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Short Communication

An ounce of prevention: A pre-randomization protocol to improve retention in substance use disorder clinical trials

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HIGHLIGHTS

- Missing data are a problem for valid inference in all areas of research.
- Substance use disorder researchers routinely report over 20% missing data points.
- Before randomization, a thorough real-world discussion of all potential retention threats may improve attendance/adherence.
- Adherence and complete data points were each over 90% following implementation of a pre-randomization retention protocol.

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ABSTRACT

Background: Missing data in substance use disorder (SUD) research pose a significant threat to internal validity. Participants terminate involvement or become less likely to attend intervention and research visits for many reasons, which should be addressed prior to becoming problematic. During a 9-month study targeting stimulant abuse, early dropouts and participant reported attendance barriers led to implementing a structured, pre-randomization protocol with participants about retention and solution-focused strategies (the "Fireside Chat"). Our aim is to outline this approach and present data on intervention participation and research visit attendance after implementation.

Methods/design: STimulant Reduction using Dosed Exercise (STRIDE) was a two-arm, multisite randomized clinical trial testing treatment-as-usual for stimulant abuse/dependence augmented by Exercise or Health Education. For both groups, study intervention visits at the site were scheduled 3/week for 12 weeks followed by 1/week for 24 weeks. During The Chat, research staff thoroughly reviewed participants' expectations, and barriers and solutions to retention. Fifteen participants were randomized (to Exercise or Health Education) prior to and fourteen were randomized after Chat implementation. Intervention and monthly follow-up attendance (before and after implementation) were compared at the site (N = 29) that developed and rigorously implemented The Chat.

Results: Individuals who participated in The Chat (n = 14) attended significantly more intervention visits during weeks 1–12 ($p < 0.001$) and weeks 13–36 ($p < 0.05$) and attended more research visits ($p < 0.001$).

Discussion: Proactive discussion of expectations and barriers prior to randomization was associated with greater study attendance. SUD researchers should consider tailoring this approach to suit their needs. Further investigation is warranted.

1. Introduction

Missing data in longitudinal substance use disorder (SUD) research pose a significant problem for drawing valid inferences, with 20% of participants routinely lost to follow-up after 3 months of participation and nearly one-third of participants missing data beyond 12 months (Hansen, Tobler, & Graham, 1990). This poses a severe threat to internal validity, and researchers are frequently faced with the dilemma of how to handle missing observations, particularly for rigorous, longitudinal SUD research. All commonly employed imputation methods within SUD research (e.g., last-observation-carry-forward, missing equals positive, multiple imputations, and full-information maximum likelihood)

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are subject to error. Further, these methods assume data are missing at random (MAR) or missing completely at random (MCAR). When the data are not missing at random (NMAR; i.e., the probability of a missing value depends on the variable that is missing) the missing data mechanism must be modeled to obtain valid parameter estimates. For this reason and others, missing information should be minimized through proactive, ongoing study staff efforts to refine and improve the recruitment and retention process and facilitate participant attendance; however, little formal research guides best practices for retaining participants.

Participants join studies for a variety of reasons (Scott, Walker, White, & Lewith, 2011), including personal relevance, altruism, and monetary compensation (Kost, Lee, Yessis, Coller, & Henderson, 2011). Also, participants terminate involvement or become less involved for many reasons, including perceived stigma, scheduling difficulties, SUD symptoms, and waning motivation (Ball, Carroll, Canning-Ball, & Rounsaville, 2006; Claus, Kindleberger, & Dugan, 2002). Most reasons can and should be addressed prior to becoming a retention issue, particularly for longitudinal research designs.

Engaging participants in a comprehensive, collaborative discussion prior to randomization about real-world barriers to research attendance may hold promise to maximize retention. Evidence supports participant comprehension as an important factor of involvement in multisite RCTs (Lipton et al., 2011). Further, team recruitment approaches have had success in a variety of studies (e.g., weight gain prevention; Stockton, McClanahan, Lanctot, Klesges, & Beech, 2012).

In response to dropouts and participant-reported attendance barriers, we initiated a structured protocol with ongoing participant collaboration, called the "Fireside Chat." This approach augmented the informed consent process with participants and was applied rigorously within the context of a multi-site, longitudinal intervention study with stimulant abusers to maximize available data and participant retention. The aims of this secondary data analysis are to describe the Fireside Chat and present data on intervention and research visit attendance for participants who did and did not participate in a Fireside Chat at one of the study sites.

2. Study background & methods

2.1. STimulant Reduction using Dosed Exercise (STRIDE) design overview

A multisite RCT (*STimulant Reduction using Dosed Exercise* [STRIDE]) was conducted by the National Drug Abuse Treatment Clinical Trials Network at nine U.S. residential substance abuse treatment programs (RTPs). STRIDE (N = 302) compared Exercise versus Health Education as augmentation to addiction treatment-as-usual in individuals with stimulant use disorders (Trivedi et al., in press). Men and women (ages 18–65) who were admitted to RTPs, used stimulants in the 30 days prior to admission, met DSM-IV criteria for stimulant abuse/dependence, and medically cleared to exercise, were eligible.

Randomization to Exercise or Health Education occurred soon after treatment admission to maximize days of study participation during the RTP stay and increase the likelihood of intervention attendance. Study visits (i.e., Exercise or Health Education intervention and research visits) occurred 3/week for three months (weeks 1–12; acute phase), followed by six months of weekly visits (weeks 13–36; continuation phase). Exercise was prescribed at approximately 50 min, 3 days per week. Health Education consisted of online, video, and written educational materials for an equivalent period of time. Complete design and rationale are described elsewhere (Greer et al., 2012; Stoutenberg et al., 2012; Trivedi et al., 2011).

2.2. Study initiation and identification of study-implementation challenges

At study initiation, staff proactively discussed and monitored participants' treatment status (e.g., outpatient treatment plans) to help ensure decisions to randomize were fully informed. Further, due to the large participant-time investment (>50 h for highly adherent participants, not including travel time), incentives were provided to increase intervention and research visit attendance. Specifically, participants received monetary compensation for weekly research visits ($15–$25) to offset participation costs (e.g., travel) and received additional adherence incentives, such as water bottles, notebooks, and monetary compensation, for completing adherence milestones.

Due to a high frequency of early dropouts at the beginning of the trial and participant reported attendance barriers that became evident only after randomization of participants had begun, the study team determined that a more structured and formal retention-related protocol should be added prior to randomization. The Fireside Chat was therefore developed to use with every participant by study teams at each site, including the site PI, before a decision to randomize was made by the team and participants. The Chat was conceptualized and developed by Houston, Texas-based study team members and study leadership.

2.3. Proactively addressing challenges with the Fireside Chat

Following implementation of the Fireside Chat (approximately midway through STRIDE recruitment at the Houston site), The Chat occurred with each potential participant and included all members of a site study team, to identify barriers to retention, minimize negative effects from these barriers and build a foundation for ongoing retention efforts. It also helped both potential participants and staff determine the "fit" between the participant and study prior to randomization. The Chat was scheduled after informed consent was obtained and after most or all screening measures were completed and all other eligibility criteria were met. This avoided overburdening participants prior to determining their likelihood of meeting eligibility criteria. Parts of the informed consent were revisited during The Chat; however, it was not simply a more in depth informed consent discussion. The Site PI typically led the discussion, using a structured guidance tool (see Table 1), over a 30- to 60-min period. This provided the opportunity for open, non-judgmental exploration of specific barriers and solutions in a thorough and structured way, and included educating participants about their study responsibilities and evaluating their understanding.

During The Chat, the study team first began by describing the reasons for The Chat and the importance of the research question. Further, study staff explicitly detailed the structure and time requirement for each visit type. Participants were asked to describe how the study might fit into their lives over nine months and were asked to prospectively identify solutions to staff-presented and participant-elicited attendance barriers during The Chat. Staff were mindful about superficial and socially desirable answers, and continued to re-state barriers to elicit a thoughtful, in-depth discussion about concerns regarding study involvement raised by both staff and participant. "What if" questions were frequently used to challenge participants to find alternative solutions to attendance barriers (e.g., What if your work schedule changes? How else could you make it to visits?). Sources of outside social support were investigated as well (e.g., What friends and family could you ask for help if you have competing demands on your time?), which often gave a clearer picture of participants' abilities to get rides from friends/family or receive childcare assistance, in order to complete study visits. The opportunity to discuss the plausible course of participation helped participants fully envision the experience prior to randomization. Participants were often randomized in the STRIDE study the day following The Chat, with some randomized on the same day.

The team considered participants' reactions before final STRIDE randomization decisions were made. Consistent with eligibility criteria in this hybrid efficacy-effectiveness trial, candidates could be excluded if deemed to be at high risk for dropping out. For example, some candidates were excluded if at risk for non-attendance due to onerous study-related travel. While this criterion was in place prior to The