
LECTURE TWO: Blinding, Intervention and Controls

Reading Assignment for Lecture 2

Required Reading:

- Designing Clinical Research (4th Edition), Chapter 10, pages 147-149.
- Fundamentals of Clinical Trials (4th Edition), Chapter 7.
- Noseworthy H, et al. The impact of blinding on the results of a randomized, placebo- controlled multiple sclerosis clinical trial. Neurology 1994 44: 16-20.
- Kirkley A, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med. 2008 Sep 11;359(11):1097-107.

Homework Assignment for Lecture 2

Total score = 16 points

Assignment file: AssignL2_2014.doc

Assignment due:

- email to Carolyn Seib & Jesus Valdez (clinicaltrials2014@gmail.com) by January 21, 2014; 5pm.
 - Make sure that your NAME is on the top of the document
 - Use this format to name your homework documents:
 LastnameFirstname_L#, for example: SmithJohn_AssignL2
 - Subject Line of email: SmithJohn_L2
- bring a copy of homework to Section I on January 23, 2014

Please give a brief answer to the following questions.

Hot flashes occur in about 2/3 of all women during the menopause transition and about 20% seek medical treatment for this problem. Estrogen therapy is highly effective, but can have adverse effects including blood clots, stroke and dementia. For this reason, many women seek non-hormonal treatment. The ideal treatment might be a behavioral intervention that has no adverse effects. The mechanism of hot flushes is not fully understood, but there is significant evidence that increased sympathetic nervous system activity plays an important role.

1. Physiologic studies have shown that practicing yoga increases heart rate variability and decreases oxygen consumption, heart rate and blood pressure, all indicative of decreased sympathetic nervous system activity. Small, uncontrolled pilot studies demonstrate that practicing Restorative Yoga resulted in a substantial decrease in the frequency of hot flashes and improvement in quality of life.

The intervention consists of learning and practicing 6 Restorative Yoga poses. Training occurs in groups of 12 to 15 that meet for 60 minutes twice per week for a month, then 60 minutes once per week for 2 additional months. The groups are taught by a certified yoga instructor using a standardized protocol. The participants

are asked to practice at home for 30 minutes at least 3 times per week, and they are provided pictures of the poses, written instructions and a video to show them how to correctly get into the poses.

You are planning a full-scale, randomized trial of this yoga intervention. Inclusion criteria are women 45 to 60 years old with at least 7 self-reported hot flashes per day or 50 per week. The main outcome is change in the number of hot flashes per day reported on a diary kept for 7 days at the beginning and the end of treatment.

- a. When designing this trial, one needs to think carefully about the control group. One option is to randomize participants to yoga or a nothing group and evaluate 3 months later. However, this is not the best option as improvement in the yoga group may be due to a placebo effect or to co-interventions such as the benefit of socializing within a group. Briefly discuss at least one other option for a control group and list at least 2 pros and/or cons of that option. (6 points)
 - b. This study is unable to be blinded because of the nature of the intervention. Given this, what additional steps need to be taken in outcome ascertainment/tactics can you take to try to limit biases? Please name at least two. (4 points)
2. Physiologic studies have also shown that paced respiration (slow breathing) decreases sympathetic nervous system activity and small, uncontrolled pilot studies show promising results. The intervention consists of using a machine called the Resperate™, an interactive device that is FDA approved for treatment of mild hypertension. Using a simple chest strap sensor, the device (the size of a portable CD player) senses the respiratory rate and rhythm and plays a different musical tone for inspiration and expiration. As the subject follows these tones, respiration is slowed and the expiratory phase is prolonged, such that almost all subjects achieve a respiratory rate of less than 10, many less than 6 breaths per minute. The device tracks the time that the respiratory rate is less than 10, and “followness”, a measure of the smooth rhythm of breathing and the avoidance of breath-holding. Participants are asked to use the Resperate for 10 minutes per day.
- a. What intervention do you plan for the control group? Why is no control intervention a bad choice? (4 points)
 - b. Could you blind this trial? Please explain why or why not. (2 points)