1.1 Fisher "The Arrangement of Field Trials" (1926),
Journal of the Ministry of Agriculture 33:503-513
(Science Library - S3.J871)
3 Fundamentals of Experimental Design

1. Local Control - Reduction of Experimental Error
   By placing competing treatments in similarly located plots (locations)

2. Replication - Necessary to obtain estimates of experimental error variance (standard errors)

3. Randomization - For valid estimates of experimental error variance

1.2 Research Plan
- Objectives
- Identifying important factors & choosing which to vary & which to hold constant
- Characteristics to be measured (outcomes, responses, endpoints)
- Procedures for conducting tests and obtaining observations
- Number of replications (sample sizes)
- Available resources and materials (budget, capacity, ...)

1.3 Experiments, Treatments, Experimental Units

- Comparative Experiments - Data collection process used to compare two or more competing circumstances
- Treatments - Circumstances or conditions created for experiment. Basis of comparison
- Experimental Unit - Subject or item or location that is independently exposed to treatment - replication.
**EXPERIMENTAL Error** - Error variation among experimental units receiving identical treatments

- Natural Variation (Subjects vary, soil conditions vary...)
- Variability in Measurement (Measurement error)
- Irreproducibility of Treatment conditions (Variation due...)
- Interaction of Treatments and Experimental Units
- Extraneous Factors (Environmental conditions)

**Observational Studies** - "EXPERIMENTS" WHERE TREATMENT ASSIGNMENT TO SAMPLING UNITS IS NOT CONTROLLED BY EXPERIMENTER, BUT RATHER BY NATURE (SELF-SELECTED OR SUBJECT TO TREATMENTS). ETHICAL CONSIDERATIONS

**Similar Method of Analysis for Controlled Experiments and Observational Studies. More Difficult to Claim "CAUSE-AND-EFFECT" For Observational Studies (Alternative Explanations)

**Research Hypotheses**

- Objective of Experiment is typically to test theories regarding treatments (Research Hypotheses)
- When active (biological or behavioral) interventions are treatments, they need to be compared to a control treatment, or benchmark (e.g., placebo in drug trials, no fertilizer in ag trials, no manipulation in behavior trials)
- One-at-a-time versus multi factor experiments. Multi-factor trials allow for simultaneous measurement of effects of multiple factors (sets of treatments) and their interaction.
1.5 Local Control of Experimental Errors

**Goal:** Powerful tests! Precise estimates of mean of experimental conditions (treatments). Want reduced experimental error (or control it).

1. **Technique** - Proper application of treatments to units, accurate measurement of outcomes.

2. **Selection of Experimental Units** - Want homogeneous experimental units. Reflective of target population.
   - Similar environmental conditions in field trials.
   - Physical in drug trials.
   - Can't be too restrictive or lose external validity.

3. **Blocking** - Experimental units grouped into homogeneous groups, all units represented in each block (or groups of units). Goal is to remove variation in blocks.
   - Criteria: Proximity (geographic), physical characteristics, time (e.g., day), managing tasks in experiment (batches), (technicians).

4. **Matching Strategies based on influential factors**:
   - Pair matching (exact value vs. caliper value).
   - Non-Pair Matching (frequency-based vs. mean-based).

Experiment Design - Arrangement of experimental units to control experimental error and handle the desired treatment design.
**Experiment Design without Blocking**

- **Treatments**
- **Replicates per treatment** \( N = r k \)
- Randomly assign tests to experimental units.

**Completely Randomized Design**

**Book Example:**
- \( t = 3 \) Engine additives
- \( r = 2 \) rep (engines) per additive.

**Experiment w/ one blocking criteria**

- **Block 1**
  - A
  - C
  - Unit 2
  - Unit 3
- **Block 2**
  - B
  - C
  - Unit 4
  - Unit 5
  - Unit 6

**Randomized Complete Block Design**

**Covariates for Statistical Control of Variation**

- Data consists of \( n \) pairs: \((x_i, y_i)\)
- Suppose \( x_i \) is pre-test score for subject \( i \)
- \( y_i \) is post-test score for subject \( i \)

**2 Tests are to be compared**

- \( \bar{y}_1 \) mean post-test score for treatment 1
- \( \bar{y}_2 \) mean post-test score for treatment 2

**Want to adjust since mean pre-test scores differ.**
Replication for Valid Experiments

- Independent replication =⇒ Reproducibility of results
- Insures against unexpected results due to accidental errors in experimental application
- Allows a means of estimating experimental error variance
- Increases precision of estimates of sample means.

Observational unit ≠ Experimental Unit (Plant in plot, single blind sample w/ Pen).

Variance of observations on experimental units having received treatment independently is experimental error, variance of observational units from the same experimental unit is not experimental error.

Example: 2 pens of animals receiving 2 ratios.
No real replication since pen is experimental unit.
Animals are observational units.

Solution: have multiple pens, look at std. err. among pen means (not among animals within pens).

How many replications? Power considerations

2 Independent samples. (Equal sample sizes) $\sigma^2 = \sigma_1^2 = \sigma_2^2 = \text{Error}$

$s = \text{Practical difference in group means } \mu_1 - \mu_2$

$H_0: \mu_1 - \mu_2 = 0 \quad H_1: \mu_1 - \mu_2 \neq 0$

Want: $P(1.28 \leq |\bar{x}_1 - \bar{x}_2| - 0 \geq \frac{2s}{\sqrt{V_0} \sqrt{\frac{1}{n}}}) \geq 2.8 \Rightarrow \mu_1 - \mu_2 = s$ 1 - $\beta$
Decision Rule: \( H_0: \mu_1 - \mu_2 = 0 \) if
\[
|Z_1| = \left| \frac{(\bar{y}_1 - \bar{y}_2) - 0}{\sqrt{\frac{2\sigma^2}{n}}} \right| \geq z_{\alpha/2}
\]

\( \Rightarrow |\bar{y}_1 - \bar{y}_2| \geq \frac{z_{\alpha/2}}{n} \sqrt{\frac{2\sigma^2}{n}} \)

Under \( H_A: \bar{y}_1 - \bar{y}_2 \sim N(\mu_1 - \mu_2 = \delta, \frac{2\sigma^2}{n}) \)

Want \( \beta \) we reject \( H_0 \) to be 1-\( \beta \) in this case

Let \( \delta = \) such that \( P(\delta = \delta) = \beta \)

Then \( \delta = \delta - 2\sigma \sqrt{\frac{2\sigma^2}{n}} \)

Solving for \( \delta \) gives the unique cut-off \( \delta \)

\[
\frac{z_{\alpha/2}}{\sqrt{\frac{2\sigma^2}{n}}} = \delta - 2\sigma \sqrt{\frac{2\sigma^2}{n}}
\]

\( \Rightarrow \delta = \left( \frac{z_{\alpha/2}}{\sqrt{\frac{2\sigma^2}{n}}} + 2\sigma \right) \sqrt{\frac{2\sigma^2}{n}} \)

\( \Rightarrow \delta^2 = \left( \frac{z_{\alpha/2}}{\sqrt{\frac{2\sigma^2}{n}}} + 2\sigma \right)^2 \left( \frac{2\sigma^2}{n} \right) \)

\( \Rightarrow \delta^2 = 2 \left( \frac{z_{\alpha/2}}{\sqrt{\frac{2\sigma^2}{n}}} + 2\sigma \right)^2 \left( \frac{\sigma^2}{\sigma^2} \right) \)

\( \Rightarrow \delta^2 = 2 \left( \frac{z_{\alpha/2}}{\sqrt{\frac{2\sigma^2}{n}}} + 2\sigma \right)^2 \left( \frac{\sigma^2}{\sigma^2} \right) \)

\( \Rightarrow \delta = 2 \left( \frac{z_{\alpha/2}}{\sqrt{\frac{2\sigma^2}{n}}} + 2\sigma \right) \left( \frac{\sigma^2}{\sigma^2} \right) \)

% CV known = 100 \( \frac{\delta}{\mu} \)

% \( \bar{Y} \) = 100 \( \frac{\bar{Y}}{\bar{Y}} \)
Factors that increase $\tau$
- $pCV$ or $\sigma^2 \uparrow$ (experimental error)
- $pS$ or $S \downarrow$ (practical difference)
- $\alpha \downarrow$ (size)
- $1-\beta \uparrow$ (power)

1.8 Randomization for valid inferences

- Random assignment of treatments to experimental units.
- Questionable whether experimental units included in an experiment are truly a random sample from population.
- Independence unlikely to hold among adjacent units in space or time.
- Fisher showed that randomization provides appropriate reference population for inferences free of distributional assumptions on observations. Normal theory tests provide reasonable approximation.
- Random allocation of treatments to experimental units simulates effect of independence and we can analyze data as if iid Normal.

Randomization Tests
- No assumptions made regarding probability distribution of data.
- Randomization Test creates a population of experiments that could have been conducted.
- Test evaluates the test statistic for all possible amounts of treatments to units for this set of observations.
- Distribution of these values under null hypothesis of no treatment effects is Randomization Distribution.
Example of Randomization Test - see Kuehl Ex. 1.3 (pp21-23)

- Fisher shows normal theory tests are good approximation for randomization tests when:
  - Treatments have been randomly assigned to experimental units.
  - Sample sizes are reasonably large.
  - Sometimes due to cost or bad luck in randomization restriction will have to be placed on randomization.
    (e.g. Split Plot Designs)

1.9 Relative Efficiency of Experimental Designs

- Measure of effectiveness of blocking in terms of reducing experimental error.
  (e.g. Comparing RBD w/ CRD).

\[ \sigma_{QQ}^2 = \frac{\sigma^2}{r} \]

Can reduce by increasing \( r \) or reducing \( \sigma^2 \) by local control.

Design 1: Experimental error variance \( \sigma_1^2 = 1 \)

Design 2: \( \sigma_2^2 = 2 \)

\[ \sigma_{Q1}^2 = \frac{\sigma^2}{r_1} = \frac{1}{r_1} \]
\[ \sigma_{Q2}^2 = \frac{\sigma^2}{r_2} = \frac{2}{r_2} \]

Equal if \( r_2 = 2r_1 \)

\[ \frac{\text{Information}}{I} = \left( \frac{f+1}{f+3} \right) \left( \frac{1}{\frac{f}{2}} \right) \]

\[ s^2 = \text{Estimated error variance w/ f d.f.} \]

\[ RE(\text{Design 1 to Design 2}) = \frac{I_1}{I_2} = \frac{(f_1+1)(f_2+3)s_2^2}{(f_1+3)(f_2+1)s_1^2} \]
Relative Efficiency

RE=1 ⇒ information from 2 designs is equal
RE>1 ⇒ Design 1 more efficient

Design 2 would have to have RE times as many replications as design 1 to have the same variance of a treatment mean.