from the primary literature.”
- “Remove the patient from the picture.”
- Limited in number, scope and “perspective”
- Often a lag between study results, analysis, publication, summary
Hierarchy of Evidence for Clinical Decision Making

- Expert opinions, editorials, perspective, ideas are based on professional experience – a key aspect of EBP!
- Animal studies often ARE the basic research studies!
- “Provide a substantial foundation”
- “Difficult to generalize to the patient sitting in front of the practitioner.”
- Not low quality
Hierarchy of Evidence for Clinical Decision Making

Key study designs for clinical research studies:

- Randomized, controlled trials (RCT)
- Clinical trials, Cohort Studies, Case Control
- Case series
- Case study / case report
Overview of Primary Research Study Designs

EXPERIMENTAL
- Investigator assigns, chooses, tests intervention, treatment or exposure
- Control / comparison
- Random allocation of study subjects
  - Randomized Controlled Trials
  - Clinical Trials
  - Community Trials
  - Laboratory Trials

OBSERVATIONAL
- Investigators study people and exposures “in nature”

Comparison / control group?
- YES
- NO

ANALYTIC
- Case-Control
- Cohort

DESCRIPTIVE
- Correlational
- Case Series
- Case Reports
- Cross-Sectional
- Migrant studies

EBP@NUHS CH5 Study Design © Barbara M. Sullivan PhD, Jerrilyn A. Cambron DC PhD, Dept. of Research NUHS 2008
Primary Clinical Research Study Designs

Randomized, controlled trials (RCT)
- Considered the “Gold Standard”
- Participants are randomly allocated into intervention (treatment) and control (placebo) groups
  - Randomization (if done) method is key
  - “other clinical trial” or “clinical trial” may have limited or no randomization
  - Random allocation vs. random selection (for surveys)
Primary Clinical Research Study Designs

Randomized, controlled trials (RCT)

- Allows rigorous evaluation of a single variable
- **Prospective**: data is collected after the study is designed and in progress
- Seeks to falsify (not confirm) its own hypothesis
- Seeks to eradicate bias through comparison and blinding
- Allows for “meta-analysis” (combining numerical results) at a later date
- Strongest study design for therapy questions
Primary Clinical Research Study Designs

Randomized, controlled trials (RCT)

- Expensive and time consuming
- True randomization is difficult to achieve
  - Incomplete randomization
  - Bias in selection and randomization
- Often impractical
- Could be unethical
- Other study designs may be more appropriate
Primary Clinical Research Study Designs

Cohort Studies

- Observational
- Measurement of the same characteristic / outcome / issue / disease
  - Patients suffering from low back pain
  - Death from heart attack
- Two groups of patients differ in one characteristic
  - For example, smokers or non-smokers
  - Surgery vs. other intervention
- Most often not randomized to intervention (selected)
- Eligibility and outcome assessments can be standardized
<table>
<thead>
<tr>
<th></th>
<th>Randomized Controlled Trial (RCT)</th>
<th>Cohort Design</th>
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<tbody>
<tr>
<td><strong>Populations studied</strong></td>
<td>Highly characterized, selected populations recruited on the basis of detailed criteria Treated at selected sites</td>
<td>Diverse populations observed in a broad range of settings (natural environment)</td>
</tr>
<tr>
<td><strong>Allocation to intervention</strong></td>
<td>Based on chance Not controlled or influenced by investigators or patient choice</td>
<td>Not randomized Allocated based on decisions made by providers or patients</td>
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<tr>
<td><strong>Outcomes</strong></td>
<td>Primary outcomes determined before patients enrolled in study; focused on predicted benefits and risks</td>
<td>Can be defined after the intervention (exposure) Can include rare or unexpected events</td>
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<td><strong>Follow-up</strong></td>
<td>Prospective studies; often short follow-up due to costs and pressure to produce timely evidence</td>
<td>May rely on history / existing experience (retrospective studies) Can provide opportunity for long follow-up</td>
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<tr>
<td><strong>Analysis</strong></td>
<td>Analysis is straightforward</td>
<td>Sophisticated multivariate techniques may be required to deal with confounding</td>
</tr>
<tr>
<td><strong>Validity</strong></td>
<td>Internal validity enhanced by minimizing selection bias and confounding</td>
<td>Vulnerable to selection bias - groups may differ in some factor related to outcome</td>
</tr>
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Primary Clinical Research Study Designs

Case Control

- Observational
- Possible associations between
  - Disease/ disorder / health issue
  - and one or more hypothesized risk factors
- Focus on the etiology of a disease or disorder
- Strongest study for questions of cause (etiology)
Primary Clinical Research Study Designs

Case Control

- Observational
- Possible associations between a disease and one or more hypothesized risk factors
- Focus on the etiology of a disease or health issue

```
Disease
   Exposed  Non-Exposed

No Disease
   Exposed  Non-Exposed
```
Primary Clinical Research Study Designs

Case Control
- **compare** the prevalence or level of the possible risk factor between

  **Case**
  * representative group of disease subjects (cases)
  * derived from the same population

  **Control**
  * representative group of disease-free subjects (controls)

  **Disease**
  - Exposed
  - Non-Exposed

  **No Disease**
  - Exposed
  - Non-Exposed
Primary Clinical Research Study Designs

Case control

- Patients with a particular health concern / characteristic / disease / disorder
- Matched with “controls:”
  - Identical patients without that issue
  - Identical patients with a different disease
  - General population
- Data is collected by searching through patient histories or through patient recall surveys
- Used to study rare conditions (strong study design)
Primary Clinical Research Study Designs

Cross-sectional surveys

• Representative sample of subjects or patients
• Interview, survey, study
• Data is collected at a single time point
• Data collection may depend on history or recall
• Establishes association, not causality
• Often used to develop further clinical research
Primary Clinical Research Study Designs

Case Study

- Detailed description a single case
- 10-30 patients = case series
- Rare events, early trends, unusual manifestations, responses
- Elucidate disease mechanisms and treatment
- Detailed, well-defined patient description
- Highly detailed and methodologically sophisticated
Primary Clinical Research Study Designs

Case Study

- Rich source of ideas, hypotheses about disease, conditions, risk, prognosis and treatment.
- Not typically useful or strong enough to test a hypothesis
- Initiate issues and trigger more decisive studies
- No statistical analysis: no determination of “chance”
- Often retrospective (looking back)
Primary Clinical Research Study Designs

Case Series

- 10 to 30 patients
- Detailed description
- Well described treatment or intervention
- All subjects receive same treatment
  - No comparison group
  - If inclusion and exclusion data were used, explicit definitions and descriptions should be provided
- Larger number of cases (than a case study) allows statistical analysis (p values, means, standard deviations)
  - Allows determination of chance
Primary Clinical Research Study Designs

Case Series

- Often retrospective (look back in time)
  - restricts value as prognosis study or determining cause and effect relationships
- Prospective (looking forward) case series studies are often designed as prospective cohort studies
  - including a control group (a benefit, strength).
Suggested Practice:

Objective:

- To search the professional biomedical literature databases for professional journal articles (papers) describing primary research studies which support clinical decisions regarding a specific patient scenario.
- Identify study design by abstract, methods

- Selected journal article characteristics:
  - Primary research study
    - Human subjects or patients who are analyzed
    - NOT reviews, analyses, guidelines, economic analyses based on primary studies etc.
    - NOT about other studies (compiled evidence reviews, systematic reviews, meta-analyses, narrative reviews, etc.)
  - Published within 3 years or less)
  - Written by the researchers who conducted the study
  - From a peer reviewed journal to ensure high quality
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Reading Resources: