Topics

• Basic principles applied to biomedical research.
• Examples of common experimental designs.
Focus on comparative experiments

• Def: Treatments can be allocated to the experimental units by the experimenter
  – A *treatment* is the diet, drug, device, delivery system, etc. that is:
    • under investigation and is under the control of the experimenter.
  – An *experimental unit* is the smallest division of the experimental material that can receive different treatments
Issues in entire process of design

• Which units?
• Which treatments?
• At what levels?
• Primary emphasis in statistical ED is on the question of how treatments should be allocated to units.
Requirements for a good experiment*

• Absence of systematic error
• Precision
• Range of validity
• Simplicity
• The calculation of uncertainty

*D.R. Cox, 1958, Planning of Experiments
Requirements (cont’d)

• Absence of systematic error.
  – Why? Gives an unbiased estimate of effects of treatment
  – How? Compare equivalent groups under different treatments
    • Usually achieved through randomization
Requirements (con’td)

• Precision
  – If experiment has no systematic error, experimental results should differ from `truth" only by random variation
  – Would like to make amount of random variation as small as possible.
Precision:
Example. Which experiment is more convincing as to differences between A and B?

Experiment 1

Experiment 2
Requirements (cont’d)

• Range of validity:
  – Can the conclusions from the controlled conditions be applied in a larger context?

• Simplicity
Requirements (cont’d)

• Calculation of uncertainty
  – Do the results provide an assessment of the uncertainty associated with the estimated effects of treatments?
Ideal experiment

• Have units that
  – if treated with A, respond with $r_A$
  – if treated with B, respond with $r_B$

• Why is this ideal?
  – Gives an unbiased, precise (known) estimate of effects of treatment
Goal of statistical ED

• Get as close as possible to ideal experiment, given constraints:
  – Generalizability
  – Simplicity/Feasibility
  – Finite resources
  – Variable experimental material
General Rules

• Avoid systematic error:
  – Randomize

• Get precision:
  – Make treatment comparisons based on units that are as similar as possible.
General Rules

• Precision for comparing two treatments depends on:
  – Variation of units receiving same treatment
  – Number of units treated
Common Designs: Completely Randomized Design

• Example:
• Assess effect of recombinant human growth hormone on recovery following bowel resection.
  – Treatments (diets): Chow, Standard, rHGH
  – Protocol: A total of 30 rats were randomized
  – Outcomes: Measure weight change, …, at day 8.

Check criteria for good experiment:

- Randomization
  - should provide protection against systematic biases in the treatment groups.
- Range of validity (?)
- Simple to implement.
- Precision and measuring uncertainty
ANOVA

• Results:
  - Chow: 593, 587, 576, …  593 18.0
  - Std : 525, 526, 540, …  533 16.5
  - rHGH: 818, 785, 791, …  806 16.5

• Why do these outcomes vary?
  - Units received different treatments
  - Unknown/unexplained/natural variation
Common Designs: Completely Randomized Design with Factorial Structure

• Example: Effect of levels of dietary nitrogen, phosphorous on plasma Ca concentrations

• Treatments

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<thead>
<tr>
<th></th>
<th>Nitro</th>
<th>Phos</th>
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<tr>
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Completely Randomized Design with Factorial Structure

• Factorial designs:
  – Treatments are combinations of factors.
  – Allow experimenter to answer questions about the *interaction* among factors.
  • Is the effect of increasing dietary nitrogen in a low-phosphorous diet equal to the effect of increasing dietary nitrogen in a high-phosphorous diet?
  • If answer is ‘Yes’, then there is no *statistical interaction*
Why is interaction important?

• With no interaction, estimate effect of nitrogen
  – Average of groups 2 and 4 (high nitro) minus average of groups 1 and 3 (low nitro)
  – Comparison based on 12 animals vs 12 animals

• Same precision as if you had devoted all 24 animals to a study of nitrogen effect
Why is interaction important?

• With no interaction, estimate effect of phosphorous
  – Average of groups 3 and 4 (high phos) minus average of groups 1 and 2 (low phos)
  – Comparison based on 12 animals vs 12 animals
• Same precision as if you had devoted all 24 animals to a study of phosphorous effect
Why is interaction important?

• With no interaction, factorial leads to a “2 for 1” efficiency:

• 24 animals gives same information as if had done two separate experiments of 24 animals each
What if there is interaction present?

- Example: Weight gains

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<th>Trts</th>
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<th>Phos</th>
<th>Avg Gain</th>
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<td>4</td>
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</table>

- Adding nitrogen to diet low in phosphorus doesn’t make much difference
Advantage of Factorials

• Interaction present:
  – Best way to discover this is with a factorial

• Interaction absent:
  – 2 for 1 efficiency
Common design: randomized block designs

- Often called a “variance reduction design”
- Group units into “blocks” such that units within blocks are relatively similar to each other
Common design: randomized block designs

• Example.
  – 10 animals assigned to each of three diets
  – Outcome: Weight change at day 8
• Line up 30 animals according to initial wgt

• A1, A2, A3, A4, A5, A6, ..., A28, A29, A30
• Block 1 Block 2 Block 10
Common design: randomized block designs

- Randomly assign diets to animals *within blocks*
  - Compares diets based on groups that are similar
  - Variability in units treated alike can be small
Common design: randomized block designs

• Can lead to highly efficient designs
  – E.g., a RB design that gives same precision of a CR design more than 2 times as large.