As a result of the randomization, treatment T_1 (low temperature) is to be assigned to package mixes 3 and 5; treatment T_2 (medium temperature) is to be assigned to package mixes 1 and 8; and so on. The experimental trials should be conducted in a random order.

Some statistical packages provide facilities for randomly permuting the treatments (or experimental units) directly, which can simplify the process considerably.

Comments

1. Randomization also can provide the basis for making inferences without requiring assumptions about the distribution of the error terms. We shall discuss this use of randomization in Section 16.9.

2. The implications of randomization may be viewed in a somewhat different fashion than that presented so far. The random errors of experimental units that are adjacent in time or space are often correlated, not independent, as a result of various systematic effects over time or space. Randomization does not eliminate this correlation pattern but, by making it equally likely that any two treatments are adjacent, tends to eliminate the correlations between treatments with increasing replications. Thus, randomization makes it reasonable to analyze the data as though the model random error terms are independent, an assumption that has been made in almost all models discussed so far.

3. Occasionally, randomization may provide a pattern that makes the experimenter uneasy. For instance, randomization of the time sequence in which four experimental units were assigned to treatment 1 and four assigned to treatment 2 may result in a randomized sequence where the four experimental units for treatment 1 are exposed first and then the four experimental units for treatment 2 are exposed. This is not a likely occurrence, but one that can take place. Some solutions have been suggested for this problem, but none provides a final answer. In practice, the experimenter typically will discard a randomization sequence that has apparent dangers of systematic effects for the particular experiment and select another randomization. ■

Constrained Randomization: Blocking

Blocking is a technique that can be used to increase precision in any experiment. To provide some context and to motivate the concept, we shall again consider the vitamin C experiment discussed earlier.

Recall that half of the children in the vitamin C example were randomly assigned to the control group, and half were assigned to the experimental group. At the end of the test period, the number of colds Y contracted by each child was recorded. A linear statistical model for the ith child's response is:

$$Y_i = \beta_0 + \beta_1 X_{i1} + \varepsilon_i \tag{15.4}$$

where:

$$X_i = \begin{cases} 1 & \text{if } i\text{th child receives vitamin C} \\ 0 & \text{if } i\text{th child receives placebo} \end{cases}$$

With X_i defined in this fashion, β_0 is the population mean response for children in the control group (i.e., those receiving the placebo), and $\beta_0 + \beta_1$ is the population mean response for children in the experimental group (i.e., those receiving vitamin C). The treatment effect parameter, β_1, represents the increase or decrease in the average number of colds per child due to the vitamin C regimen. Finally, the experimental error ε_i is the deviation of the number of colds for the ith child from the true mean of the child's treatment group—sometimes called the specific effect associated with the ith experimental unit. The variance of the experimental error is $\sigma^2 = \sigma^2\{\varepsilon_i\}$.

We shall assume that the goal of the study is precise estimation of (or inference about the treatment effect, β_1. Then a key quantity of interest is the variance of the least squar estimator, b_1, of this effect. From (2.3b), we have:

$$\sigma^2\{b_1\} = \frac{\sigma^2}{\sum(X_i - \bar{X})^2} \tag{15.5a}$$

It is easy to show, when the number of children in the two treatment groups are the same, that the variance of b_1 is:

$$\sigma^2\{b_1\} = \frac{4\sigma^2}{n} \tag{15.5b}$$

Thus for a given sample size (here $n = 868$), increased precision can only come about through reductions in the experimental error variance, σ^2.

One way to reduce $\sigma^2\{\varepsilon_i\}$ is to identify and control factors that contribute to variation in the ε_i. In the vitamin C example, some factors (other than vitamin C) that might affect the numbers of colds contracted by the ith child might include: the gender of the child, the age of the child, the general health status of the child, the nutritional habits of the child, and so on. These factors, which affect the response but are not of primary interest to the investigator, are referred to as *nuisance* or *confounding* factors. For simplicity, we will assume that there is just one nuisance factor in the experiment other than the treatment effect, namely, gender. This source of variation could be removed from experimental error by using only males or only females.

For example, if only females are used as subjects, the model for our response is now:

$$Y_i = \beta_0 + \beta_1 X_{i1} + \varepsilon_i^F \tag{15.6}$$

where ε_i^F is the experimental error when subjects are exclusively female. If females tend to have fewer (or more) colds than males, then the female experimental units are more homogeneous and the experimental error variance will be reduced.

Of course there are disadvantages to limiting the experiment to one gender. First the sample size n is reduced, which increases the variance of our estimated treatment effect in (15.4b), and second, we would not be able to generalize the results of the experiment to the gender that was omitted. These disadvantages are overcome by a technique known as blocking.

In a *blocked* experiment, the heterogenous experimental units are divided into homogeneous subgroups called *blocks*, and separate experiments are conducted in each block. For example, blocking on gender in the vitamin C example would be accomplished by conducting separate experiments on males and females. Because gender does not vary within blocks, the effect of vitamin C is more efficiently estimated within each block. The overall effect of the experimental factor is obtained by combining the estimated effects from each of the blocks.

Note that because blocking requires that separate experiments be conducted in each block, it follows that separate randomizations of treatments to experimental units (or vice versa) must be carried out within each block. The within-block randomization is sometimes referred to as a *restricted randomization* because assignments of treatments can only be made to experimental units within the given block.

Figure 15.5 Randomized Complete Block Design—Vitamin C Example.

	Restricted Randomizations						
Male	1	2	3	4	...	433	434
Treatment:	Vitamin C	Vitamin C	Placebo	Vitamin C	...	Vitamin C	Placebo
Female:	1	2	3	4	...	433	434
Treatment:	Placebo	Vitamin C	Placebo	Vitamin C	...	Placebo	Vitamin C

An example of a blocked layout for the vitamin C example is given in Figure 15.5. Notice that each block consists of 434 subjects (assuming half of the 868 subjects are male and half are female), and that the control and experimental treatments are each assigned to half of the subjects in each block. This is accomplished with two restricted randomizations.

The advantages of a blocked experiment over a completely randomized design should be evident in this example. Randomization alone cannot guarantee that the same number of males and females will receive each treatment. Thus if one gender tends to have fewer colds, differences in the treatment groups may be observed even when the experimental treatment has no effect. Another benefit of blocking is that it can increase the range of validity for the conclusions from the experiment. Blocking of experimental units according to their characteristics (e.g., by age) can be employed to provide sufficient variability between groups of experimental units in different blocks for a wide range of generalizability and yet achieve high precision because of small experimental errors within blocks.

As a general principle, an experimenter should always try to remove any known or potential sources of variability, either by holding the nuisance factors constant throughout the experiment or by blocking. Randomization within blocks provides additional protection against any unknown sources of variability that may be present.

Comments

1. The amount of variance reduction achieved by blocking can be seen from a regression context. Suppose in the vitamin C example that the model for the response of the jth subject having gender i ($i = 1$ if female; $i = 0$ if male) is:

$$Y_{ij} = \beta_0 + \beta_1 X_{ij1} + \beta_2 X_{ij2} + \varepsilon_{ij} \tag{15.7}$$

where:

$$X_{ij1} = \begin{cases} 1 & \text{if } ij\text{th child receives vitamin C} \\ 0 & \text{if } ij\text{th child receives placebo} \end{cases}$$

$$X_{ij2} = \begin{cases} 1 & \text{if } i\text{th child is female} \\ 0 & \text{if } i\text{th child is male} \end{cases}$$

Here β_1 can again be interpreted as the change in mean response due to receiving vitamin C (relative to receiving the placebo) and β_2 is the change in mean response for females (relative to males). We will consider this new model which takes into account the potential effects of gender to be the "full" model. If gender is ignored in the design of the study, the appropriate "reduced" model is (15.4). Let $SSE(F)$ denote the sum of squares for the full model—corresponding to the blocked design,

and let $SSE(R)$ denote the sum of squares for the reduced model—corresponding to the completely randomized design. Then we have:

$$SSE(F) = SSTO - SSR(X_1, X_2) = SSTO - [SSR(X_1) + SSR(X_2|X_1)] \quad (15.8)$$

If the number of observations in each block is the same, it can be shown that X_1 and X_2 are uncorrelated (i.e., orthogonal), hence $SSR(X_2|X_1) = SSR(X_2)$. Thus:

$$SSE(F) = SSTO - [(SSR(X_1) + SSR(X_2)] \quad (15.9)$$

From reduced model (15.4),

$$SSE(R) = SSTO - SSR(X_1) \quad (15.10)$$

and it follows from (15.9) and (15.10) that $SSE(F) = SSE(R) - SSE(X_2)$. Therefore $SSR(X_2)$ represents the reduction in the error sum of squares achieved with blocking.

2. When blocking on a nuisance factor is not possible at the design stage, variance reductions can sometimes be achieved at the analysis stage by including the nuisance factor as an additional predictor in the linear model for the response. Returning to the vitamin C example, suppose that blocking by prior gender was not possible. Nevertheless, model (15.7), which considers gender effects, could be employed at the analysis stage if the gender of each subject is recorded. By adding gender (X_2) as an additional predictor to model (15.4), we may realize variance reductions similar to those described in Comment 1 for blocking. This approach, called the *analysis of covariance*, is discussed in Chapter 22. ■

Measurements

The measurement process is another important element of experimental designs. Ideally, the measurement process should produce measurements that are unbiased and precise. *Measurement bias* can cause serious difficulties in the analysis of a study. An important source of measurement bias is due to unrecognized differences in the evaluation process. For example, a group of plants randomly assigned to a new fungicide treatment might unintentionally be evaluated by the investigators to be responding better to the treatment than actually is the case because of a desire to show the new treatment to be effective. When the experimental unit is a person, knowledge of the treatment by the person may also influence the measurement obtained. For instance, a person who knows that the food additive is salt may respond differently in the evaluation of the tastiness of a vegetable than if the additive were unknown. This source of measurement bias can be minimized by concealing the treatment assignment to both the experimental subject and the evaluator. A study using this kind of concealment is called a *double-blind study*. When knowledge of the assignment is withheld only from the experimental subject or the evaluator, the study is called a *single-blind study*.

15.3 An Overview of Standard Experimental Designs

In this section, we give an overview of the best-known and most frequently used experimental designs. In addition, we provide linear statistical models associated with the most basic of these designs. Each of the designs introduced here will be treated in greater detail in the chapters that follow.