

Reflexology: An Intervention for Advanced Breast Cancer. **National Cancer Institutes funded study grant- Improving quality of life for cancer patients.**

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It is a pleasure to have been asked to speak at your annual conference in May, 2008. In thinking about some of the issues you might like to hear about, I thought this article could set the stage for my conference presentation. There are a number of key methodological issues in complementary therapy (CT) research. In order to provide an illustration of the basic principles of sound research methodology that I'll be discussing, I will use my currently funded National Institute of Health- NIH grant. I am the principle investigator and Dr. Alla Sikorskii is my co-investigator. The National Cancer institute- NCI funded grant is entitled, *Reflexology: An Intervention for Advanced Breast Cancer*. My research is exclusively in the area of improving quality of life for cancer patients.

First, I would like to clarify definitions related to this field of work. **Alternative therapies** has come to mean "in place of conventional medicine." **Unconventional therapies** often has a negative connotation, since most cancer patients are not comfortable with the term health care. **Traditional** is often confused with conventional medicine, when in fact it can mean the practices indigenous to a particular culture or population. For purposes of this article, I will use the term **Complementary Therapies**, since these modalities are not meant to replace conventional medicine, but to work with it. For a working definition, I favor the one put forth by Cassileth in 1998, "therapies used along with conventional medicine that are non-invasive, pleasant, stress-reducing, and can be used in states of sickness or health."

It is hard to say when people began using Complementary Therapies-CT. People have been using indigenous medicines, or "home remedies," since the beginning of time. But, it has only been since the early 1990s that the health care professions have acknowledged widespread use of CTs. One of the first studies to explore the prevalence, costs, and patterns of use was the Eisenberg Study, published in *The New England Journal of Medicine* in January, 1993. Physicians and other advanced practitioners began to acknowledge that use of CT was widespread, since Eisenberg estimated that 33.8% of the general public used some form of CT. Based on this sample of consumers, about 72% did not inform their primary care provider that they were using CT (Eisenberg, 1993). In a 1998 follow-up study, Eisenberg reported that use of at least one complementary therapy increased from the previously reported 33.8% to 42.1%. The rate of patient disclosure to physicians remained nearly the same.

The total 1997 out-of-pocket expenditures for CT are conservatively estimated at \$27 billion, which is comparable to the 1997 out-of-pocket expenditures for physician services.

It is now estimated that 60-80 % of cancer patients use some form of CT. It is vital that patients feel comfortable informing their primary providers about the therapies they are using. Although many of the complementary therapies offer safe and effective care, others pose risks. Well-conducted CT research is needed to inform nursing practice.

To date many CT research findings have been inconsistent due to design and methodological issues. Many of the early studies were at the descriptive level due to sample size and the mixture of types of patients included. Existing publications often lack information on: 1) the number of sessions of the experimental intervention, 2) the duration of each session, 3) the amount of time between sessions, 4) details on the methodology, 5) adequate power, 6) a 3-group design (to distinguish between “attention” and the “active ingredient”), and 7) both self-report and biological measures combined in one randomized clinical trial.

In past research, investigators have designed control groups (placebo) in various ways, such as a mimic group, bedside chat, or music attention. These approaches each have limitations. With a mimic treatment, the researcher must be sure that the person delivering the treatment has not been trained in the specific therapy under investigation. A bedside chat, if scripted, may contain therapeutic content that could alter the outcome variable. A control such as music would be considered an intervention by a music therapist and not a non-treatment at all. In addition to any attention control or placebo group, it is also necessary to have a standard care group. Thus, there are many challenges to CT research. While many of their early studies had their flaws, still, they offer encouraging data to pursue more rigorous investigation.

Level of evidence refers to sources of data relevant to a particular clinical problem. Evidence is ranked according to the strength or rigor of a research study using an evidence hierarchy. A number of valid evidence-based hierarchies exist, but I've chosen to use the hierarchy created by the Agency for Health Care Policy and Research (1994). I like this hierarchy because it is used consistently in the literature and it illustrates the divisions between levels of evidence well.

A meta-analysis of the RCTs is the highest level of evidence. The randomized clinical trial is the “gold standard” of evidence. Then on the other end of the scale are nonexperimental studies and expert opinions representing the weaker forms of evidence to support health care practices. Funding agencies, such as NIH, expect CT researchers to adhere to the same standards as researchers in more traditional areas of investigation.

The purpose of this article is to address some of the issues that confront CT researchers. Hopefully, these ideas will better position CT researchers to obtain funding, and clinicians to understand the issues involved in this type of research.

The Wyatt Quality of Life Model provides the conceptual framework for our overall program of research. The Model emerged from a series of carefully designed qualitative studies and then quantitative testing's of the model. Four domains constitute the key elements of the model: physical well-being, psychological well-being, social well-being, and existential/philosophical well-being.

There are several ways to design and conduct a strong CT research study.

1. The RCT provides the strongest source of evidence.
2. A second strength is the use of a three- group design.
 - a. The experimental group receives the true experimental treatment.
 - b. The placebo group receives a treatment that mimics the true CT, but the “active ingredient” of the true CT is not present.
 - c. The control group receives standard care as usual, as do the experimental and placebo groups.

Another way to strengthen the study is the longitudinal design. A pre-test/post-test design will only capture the immediate effect of the intervention, that is immediately after it is completed. A longitudinal study employs at least three data collection points: baseline and at least two additional data collection points interviews at predetermined intervals that are appropriate for the specific intervention. The intervention is administered between baseline and the second data point.

By administering the instruments at predetermined intervals, for example seven and thirteen weeks for the study I am currently working on, we are able to measure the sustainability of the intervention. Besides learning if the intervention is immediately efficacious, we can also learn if it has a sustained effect.

In regard to CT, we don't know the sustainability of most therapies. Thus the schedule of administering the instruments in a longitudinal study is a very important part of the testing, and consistency of timing of the data points is of paramount importance.

Randomization of participants is an essential part of the study design. A researcher has choices to make, and each strategy has its own strengths. What is desired is an equalization of the conditions and differences in the inherent characteristics of the participants spread across the three groups at baseline. This allows for the differences among groups post-intervention to be attributed to the intervention and not to differences between groups at baseline. The goal is to start with equivalent groups. A couple of possibilities exist, including simple randomization, blocked randomization, and stratified randomization.

The technique used in our study is computerized minimization, which is a compromise between randomization and stratification. The researchers agree on the variables most likely to impact the primary outcomes and balance the groups on these variables. In our current study, the four balancing variables are recruitment location, or the oncology clinic setting; the levels of pain and fatigue assessed at baseline; and the goal of therapy, i.e. maintenance, palliative, curative. Computerized minimization balances the three groups on four variables. It is a step-wise procedure that, at each step (each participant assignment), adjusts the probabilities of assignment based on the history of randomization in order to minimize the dis-balance among the groups.

The power and sample size calculation was based on the primary outcome variable, Quality of Life. The sample size will ensure adequate power to detect clinically significant differences in the means of outcome measures across the three groups. We will need 100 participants per group to complete the three data points. The recruitment goal of the study is to over sample to 350 participants to offset attrition. That number should be sufficient to offset attrition and provide the full data for 300 subjects, or 100 for each group.

We will analyze data following the “Intention to treat” approach. In other words, subjects’ data will be analyzed as they were randomized, even if they do not complete all of the intervention or the interviews. For the purposes of the reflexology study, the protocol for dose factor is that three out of four interventions are considered to be a full dose. “Intention to treat” gives a more conservative estimate of the intervention effect compared to “per protocol” analysis.

The longitudinal design will allow the researcher to evaluate the time trends in outcomes. In the example study, there are three measures of all of the instruments: baseline, 7 weeks, and 13 weeks. This allows us to evaluate the immediate and the sustained effects of the intervention.

Much of the variation in outcome at seven weeks and at thirteen weeks can be explained by baseline scores of individuals, so baseline values of the outcomes will be included as covariates in the models. Interaction between group and outcome variables at baseline will be also be explored.

Sequencing of specific aims refers to the three-arm design of the study. Following comparisons of all three groups, it will be possible to compare the groups pairwise. We will be able to compare group A (reflexology) to group B (placebo), group A to group C (control), and Group B to group C. If there is difference among the three groups, we will be able to detect which of them are different from each other. Most previous CT research compared the intervention group to a standard care group. By comparing the placebo group as well, we can test for the placebo effect of simply having similar attention as the true intervention group.

This reflexology study falls in nearly the highest level of the hierarchy of evidence, so will produce very valuable data. The design decisions will contribute to the researcher’s ability to conduct complementary therapy research that will inform and translate to practice. The specific areas outlined in this article are intended to strengthen the design and research methodology, and increasing the practitioners awareness of the elements of a solid research project.

Read more at;

<http://news.bio-medicine.org/medicine-news-3/Breast-cancer-patients-turn-to-reflexology-for-comfort-8357-1/>

<http://www.medicalnewstoday.com/articles/31689.php>

http://www.aphroditewomenshealth.com/news/20050906211107_health_news.shtml