KUEHL - Chapter 1

(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, computing, ...)

(1.3) EXPERIMENTS, TREATMENTS, EXPERIMENTAL UNITS

- Comparative Experiment - Data collection process used to compare two or more competing circumstances.
- TREATMENTS - Circumstances or conditions created for experiment. Bases 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 (Varying dose...)
  - 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-SELECTION OF SUBJECTS TO TREATMENTS). ETHICAL CONSIDERATIONS

(*) SIMILAR METHODS OF ANALYSIS FOR CONTROLLED EXPERIMENTS AND OBSERVATIONAL STUDIES. MORE DIFFICULT TO CLAIM "CAUSE-AND-EFFECT" FOR OBSERVATIONAL STUDIES (ALTERNATIVE EXPLANATIONS)

(1.4) 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 means 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.

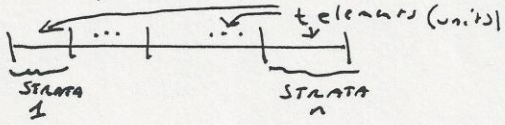
(3) **Blocking** - Experimental units grouped into homogeneous groups, all trts represented in each block (or groups of trts). Goal is to remove variation in blocks.

Criteria - Proximity (Geographical)
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)

Frequency:



Experiment Design - Arrangement of experimental units to control experimental error **and** handle the desired treatment design.

EXPERIMENT DESIGN w/OUT BLOCKING

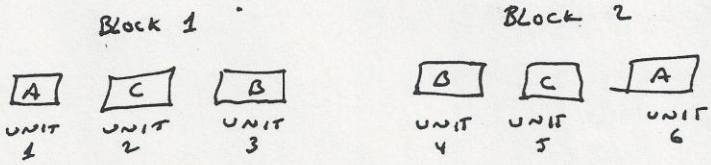
t TREATMENTS
r Replicates per TRT $\quad N = rt$

Randomly assign trts to experimental units

COMPLETELY RANDOMIZED DESIGN

Book EXAMPLE: $t = 3$ Engine additives
$r = 2$ reps (engines) per additive.

EXPERIMENT w/ ONE BLOCKING CRITERIA



RANDOMIZED COMPLETE BLOCK DESIGN

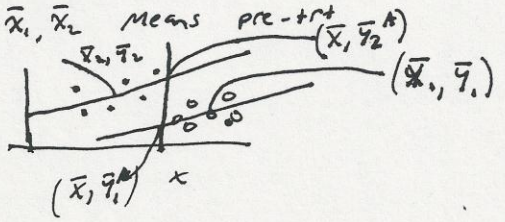
COVARIATES FOR STATISTICAL CONTROL OF VARIATION

Data Consists of n pairs: (x_i, y_i)

Suppose $x_i \equiv$ Pre-Trt test score for subject i
" $y_i \equiv$ Post-" " " " " "

2 TRTS ARE TO BE COMPARE ~~(1,3)~~ (1,2)

$\bar{y}_1 \equiv$ Mean post-trt score for TRT 1
$\bar{y}_2 \equiv$ " " " " " TRT 2
$\bar{x}_1, \bar{x}_2$ Means pre-trt



WANT TO Adjust since mean pre-trt scores differ.

(1.6) 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 "may" $\neq$ Experimental Unit (Plant w/in plot, single blood sample w/in patient).

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

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

Solution - have multiple pens, look @ std. dev. among pen means (not among animals within pens).

(1.7) How many replications? Power considerations

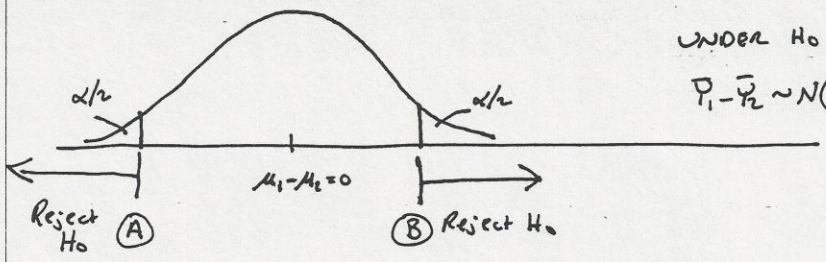
2 Independent samples. (EQUAL SAMPLE SIZES w/ $\sigma_1^2 = \sigma_2^2 = \sigma^2$ known)

$\delta \equiv$ Practical difference in group means $\mu_i - \mu_j$

$H_0: \mu_1 - \mu_2 = 0$ $H_A: \mu_1 - \mu_2 \neq 0$

WANT: $Pr\{|Z| = \left| \frac{(\bar{Y}_1 - \bar{Y}_2) - 0}{\sqrt{\sigma^2(\frac{2}{r})}} \right| \geq Z_{\frac{\alpha}{2}} \Big| \mu_1 - \mu_2 = \delta \} = 1 - \beta$

$\rightarrow$



UNDER H_0

$\bar{Y}_1-\bar{Y}_2 \sim N(\mu_1-\mu_2=0, \frac{2\sigma^2}{r})$

Decision Rule: Reject $H_0: \mu_1-\mu_2=0$ if

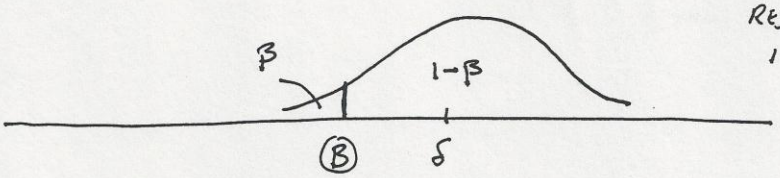
$$|z| = \left|\frac{(\bar{Y}_1-\bar{Y}_2)-0}{\sqrt{\sigma^2(\frac{2}{r})}}\right| \geq z_{\frac{\alpha}{2}}$$

$$\Rightarrow |\bar{Y}_1-\bar{Y}_2| \geq z_{\frac{\alpha}{2}}\sqrt{\frac{2\sigma^2}{r}} \Rightarrow$$

$$\boxed{\begin{aligned} (A) &= -z_{\frac{\alpha}{2}}\sqrt{\frac{2\sigma^2}{r}} \\ (B) &= +z_{\frac{\alpha}{2}}\sqrt{\frac{2\sigma^2}{r}} \end{aligned}}$$

UNDER H_A: $\bar{Y}_1-\bar{Y}_2 \sim N(\mu_1-\mu_2=\delta, \frac{2\sigma^2}{r})$

WANT PROB WE REJECT H_0 TO BE $1-\beta$ in this CASE



Let z_β BE SUCH THAT $P(z \geq z_\beta) = \beta$

Then (B) = $\delta - z_\beta\sqrt{\frac{2\sigma^2}{r}}$

Solving for r That gives the unique cut-off (B)

$$z_{\frac{\alpha}{2}}\sqrt{\frac{2\sigma^2}{r}} = \delta - z_\beta\sqrt{\frac{2\sigma^2}{r}}$$

$$\Rightarrow \delta = (z_{\frac{\alpha}{2}} + z_\beta)\sqrt{\frac{2\sigma^2}{r}}$$

$$\Rightarrow \delta^2 = (z_{\frac{\alpha}{2}} + z_\beta)^2\left(\frac{2\sigma^2}{r}\right)$$

$$\Rightarrow r = 2(z_{\frac{\alpha}{2}} + z_\beta)^2\left(\frac{\sigma^2}{\delta^2}\right)$$

% CV KNOWN $= 100\frac{\sigma}{\mu}$

% δ " $= 100\left(\frac{\delta}{\mu}\right)$

$$\Rightarrow r = 2(z_{\frac{\alpha}{2}} + z_\beta)^2\left(\frac{\%\,CV}{\%\,\delta}\right)^2$$

Factors that increase r

- % CV or σ^2 ↑ (experimental error)
- % δ or δ ↓ (practical difference)
- α ↓ (size)
- $1-\beta$ ↑ (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 populations for inferences free of distributional assumptions on observations. Normal theory tests provide reasonable approximations
- 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 arrangements 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).

$\sigma^2_{\bar{y}} = \frac{\sigma^2}{r}$ Can reduce by increasing r or reducing σ^2 by local control

Design 1: Experimental error variance $\sigma_1^2 = 1$

Design 2: " " " $\sigma_2^2 = 2$

$$\sigma^2_{\bar{y}_1} = \frac{\sigma_1^2}{r_1} = \frac{1}{r_1}$$

$$\sigma^2_{\bar{y}_2} = \frac{\sigma_2^2}{r_2} = \frac{2}{r_2}$$

} EQUAL IF $r_2 = 2r_1$

Information

$$I = \left(\frac{f+1}{f+3}\right)\left(\frac{1}{s^2}\right)$$

s^2 = 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

$RE = 1 \Rightarrow$ information from 2 designs is equal

$RE > 1 \Rightarrow$ 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.