Designing Clinical Research Studies: Part II

Joyce Colling

This is part two of the discussion on research design. Part one (Colling, 2003a) covered common types of study designs for quantitative and qualitative studies and a discussion about the study setting. Prior articles included defining a research problem and the important aspects of a literature review (Colling, 2003b, 2003c). In this article, sample selection and determining the number of subjects needed for the study will be addressed. In addition, two other components of the design section of the study will be discussed: the intervention (for a clinical trials study) and the procedures. The final part of the design, how to plan to measure attributes within the study question, will be covered in part three of this series (February 2004). Future articles will include material on collecting and analyzing data, where to find money to conduct the study, how to write a budget, and finally how to write up the findings from the study and disseminate study results.

The decision points along the research journey are like crossroads in highways. They require thought and study to make the best decisions in order to reach your destination. Some decisions may lead to a smoother journey while others to a more tangled journey and unclear destination. Mapping the entire route (design) prior to beginning your research journey will take more time and planning but will increase the strength of the study and get you to your goal more quickly.

Sample Selection

Studies rarely gather information from an entire population of interest. Instead, a sample is selected. Sampling saves time and expense. A major concern in selecting a sample is how representative the sample is to the population; that is, how closely does the sample mirror the characteristics of the entire population of interest. While books have been written on sample selection, several common sampling strategies are presented in Table 1.

Convenience sample. This type of sampling is easy and usually inexpensive. It is a weak strategy to use, however, unless no other alternatives are possible or you are doing a pilot study (a small preliminary study prior to conducting a larger study). The researcher has no control over the characteristics of the sample which may mean the sample may be quite different from the population to which the study results are expected to be relevant. Thus, it is wise to consider an alternative to this sampling method or employ some additional strategies to decrease the sampling bias built in to this strategy. For instance, identify factors that might influence the outcome of the study. If you are studying how patients with chronic UTI describe their discomfort, consider factors that may influence their responses. Some of these might be the presence of other chronic painful conditions, the length of time they have suffered with UTI, their age (elderly persons with UTI may not experience pain as a symptom), and drugs they may be taking for pain relief. Common characteristics that can affect many study outcomes are socioeconomic status, gender, age, and cultural differences. The investigator should always consider these in deciding which to include/exclude or how to manage the potential biasing effects of these characteristics. Bias can be decreased by excluding subjects from the study who fail to meet certain characteristics. Information from the literature review, expert knowledge about the study population, and sometimes brainstorming with other nurses familiar with the population you are planning to study can help determine which characteristics or factors may be problematic and cause bias and which factors are important to study.

Another strategy is to sample two or more different locations (for example, hospitals, clinics). This can sometimes decrease the built-in bias of a single sampling site. These sampling decisions should be made prior to beginning the study.

Small nonrandom samples are almost always used in qualitative studies. Nevertheless, the quality of the sample is important. The investigator is usually interested in gaining understanding of how persons experience a particular phenomenon by asking

Joyce Colling, PhD, RN, FAAN, *is Professor Emeritus, Oregon Health and Sciences University, School of Nursing, Portland, OR.*

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Table 1.
Examples of Sampling Strategies

Sampling Strategy	Characteristics
Convenience	Recruiting all available subjects during a given time who fit the study criteria. It is relatively easy and inexpensive, but considered a weak strategy since unknown biases can exist in the sample. May be an acceptable strategy if you can decrease biases. (See discussion below.)
Quota	A type of convenience sampling which divides the target population into subgroups so there is more potential that the sample will be representative of the total population.
Purposive	The conscious selection of certain subjects or elements for inclusion in the study. Requires use of judgment on the researcher's part to carefully select differing characteristics of subjects which have meaning to the research question in the study. May be particularly useful in qualitative studies.
Network	Subjects refer researcher to others that they know who have similar characteristics needed to answer the study question. Especially good for studies in which the study sample may be hard to find such as drug addicts, prostitutes, grieving widows, etc.
Simple random sample	Selection of subjects on a random basis, using a table of random numbers or other ways to achieve random selection (see discussion below). Strengthens the design of any study, but strongly recommended in intervention studies.
Stratified random sample	Dividing the sample into subgroups such as males, females, young, old, high-education level, low-education level, and then selecting randomly from the subgroups using a table of random numbers. Useful to ensure an adequate number in a subgroup for measurement purposes.

open-ended questions and recording verbatim what the subject says. The goal is to continue to ask the same questions until the researcher hears no *new* information from subjects. Then the recordings are analyzed for common themes or ideas which emerge from the material obtained from the subjects. There are, however, guidelines and criteria for subject selection and for sample size. When planning a qualitative study, find a mentor to assist you or consult a comprehensive book on qualitative research such as Leininger (1985).

Simple random sample. This sampling strategy provides that each person in a population has an equal chance of being selected for the study. For instance, if you will be studying a set of characteristics of all the patients treated in your clinic for prostate cancer for the last 2 years, you would list the entire population who meet the study criteria. A sample from this population would then be randomly selected. One way to accomplish this is to put names or patient record numbers in a container and draw the names/numbers randomly. Another way is to flip a coin. If the toss is heads the person is selected, if it is tails the person is not selected. A more sophisticated method is to use a table of random numbers. If the design has more than two groups, the table of random numbers may be necessary. Many research books have these tables in their appendices (see resources at the end of this article). It is not a difficult procedure, but random sampling greatly strengthens the design of the study by reducing potential selection biases.

Regardless of the sampling strategy used, keep a careful record of the sampling decisions and identify how many people began the study, how many completed the study, and why subjects left the study before completing it. Keep a record of those who refused to participate in the study These records will be of great value to identify potential biases in the study results, to provide a clear narrative of the sampling strategy, as well as to interpret the study findings more precisely.

Sample Size

Determining sample size is an extremely important part of the study. If subjects are hard to get or expensive to enroll in the study, use as few as possible to still have a credible study. After a reasonable number of subjects are enrolled in the study, a law of diminishing returns sets in where adding subjects adds very little information to the study. However, too few subjects could result in sampling error. Studies with too few subjects to reliably "see" an effect have low "power" where tests of statistical significance are less likely to indicate significance even if your study has a real effect (particularly if the effect is small relative to the variability of the sample). For instance, suppose you are planning a chart review study to determine if men who had prostate surgery under the age of 65 had as much postsurgery incontinence as those who were over 65. Your practice did a total of 200 prostate surgeries in the last 2

Table 2.
Sample Size Considerations

Item	Discussion
Complexity of the study	The more complex the study, the larger the sample size. A rule of thumb is that 30 subjects are needed for each variable (concept or characteristic) that will be analyzed.
Attrition from the study	Larger sample is needed if attrition (drop out rate) is expected to be high as with longer studies or vulnerable populations (elderly, dying).
Effect size	If the strength of the relationship or differences among research variables are expected to be great, then a smaller sample is adequate. The literature review should provide evidence of this expectation.
Measurement sensitivity	More precise reliable measurement instruments permit smaller samples. For instance, temperature can be measured precisely, whereas social support measurement is less.

years and you randomly select to review 20 charts of those under 65 and 20 of those over 65. From the literature review, you expect that the incidence in older men will be much greater than for the younger age group. However, the incidence in your sample is only moderately greater in the over 65 age group. When you apply a test for the significance, the statistic is not significant. Thus, even though there was an effect, the number of subjects was too low to be statistically significant. It is likely that with so few subjects, the variability (whether the sample is homogeneous or heterogeneous) was too homogeneous and may not have reflected the true rate of incontinence in the entire population. However, what you found may have been true for this population, in which case, the findings would lead you to examine other factors as to why the incidence of incontinence among these men is lower than what the literature would lead you to expect. In fact, uncovering why this population had a lower incidence of incontinence would be a very important clinical finding.

Computing a power analysis is the gold standard in determining sample size. It increases the probability that the results are true results and not due to factors not considered. If the study is complex or if computing a power analysis seems daunting, consult a statistician or resources on the Web (see reference list). If you do not compute a power analysis, or if it is not feasible to do so, select as large a sample as you can within your time and budget constraints. Many nursing studies which are otherwise good studies suffer from small sample size. Table 2 presents some specific considerations for sample size when not computing "power." One item is not more important than another. They are listed so that you can make a more thoughtful decision about the size of the study.

Intervention Studies

Intervention studies are sometimes called clinical trials or experimental studies. They are designed to answer the "why" questions in research. This means the investigator tests an intervention rather than just observing what occurs naturally in a given setting. There are three main characteristics of intervention studies:

1. *Randomization.* Subjects are assigned to either a control or experimental group(s) on a random basis.
2. *Control.* Use of a control group where part of the subjects do not receive the experimental treatment.
3. *Manipulation.* The introduction of an intervention by the investigator to determine the effect of the intervention on the subjects.

For instance, to determine whether women with fibromyalgia who are incontinent become continent more quickly when taught to do daily Kegel exercises alone, medication alone, or in combination with Kegel exercises and medication, there would be three intervention groups and a control group. The control group has no treatment, treatment group 1 has Kegel exercises only, treatment group 2 has medication only, and treatment group 3 has both exercises and medications. Prior to beginning the study, subjects must be randomly selected into the 4 groups using a table of random numbers.

Procedures

Procedures are the protocols of how you will conduct the study. They describe how subjects will be accessed, who will contact them, what kind of consent will be obtained, how data will be collected from subjects, how often data will be collected (if it is more than one time), what instruments will be

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used to collect the data, and who will collect the data. If the study includes an intervention, describe how, when, and by whom it will be carried out. This detail is useful to ensure that you have thought through each step of the study.

Summary

The focus of this article has been to describe common sampling strategies, determine how to decide sample size, consider the three hallmarks of an intervention study, and to describe what should be included in the procedures of the methods section of the study. An effort was made to emphasize material necessary for beginning investigators who would be designing small quantitative clinical studies. Resources are provided for further clarification and amplification. ◙

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Web site for finding a statistician and general statistical resources: http://www.amstat.org/education/

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