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A Health Education Intervention as the Control Condition in the CTN-0037 STRIDE multi-site exercise trial: Rationale and Description

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Abstract

The selection of a control condition in a randomized controlled trial (RCT) is critical in determining the effect of the experimental treatment. While the use of a placebo pill can be an ideal control in pharmaceutical trials, RCTs of behavioral interventions present unique challenges in the selection and implementation of the appropriate control condition. Investigators must not only consider the control condition's ability to protect against threats to internal validity and its plausibility as a possible intervention, but must also carefully implement the control condition so it does not introduce bias from either the investigators or the participants. The purpose of this paper is to provide the rationale for the use of a health education intervention (HEI) as the control condition in the CTN-0037 Stimulant Reduction Intervention Using Dosed Exercise (STRIDE) trial. In this paper, we will describe the careful design of the HEI to ensure proper implementation and discuss alternative control conditions considered.

Keywords

Control condition; Health Education; Exercise; Design

The thoughtful selection and careful implementation of a control group is essential to the success of randomized controlled trials (RCTs). In RCTs, the primary purpose of a control condition is to protect the internal validity of the trial. While the use of placebo medications is a clear choice in pharmacological RCTs, there is no such option in RCTs with behavioral experimental conditions. A great deal of literature describes the merits of different control conditions in behavioral RCTs and more recent work presents factors to consider in the selection of a control condition (Freedland, Mohr, Davidson, & Schwartz, 2011; Mohr et al., 2009). This work also highlights the rigor by which the control condition is implemented to ensure the success of the RCT. The purpose of this paper is to: 1) describe the rationale for the selection of the control condition used in the CTN-0037 Stimulant Reduction

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Intervention using Dosed Exercise trial (STRIDE); 2) describe design factors used within the control condition to ensure its successful implementation; and 3) provide a detailed description of the Health Education Intervention (HEI) used as the control condition in the STRIDE trial.

Study Overview

The STRIDE trial aimed to examine the efficacy of an aerobic exercise intervention as augmentation to treatment as usual (TAU). Patients with stimulant abuse in nine residential treatment programs (RTPs) were recruited to participate. Participants (N=302), after providing informed consent and completing a screening process, were randomized to receive augmentation of TAU with either aerobic exercise or health education. Participants in both conditions attended 3 intervention sessions per week during the 12-week acute phase of the study. The exercise dose was 12 kilocalories per kilogram of bodyweight (KKW). The 12 KKW dose was selected as it equivalent to the current American College of Sports Medicine physical activity recommendations (Haskell, Lee, & Pate, 2010). The primary outcome for the STRIDE trial was the percent days of abstinence from stimulants during this 12-week period. A more thorough description of the study design and outcomes has been published elsewhere (Stoutenberg et al., 2012; Trivedi, Greer, Grannemann, et al., 2011; Trivedi, Greer, Potter, et al., 2011).

Rationale

In selecting the appropriate control condition, we considered several options including: TAU, a low dose exercise intervention, and a health education intervention. We ultimately chose the HEI as the control condition; below we describe the rationale for that decision.

The STRIDE trial design augmented TAU with exercise; therefore, we first considered using TAU alone as a control condition. In this study design, the results would have indicated whether TAU + exercise is better than TAU alone. The advantage of this trial design would be that it would most accurately reflect if exercise augmentation would improve outcomes of the current treatment regimen. However, there are disadvantages to the use of a TAU control condition in this study. First, participants assigned to the TAU condition may become disenfranchised, thus reducing retention in the control condition. Second, while the results would indicate the efficacy of the exercise intervention in improving treatment outcomes, those improvements could not be attributed specifically to the exercise itself. In STRIDE, as with any other exercise trial, the primary threat to internal validity is the attention participants receive through contact with study staff. Participants in the exercise condition would receive additional attention through their interactions with study staff. Therefore, any differences between the two groups at the end of the study could be attributed to that increased attention. This may be especially true in the STRIDE trial, as increased attention is associated with improved treatment adherence in substance abuse patients (Stark, 1992). Therefore, we determined that the control condition must provide comparable staff contact to the exercise intervention.

We considered two options for an attentional control group. First, was a low dose exercise group. We have successfully used low dose exercise groups in previous trials (A. L. Dunn, Trivedi, Kampert, Clark, & Chambliss, 2002; A.L. Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005; Trivedi, Greer, Potter, et al., 2011; Trivedi, Greer, Grannemann, Chambliss, & Jordan, 2006; Trivedi, Greer, Grannemann, Church, et al., 2006). The advantage to a low dose exercise group is that the structure and contact with study staff would be identical across the two groups. The disadvantage of using a low dose exercise group is the unknown effect of exercise in this population. The DOSE and TREAD trials were preceded by other trials supporting the antidepressant effects of exercise. Therefore,

these trials could examine differential response to two doses of exercise. Because STRIDE is the first trial to examine the effects of aerobic exercise on stimulant use, effects of a low dose of exercise on this population is unknown. It is possible that both a low dose of exercise and a higher dose of exercise could be efficacious and thus treatment effect would not be detected. Therefore, we chose not to use a low dose exercise control condition. However, if the STRIDE trial provides results suggesting a benefit of exercise in the treatment of stimulant abuse and dependence, future trials could then aim to identify the optimal dose of exercise and the related biological mechanisms.

We ultimately chose a Health Education Intervention (HEI) as our control condition. The HEI consisted of a schedule of sessions identical to the exercise intervention, thus ensuring equivalent staff contact with participants across the two conditions. The HEI has been established as an ineffective, yet attentionally equivalent control condition in studies of exercise (Marcus et al., 1999; Pahor et al., 2006; Rejeski et al., 2005). However, it is possible that HEI may have an effect on substance abuse. Engaging in the HEI may have effects on psychosocial factors related to improved treatment outcomes including increased self-efficacy, increased social support and increased participant autonomy. This may ultimately reduce the observed effect size. Though the effect size may be diminished, a clinically meaningful effect size, if present, will be detected due to the large size of the trial. Additionally, the HEI was designed to minimize its effect on psychosocial factors. Beyond the act of attending the HEI session, participants in the HEI were not provided specific goals to achieve during these sessions. This is in contrast to the exercise condition, in which participants had a defined exercise dose goal to achieve. Furthermore, the exercise condition involved skill acquisition due to the fact that participants in the trial were sedentary. Conversely, the HEI, as described below, consisted mainly of watching informational videos. Members of the STRIDE Protocol Development Team had previous experience in using HEI as a control condition and the knowledge gained from their experience helped ensure its effective implementation.

HEI Design Considerations

While control conditions are implemented primarily to protect a study's internal validity, the characteristics of the control condition may have unintended effects that negatively impact a trial's success. One important principle in the conduct of RCTs is equipoise (Freedman, 1987). In biomedical research, equipoise is the assumption that one treatment is not superior to another. This is especially important in behavioral RCTs in which double blinding is often not possible. A lack of equipoise can introduce both researcher and participant biases.

In psychotherapy RCTs, therapist allegiance has been identified as a potential source of bias (Luborsky et al., 1999). This phenomenon can also apply to other behavioral interventions, such that the person administering the intervention must feel that they are delivering a legitimate treatment. As such, several strategies were implemented to legitimize the HEI. Though previous work had shown this HEI to be ineffective, it was not presented as such to the study staff. The STRIDE trial was framed as a “health intervention study” that compared two health interventions: 1) aerobic exercise and 2) health education. Furthermore, the HEI was manualized, the interventionists were trained to administer the HEI as described in the manual, and the study lead team monitored intervention fidelity and adherence consistently across the two interventions.

These steps were also anticipated to have effects on participant expectations and engagement in the intervention. The success of STRIDE, as with other behavioral RCTs, is dependent upon participant adherence to the intervention. If participants believe they are assigned to the control condition, they will be less likely to adhere to the intervention. In

fact, outcomes are worse for participants who are aware that they have been allocated to a control condition (Basham, 1986; Gaudiano & Herbert, 2005; Harris & Miller, 1990). Since participants could not be blinded to the treatment allocation, the study staff presented the STRIDE trial to participants as a comparison of two health interventions to avoid participants becoming disenfranchised by assignment to the control condition. Furthermore, procedures in the HEI also matched those used in the exercise intervention. Participants in the HEI group were monitored similarly to participants in the exercise condition, and they received behavioral adherence strategies on the same schedule as exercise participants. All attempts were made to address barriers to retention in the HEI, as in the exercise intervention.

HEI Design

The HEI was structured to provide equivalent contact to that of the exercise intervention. In the Acute Phase (the first 12 weeks), supervised sessions were conducted three times per week, during which participants viewed educational items such as didactical presentations, readings, websites, and audio and video materials. Health Education Facilitators (HEFs) instructed participants to log the materials reviewed. In both interventions, contact and conversation between facilitators and participants were limited to focus on assistance with implementation of the session, and session content. Visits occurred weekly in the Continuation Phase (months 4-9). Missed intervention sessions were not made up in subsequent weeks (i.e., once an intervention week ended, participants planned the new week with no carry-over from the previous week). For sessions missed during a week, every effort was made to ensure that a make-up session was scheduled within that week.

The HEI sessions were designed to last about as long as the exercise sessions: approximately 30-45 minutes. Like with the exercise sessions, the HEI participants scheduled individual times for their HEI sessions, but for HEI, there may be more than 1 participant in the room at one time. The interventions were not designed as a group intervention, so care was taken by the facilitators to discourage group formation. The participants could attend sessions where other participants were present, but there was to be minimal group interaction. The HEF would interact with the participants individually during the sessions and not encourage group discussion. If considerable social interaction occurred among participants at HEI sessions, the HEF would attempt to redirect the discussion to the content being presented.

The HEI was made up of various health topics and corresponding activities specific to each topic. Instructional topics included areas such as healthy eating habits, recipes for healthy eating, preventive health care and recommended health screenings (e.g., cancer prevention, cardiovascular disease prevention), accessing health care resources, and other health related topics that were relevant to adults with substance use disorders. Activities included watching DVDs, reading handouts/brochures, reading magazines, going to specific health websites, games, and hands-on tasks. See Table 1 for the list of HEI topics and activities. Participants were encouraged to suggest topics of interest to help maintain their involvement and engagement in the sessions throughout the duration of the study. Some activities last longer than others, so participants could spend several sessions on the same activity. For example, some DVDs would take several sessions to finish. Additional materials were given to correspond with the particular topic and help to enhance the education and participant interest (i.e., floss and toothbrushes for the Dental Hygiene topic). Similar topics were used in previous trials using an HEI as a control condition and were found to be feasible to deliver and acceptable to participants (Marcus et al., 1999; Pahor et al., 2006; Rejeski et al., 2005).

Available topics for the participant to choose from varied from the Acute Phase to the Continuation Phase. There was a subset of fewer topics available in the Acute Phase, but all topics were available in the Continuation Phase. The HEF would help the participant choose topics and activities that were of interest to them and to plan for their HEI sessions. A participant could stop in the middle of an activity if they lost interest and switch to a new activity. Similarly, the participant could begin a topic one session, but move on to a different topic the next session without finishing the activity (i.e., without watching the entire accompanying DVD).

HEI Monitoring and Documentation

During HEI sessions, the HEF completed the *Health Education Session Checklist/Progress Note* and provided comments on the session in the Progress Notes section. Participants also completed the *Health Education Log* detailing the HEI sessions attended, the topic and activity. All data from the HEI sessions were immediately entered into the STRIDE website at the conclusion of the HEI session.

HEI Adherence

Several strategies were implemented to ensure maximal adherence to both interventions. The strategies relevant to the HEI are described below; however, identical strategies were implemented in the exercise condition.

Introductory Session

The Introductory HEI Session was the first meeting between the participant and the HEF. During the Introductory HEI Session the HEF provided an overview of the HEI to the participant. This session also served as an initial opportunity to build rapport with the participant. At the Introductory HEI Session, participants received: 1) a general outline of HEI and the schedule (including each of the phases of the study), participant requirements, and information in the STRIDE Binder; 2) instruction on use of the study equipment (computers, TV and DVD player); 3) instruction in accurate self-monitoring and recording of HEI session data; 4) psychoeducation about the need to achieve adherence goals, including discussion of planning, prompting, the incentive plan, and discussion of possible barriers to adherence. Participants were then guided in developing their 1st weekly HEI plan using the Health Education Initial Planning Worksheet and Behavioral Contract. This worksheet served two purposes: first, it allowed the participant to schedule the remaining two HEI sessions required for the 1st week; second, the participant signed the Behavioral Contract showing his/her intent to fulfill the health education agenda.

Weekly Planning and Monitoring

A similar planning session occurred prior to the first HEI session of each week. During the weekly HEI planning, the HEF reviewed adherence from the previous week with the participant. Participants were eligible to earn adherence awards for meeting specific adherence goals (Table 2). For participants who did not achieve 100% adherence, the HEF discussed any barriers to adherence and provided feedback and helped participants develop strategies to address the relative HEI barriers. Finally, the HEF worked with the participant to develop an overview of the HEI training plan for the upcoming week.

Participants were monitored weekly and contacted to reschedule missed HEI sessions. The study staff, along with the Lead Team closely monitored adherence to the weekly HEI sessions. To aid the Lead Team in monitoring HEI adherence, the HEF completed a Daily Adherence Report at the end of each day that was sent to the Lead Team. HEI session adherence was calculated each week (% sessions completed throughout the week divided by

the number of sessions required for the week). HEFs would provide the participant with verbal reinforcement related to adherence. If adherence goals were met, the HEF would congratulate the participant for his/her hard work. If goals were not being met, the HEF worked with the participant to help him/her achieve the targeted number of sessions for the week.

Conclusion

The STRIDE trial aims to examine the effect of augmenting TAU for stimulant abuse with exercise. As we have described above, the internal validity of the STRIDE trial is dependent upon the selection and implementation of an appropriate control condition. As a result, differences between the exercise group and the control condition group at the end of the trial can only be attributed to the effects of the exercise intervention. After considering several alternatives, we ultimately chose a health education intervention as the control condition. This decision was based on identifying a control condition that not only would provide equivalent attention across the two conditions, thus protecting against the trial's internal validity, but also could be implemented in such a manner that would not introduce investigator or participant bias. Variation in the design and goals of each RCT of a behavioral intervention necessitates a range of control conditions (Freedland et al., 2011; Mohr et al., 2009); however, the factors that affect the selection of the appropriate control condition are constant. This paper provides a real-world example of the process and rationale for selecting a control condition in an RCT of a behavioral intervention, and therefore serves as an aid to researchers in this critical study design decision. Finally, we describe in detail the structure of the HEI used as the control condition in the STRIDE trial. Though not appropriate for all trials, this description highlights critical design features to consider for successful implementation of a control condition in a behavioral RCT.

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Highlights

- Rationale for a health education intervention (HEI) control condition
- Advantages of using the HEI in exercise trials assessing psychological outcomes
- Careful design of the HEI to ensure proper implementation
- Discussion of alternative control conditions considered

Table 1
Health Education Intervention Topics and Activities

Acute Phase		Continuation Phase	
Topic	**Activity**	**Topic**	**Activity**
Cancer	The Truth About Cancer (DVD, 116 minutes)	Sleep	Good Night with the Sleep Doctor (DVD, 79 minutes)
	Secrets for Reducing Your Breast Cancer Risk (DVD, 80 minutes)	Healthy Eating	Handouts: "Just Enough for You: About Food Portions, "Bacteria and Foodborne Illness", and "Weight-loss and Nutrition Myths"
Alzheimer's	The Forgetting (DVD, 90 minutes)		Websites: www.cookinglight.com www.hearthealthyonline.com
Obesity	Fat: What No One is Telling You (DVD, 90 minutes)		Handouts: "10 Things to Know about Evaluating Medical Resources on the Web" and "Online Health Information: Can You Trust It?"
Heart Disease	Heart Disease in America: The Hidden Epidemic (DVD, 116 minutes)	Finding medical info online	Websites: www.WebMD.com www.health.nih.gov www.cdc.gov
Depression	Depression: Out of the Shadows (DVD, 90 minutes)		The New Medicine (DVD, 114 minutes)
Common Illness	Nurse's Notebook: Hints for Health (DVD, 75 minutes)		Handouts: "Are You Considering Using CAM?", "Using Dietary Supplements Wisely", "Massage Therapy: An Introduction", "Acupuncture: An Introduction", "Meditation: An Introduction"
Mental Health	This Emotional Life (DVD, 360 minutes)	Alternative Medicine	Materials: stress ball, aromatherapy oil
Dental	Handouts: "Finding Low-Cost Dental Care", "Plaque: What it is and how to get rid of it", and "Dry Mouth"		Healing Words: Poetry and Medicine (DVD, (DVD, 60 minutes)
	Materials: toothbrush, toothpaste		Materials: art kit
HIV/AIDS/Hepatitis	Handouts: "HIV and AIDS: Are You at risk?", "HIV and Its Treatment: What You Should Know", "Hepatitis A General Information", "Hepatitis B General Information", "Hepatitis C General Information", and "Viral Hepatitis: A through E and Beyond"	Art	Handout: synopsis from LT
		Laughter	Materials: comics, books, videos, websites
General	Human Body: Pushing the Limits (DVD, 172 minutes)	Brain Health	The Secret Life of the Brain (DVD, 300 minutes)
			Websites: www.fitbrains.com www.brainhealthandpuzzles.com Materials: Sudoku books, puzzles

Table 2
Health Education Intervention Adherence Criteria and Awards

Week	Adherence Criteria and Award
Week 1	Participants who attend all planned sessions will receive a pen & notebook.
Week 2	Participants who achieve > or = 80% adherence will receive a travel alarm clock.
Week 4	Participants who attend all of the planned health education sessions for week 4 (or the participants first week outside the residential setting) will receive a $10 gift card.
Week 6	Participants who achieve an average of 80% or better adherence for Weeks 5 and 6 will receive a $25 gift card.
Week 12	Participants who achieve an average of 80% or better adherence for weeks 10, 11, and 12 will receive a $50 gift card.