Published in final edited form as:

Drug Inf J. 2009 July ; 43(4): . doi:10.1177/009286150904300411.

Effective Strategies for Maintaining Research Participation in Clinical Trials

Allen Zweben, DSW [Professor and Associate Dean],
Columbia University, School of Social Work, New York, New York

Lisa M. Fucito, PhD [Postdoctoral Fellow], and
Yale University School of Medicine, Department of Psychiatry, New Haven, Connecticut

Stephanie S. O'Malley, PhD [Professor of Psychiatry]
Yale University School of Medicine, Department of Psychiatry, New Haven, Connecticut

Abstract

Achieving high protocol adherence is essential for ensuring the overall success and scientific merit of clinical trials. Strategies for maximizing recruitment and treatment adherence have been previously explored in the literature. There has been less focus, however, on effective methods for maintaining participants in research follow-up. This article examines factors associated with poor follow-up rates as well as strategies for facilitating research commitment and addressing sources of nonadherence. Special attention is devoted to alcohol- and substance-dependent populations, groups known to have poor adherence rates. Examples are drawn from the COMBINE Study, an NIAAA-funded, nationwide, multisite, combined behavioral and pharmacotherapy trial for alcohol problems that achieved high one-year follow-up rates. The important role of coordinating centers in facilitating research retention is also discussed.

Keywords

Research retention; Clinical trial; Alcohol and substance dependence

INTRODUCTION

The randomized controlled trial (RCT) design is the most scientifically rigorous methodology for evaluating treatment efficacy (1). The success of RCTs is contingent upon adequate retention of research participants (2–4) and there is evidence that rates could be improved (5–7). Poor retention may increase study duration and costs and, in the worst cases, result in premature termination of research (3,6,8). The treatment literature has devoted more attention to examining recruitment barriers and less to retention, particularly among special populations such as those with substance use problems, a group known to have poor adherence rates (9–12). In addition, the current literature on retention has been limited by not always making a clear distinction between research retention and treatment retention in RCT (13,14).

Copyright © 2009 Drug Information Association, Inc.

Correspondence Address: Allen Zweben, DSW, Columbia University, School of Social Work, Mail Code 4600, 1255 Amsterdam Avenue, Room 619, New York, NY 10027, az173@columbia.edu.

Allen Zweben and Lisa M. Fucito report no conflicts to disclose. Stephanie O'Malley has disclosed that she has received other financial or material support from the Association for Medical Education and Research on Substance Abuse, and the American College on Neuropsychopharmacology Alcohol Medication Development Workgroup. She further discloses that she is a partner in Applied Behavior Research.

Failure to retain a sufficient number of participants in the protocol may threaten the internal and external validity of RCTs (11,15,16). High rates of attrition from follow-up may produce bias; results may not be due to treatment effects but rather to a disproportional loss of participants who were more or less symptomatic or unresponsive to the study medication than other participants (3,17). Furthermore, high attrition rates may result in significant differences between participants who remain in research and those who drop out, thereby limiting the generality of findings to the population of interest (3,17). Also, high attrition limits statistical validity by reducing the power to detect true differences between treatments (3).

Previous research has revealed that high study demands (eg, frequent appointments, long study duration, and extra, inconvenient, or uncomfortable procedures) and greater travel and travel costs may deter participants from remaining in research (17–21). Participants' concerns about taking medication, experiencing adverse events, or being assigned to a placebo condition may also increase attrition (18–20). Other participant factors including greater problem severity and distress, lower socioeconomic status and education, lack of social support, and minority status may also play a role, though research is equivocal (19–22).

Conducting RCTs with alcohol- and substance-dependent participants poses additional challenges since it is well documented that retention is poor among this population (5,13,14,23,24). For instance, a review of alcohol treatment outcome studies from 1970 to 1998 found that only 56% achieved sufficient retention rates (ie, 80% or more) (5). A lack of social stability often linked to alcohol and substance dependence (eg, unstable living, relationship, and employment situations; legal problems) may result in poorer retention and greater difficulty maintaining contact with participants (11,23,24). The high degree of ambivalence associated with alcohol and substance dependence may also decrease motivation to continue participation (25,26). Furthermore, incentives to increase motivation, particularly cash payments, may raise ethical dilemmas regarding triggering substance use or being coercive to a typically disadvantaged population (27–32). Fear of social stigma and concerns about confidentiality may also serve as barriers (33,34).

This article examines strategies found to be effective in achieving high research retention rates in pharmacotherapy trials. Special attention is devoted to strategies geared to alcohol- and substance-dependent populations who are reluctant to continue research assessments. These participants can be distinguished from those who are lost or cannot be found and require more extensive tracking and monitoring procedures (see section on nonroutine strategies). Examples are drawn from the COMBINE Study, an NIAAA-funded, nationwide, multisite, combined behavioral and pharmacotherapy trial for alcohol problems. This study achieved relatively high retention rates throughout the one-year follow-up period.

PRACTICAL STRATEGIES FOR IMPROVING PROTOCOL ADHERENCE

OVERVIEW

Discontinuation of treatment does not need to equal discontinuation from assessment provided that study personnel take steps to ensure continued participation from the outset. With well-articulated strategies and commitment to following participants, retention in research assessment can be high even with alcohol- or substance-dependent participants. In the COMBINE study, a large multisite study of combining medications and behavioral treatments for alcohol dependence, approximately 78% completed one or more aspects of treatment, whereas 94% provided complete drinking data used to evaluate the primary efficacy endpoints (35). Similarly, Project MATCH, an earlier multisite study of psychotherapies for alcohol dependence, found that although treatment and research

compliance were highly associated, a substantial proportion of those with only low to moderate treatment compliance achieved moderate to high levels of participation in research assessment (11). A study of individuals admitted to methadone maintenance successfully interviewed 98% of participants at one-year follow-up, although only 51% were still in treatment at the center (36). Several routine and nonroutine strategies can be implemented to enhance retention in research (13,14,16) even with participants who failed to comply with study treatments.

Table 1 delineates how to employ retention strategies to address sources of nonadherence associated with various adherence risk levels among alcohol- or substance-dependent populations. As outlined in the table, strategies aimed at low-risk participants primarily involve establishing a user-friendly environment. This comprises having flexible appointment times; ensuring confidentiality; orienting participants to the study demands, tasks, and responsibilities; and providing incentives for visits such as reimbursing participants for their travel and time. For the majority of participants, these routine strategies are sufficient to address potential adherence problems. However, despite careful planning, a minority of participants may have difficulty meeting protocol requirements. The current circumstances and conditions of such participants as well as their individual experiences in the trial may interfere with their commitment to the research. Consequently, strategies need to be devised and adapted to address the circumstances, conditions, and experiences (eg, dissatisfaction with the medication or behavioral treatment) of participants in the trial to facilitate or retain a commitment to the study protocol.

EMPLOYING ROUTINE STRATEGIES

Create a Welcoming Environment—Of course, the first step in enhancing retention is to make participants' experiences with the study as smooth and enjoyable as possible. Welcoming and respectful staff is the minimum requirement for achieving this aim; a nonjudgmental and accepting attitude is essential for patients with addictive disorders. Conducting interviews in areas that afford privacy is also important. Other gestures such as offering coffee or tea can be made as well.

Establish an Efficient Tracking System—Retention in research assessment depends on being able to locate the participant. Several procedures can make this more likely. Participants are asked to provide email addresses and to indicate the best times to contact them and whether messages can be left. The names and contact information of up to three people who can be contacted for assistance with locating participants are also requested. Written informed consent to contact these individuals is obtained, including a description of the scope of the information to be obtained (eg, forwarding addresses versus questions about the clinical status of the participant). Obtaining consent to use driver's licenses and Social Security numbers to locate participants is useful in addition to verifying and updating contact information at subsequent appointments. Safeguards for maintaining participants' confidentiality should be considered in all of these communications (37).

Educate Participants About Their Role as Research Participants—As in any study, prospective participants are informed about the various components of the treatment and research protocol during the process of obtaining informed consent. However, in an effort to enhance retention, it is important to highlight the significance of research follow-up even if participants decide to discontinue the treatment intervention. Explaining how their experiences with the treatment, whether positive or negative, is critical to evaluating the treatment under study can increase their understanding of the research process and lay the groundwork for future discussions about the importance of completing research assessments.

Anticipated barriers to attending appointments such as transportation, work schedules, vacations, and child care can be reviewed up front and resolved (13,14).

Establish a Routine While Maintaining Flexibility—Just as establishing a routine for taking medication can enhance medication adherence, scheduling recurring appointments at the same time each week can reduce no-shows due to forgetting. Reminder letters and phone calls about appointments should be used for all appointments, and rapid follow-up of missed appointments should be incorporated into the protocol. However, flexibility in scheduling research appointments may be required to keep participants engaged in both the treatment and assessment components of the study.

Provide Incentives for Participation—Providing payment for completion of research assessments can increase the likelihood that critical safety and outcome data will be obtained. The use of incentives, however, can pose a variety of potential ethical issues. Some concerns are that payments, depending on the size, may reduce the voluntary nature of participation or induce individuals to accept greater risks, or that economically disadvantaged participants will be more likely to participate, among other concerns (27,38). However, these potential negative consequences might be reduced if patients are informed that they are being reimbursed for their efforts in completing assessments along with the expenses incurred from study participation, such as transportation, parking, and meals. Such an approach appears to be acceptable to both government- and industry-sponsored trials.

Among substance abusers, an additional concern is that subject payments will be used to purchase drugs or alcohol, and so in-kind payments rather than cash are sometimes used. The existing research data suggests that participants, whether in treatment (37,39) or nontreatment studies (40), may prefer cash payments to other forms of compensation. Festinger and colleagues specifically tested the effects of different modes of compensation (cash versus gift certificates) and the value of the remuneration (\$10, \$40, or \$70) on rates of participation in a six-month follow-up interview and on substance use following payment (41). Higher payments and cash payments were related to greater follow-up rates and did not influence substance use, which was low across all conditions. These data suggest that providing monetary incentives for completing assessments may be particularly helpful in motivating participants to remain in the research component of the study.

EMPLOYING NONROUTINE STRATEGIES

Given the variety of factors associated with nonadherence, a sizeable proportion of participants may be reluctant to attend the assessment interviews. Some participants may be performing quite well after treatment but do not come to the research appointments because they do not want to be reminded about their former substance use problems. Others may be experiencing serious hardships that interfere with attending research appointments. Whatever the reasons, staff members need to be attentive and persistent about addressing adherence problems in order to maintain clinical trial integrity.

Nonroutine strategies are employed when it is clear that a participant is nonresponsive to the research protocol and the aforementioned routine strategies have not produced a positive response. This situation is typically characterized by participants who frequently cancel sessions without rebooking, fail to appear for scheduled appointments, are unresponsive to rescheduling efforts, or attend follow-up sessions but are reluctant to schedule the next appointment or express a desire to drop out. These participants are considered to be in a medium- or high-risk category for protocol adherence.

Staff Training—To start, staff members need to be educated about and prepared to recognize and address adherence issues in clinical research. To achieve this objective, a manual of operations that includes the following procedures should be developed: (a) conducting an adherence assessment, (b) formulating a working hypothesis for attending to adherence issues, (c) developing a range of options for addressing adherence issues, and (d) implementing and evaluating risk reduction strategies. After devising the manual, staff members are trained in the use of adherence procedures. The training process entails the screening of videotapes of adherence interviews, role-playing adherence sessions, and receiving feedback on role-play performance. The content of the training includes: (a) orienting participants to the follow-up, (b) obtaining an adherence history, (c) identifying research task demands, and (d) attending to adherence issues. Staff members are also taught how to use risk levels (see Table 1) to address nonadherence and to explore all possible sources of nonadherence with the assumption that no participant is immune to premature research dropout regardless of how well she or he is progressing in the treatment period.

Conduct an Adherence Assessment—If staff members are successful in locating the nonadherent participant, then an attempt should be made to arrange an in-person (preferred) or telephone assessment interview. Participants who are not responsive to telephone calls or letters requesting a follow-up appointment should be sent a strategic letter (see below). In the assessment interview, staff members seek to discover factors that interfere with participating in follow-up. Staff members review the chain of events associated with nonadherence. Thus some participants may reveal that they are too embarrassed about their drinking to attend the follow-up appointment. Others may indicate that they are too overwhelmed or preoccupied with legal, financial, or domestic matters to attend sessions or may not attend appointments as a consequence of their anger or frustration over the feeling that they received a placebo rather than the active study medication. (Whether these feelings are justified or not are less important than participants' perceptions or beliefs of what has occurred during their participation.)

Formulate a Working Hypothesis—Once participants have communicated their concerns, study personnel devise a working hypothesis to account for nonadherence. To obtain a consensus with the participant, staff members enumerate potential risk factors that may have interfered with adherence. Participants are then asked to comment, clarify, or correct the putative barriers to adherence. Participants are also asked to rank which risk factors represent the greatest threat to their adherence. For example, some participants may view having a slip or setback as the greatest threat to adherence, while others may consider confidentiality concerns to be a major source of nonadherence.

Identify a Range of Options for Addressing Adherence—If consensus can be reached, potential solutions may be considered to address nonadherence. The tentative solutions are presented as a menu of options that represent suitable alternatives to what has been occurring (eg, no-shows) in follow-up. Having participants choose from an array of options helps to facilitate their cooperation.

One of the options to consider is reducing the extensive task demands placed upon participants. Individuals struggling with sobriety and related hardships (eg, family, social, legal, and economic matters) often find it difficult to meet the extensive and varied demands of the research protocol. Allowing participants the opportunity to scale down the study requirements during times of hardship can be useful in sustaining their involvement. This could entail obtaining partial data on participants. For example, the Form 90 alcohol consumption measure can be abbreviated to a Form 90Q (quick screen) version (42). This procedure enables staff to gather data just on the critical questions related to drinking that

are used to derive the primary endpoints rather than the day-by-day reports of drinking obtained with the full interview. These limited questions include: “How many days during the period from May 1st to July 1st did you have at least one drink containing alcohol? Now on those days you did drink, how much did you drink on average? And when was the first day that you had five (four for women) or more drinks in the same day?”

Reducing the frequency of blood draws might be another practical strategy. However, such an approach is only recommended when blood samples are drawn for research purposes, for example, as a secondary measure of treatment response. It is not considered appropriate where blood samples are necessary for monitoring the safety of the drug, for example, to detect a drug-related reaction such as renal or hepatic effects.

Furthermore, another strategy might involve administering a reduced assessment battery. For example, staff might administer instruments pertaining to primary outcomes of alcohol or substance use and omit assessments pertaining to secondary outcomes such as drinking-related consequences. Administering the full assessment package might be resumed at a later time when the participant’s difficulties have subsided. Note that investigators should consider limiting the data collection burden in the design phase of the clinical trial.

For some participants, especially those in serious crisis or experiencing severe hardships, the only feasible solution may be to postpone the follow-up appointment (16,43). For others, an intention to withdraw may seem to be the most reasonable plan, despite the suggestion to postpone the next visit. Such participants may find it difficult to fulfill demands that are perceived as unrelated to their crisis situation. As an alternative, staff may suggest that participants delay the decision to withdraw to a later time rather than finalize the decision. This gives participants an opportunity to resolve the crisis so that they can resume involvement at a later time and confirm their earlier commitment about the importance of the research. In other words, the temporary refusal may be more reflective of their current circumstances or conditions rather than a clear intention or preference to drop out (43). However, it is important to specify the period of opportunity for reconsideration or set a deadline for the final decision so participants do not remain forever in this suspended state.

Use of Strategic Letters—If participants are unavailable for face-to-face interviews or telephone calls, strategic letters serve as a useful alternative (44). These letters are tailored to the needs of the participants. The letter should restate the rationale for participant involvement and discuss the importance of the research interview to the success of the study. Consideration should be given to participants’ beliefs and expectations in discussing their reasons for nonadherence. Emphasis is placed on maintaining a respectful posture and normalizing the inaction rather than moralizing or blaming participants for their nonadherent behavior: “We know that a lot can happen in a person’s life that may make it difficult to follow through with the interview.”

The letters should also include a proposed plan for addressing adherence difficulties. The plan comprises an array of options that are expected to address underlying sources of nonadherence and facilitate continued involvement. For participants who have prematurely dropped out of treatment, it may be useful to clarify the differences between clinical and research participation: “Please remember that we still consider you a part of the research project even if you decided to terminate treatment early.” For participants who have resumed drinking or substance use, it is important to remind them that “we are interested in *all* outcomes of treatment and have no set expectations about what should be happening in your life.” The letter should reinforce the notion of the importance of knowing what is actually happening in their lives to draw accurate conclusions about their progress following treatment. For participants who require a reduction of the task demands, potential

modifications such as conducting interviews at a more convenient location are offered: “We want to make the visit as convenient as possible, so let us know if the suggestions are responsive to your current needs.” In sum, strategic letters are employed to communicate understanding and sensitivity of the circumstances associated with nonadherence, to support self-efficacy (“you can do it”), and to foster a renewed commitment to the research.

It should be mentioned that not all participants will be responsive to the aforementioned strategies. In such cases, it is advisable to accept participants’ intention to withdraw respectfully and express appreciation for their time and involvement in the study (43).

ROLE OF COORDINATING CENTER IN FACILITATING RETENTION

Congruency among research staff in carrying out the aforementioned procedures and strategies facilitates retention. This is particularly important in multisite clinical trials, in which differences in sustaining performance standards across sites can be detrimental to the validity of the study findings. In such cases, a centralized coordinating center is devised to establish a studywide infrastructure to supervise and monitor the tracking of participants, develop performance standards, identify strategies and procedures for addressing retention issues, and make recommendations for improving the handling of data-gathering activities. In single-site studies, a member of the staff may be assigned to the role of coordinating these tasks and responsibilities (16,45).

The coordinating center is responsible for training sites in retention strategies and clarifying performance expectations. The coordinating center should also promote staff enthusiasm and perseverance, high morale, and compassion to bond with patients, important mechanisms in achieving high retention rates (23). Study sponsors also need to ensure that sites receive the funding needed for these retention activities, including follow-up interviews of participants who have discontinued treatment.

Following the training, teleconference calls and on-site visits to monitor trialwide data-gathering activities should be scheduled. At these meetings, participant attendance and the reliability of data-gathering procedures are assessed to determine whether the research sites are fulfilling performance goals. Sites not meeting expectations are provided with recommendations for engaging or reengaging participants in follow-up. Recommendations may include improving tracking systems, encouraging the facility to become more user friendly, identifying a particular staff member who will be responsible for follow-up interviews, and implementing retention strategies such as sending out strategic letters. Sites not meeting expectations are also sent letters requesting that they provide the coordinating center with remedial plans for improving retention rates. To assist with the process, the coordinating center arranges conference calls between high-performance and low-performance sites to discuss useful methods for retaining participants in follow-up. This procedure enables low-performance sites to obtain firsthand knowledge about effective retention strategies.

SUMMARY

This article demonstrates how adequate attention to retention issues can reduce the threat to the scientific rigor of clinical trials. A particular challenge is how to sustain perseverance of site personnel while attending to the needs of nonadherent participants. A wide range of strategies are offered to address adherence issues as well as to sustain staff commitment to the research.

Acknowledgments

This research was supported in part by NIAAA grants R01AA13848, U10AA011773, K05 AA014715, R01 AA17173, U01 AA 11787, U10 AA11715, 01 AA012788, and T32 AA015496.

References

1. Sibbald B, Roland M. Understanding controlled trials: why are randomised controlled trials important? *Br Med J*. 1998; 316(7126):201. [PubMed: 9468688]
2. Cramer, J.; Spilker, B. *Patient Compliance in Medical Practice and Clinical Trials*. New York: Raven Press; 1991.
3. Friedman, L.; Furburg, C.; DeMets, D. *Fundamentals of Clinical Trials*. New York: Springer-Verlag; 1998.
4. Spilker, B.; Cramer, J. *Patient Recruitment in Clinical Trials*. New York: Raven Press; 1992.
5. Moyer A, Finney J, Swearingen C. Methodological characteristics and quality of alcohol treatment outcome studies, 1970–1998: an expanded evaluation. *Addiction*. 2002; 97(3):253–263. [PubMed: 11964099]
6. Pich J, Carne X, Arnaiz J, Gomez B, Trilla A, Rodes J. Role of a research ethics committee in follow-up and publication of results. *Lancet*. 2003; 361:1015–1016. [PubMed: 12660062]
7. Wittes R, Friedman M. Accrual to clinical trials. *J Natl Cancer Inst*. 1988; 80(12):884–885. [PubMed: 3398064]
8. Easterbrook P, Matthews D. Fate of research studies. *J R Soc Med*. 1992; 85(2):71–76. [PubMed: 1538384]
9. Edwards A, Rollnick S. Outcome studies of brief alcohol intervention in general practice: the problem of lost subjects. *Addiction*. 1997; 12:1699–1704. [PubMed: 9581002]
10. Howard K, Cox W, Saunders S. Attrition in substance abuse comparative research: the illusion of randomization. *NIDA Research Monograph*. 1990; 104:68–79.
11. Mattson M, DelBoca F, Carroll K, et al. Compliance with treatment and follow-up protocols Project MATCH: predictors and relationship to outcome. *Alcohol: Clin Exp Res*. 1998; 22(6): 1328–1339. [PubMed: 9756050]
12. Thomson C, Morley K, Teesson M, Sannibale C, Haber P. Issues with recruitment to randomised controlled trials in the drug and alcohol field: a literature review and Australian case study. *Drug Alcohol Rev*. 2008; 27(2):115–122. [PubMed: 18264870]
13. Carroll, K., editor. *Enhancing Retention in Clinical Trials of Psychosocial Treatments: Practical Strategies*. Washington, DC: Government Printing Office; 1997.
14. Onken, L.; Blaine, J.; Boren, J., editors. *NIDA Research Monograph No. 165. DHHS Publication No. (ADM) 97-4142; No. 165. Beyond the Therapeutic Alliance: Keeping the Drug-Dependent Individual in Treatment*.
15. Group PMR. Project MATCH: rationale and methods for a multisite clinical trial matching alcoholism patients to treatment. *Alcohol Clin Exp Res*. 1993; 17(6):1130–1145. [PubMed: 8116822]
16. Zweben A, Barrett D, Berger L, Murray K. Recruiting and retaining participants in a combined behavioral and pharmacological clinical trial. *J Stud Alcohol*. 2005; 66(Suppl 15):72–81.
17. Flick S. Managing attrition in clinical research. *Clin Psychol Rev*. 1988; 8:499–515.
18. Atwood J, Haase J, Rees-McGee S, et al. Reasons related to adherence in community-based field studies. *Patient Educ Counsel*. 1992; 19(3):251–259.
19. Bender B, Ellison M, Gleason M, Murphy J, Sundstrom D, Szeffler S. Minimizing attrition in a long-term clinical trial of pediatric asthma. *Ann Allergy Asthma Immunol*. 2003; 91:168–176. [PubMed: 12952111]
20. Cassidy E, Baird E, Sheikh J. Recruitment and retention of elderly patients in clinical trials. *Am J Ger Psychiatry*. 2001; 9:136–140.
21. Moser D, Dracup K, Doering L. Factors differentiating dropouts from completers in a longitudinal, multicenter clinical trial. *Nurs Res*. 2000; 49(2):109–116. [PubMed: 10768588]

22. May D, Kratochvil C, Puumala S, Silva S, Rezac A, Hallin M. A manual based intervention to address clinical crises and retain patients in the treatment of adolescents with depression study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006; 46(5):573–581. [PubMed: 17450048]
23. Cottler L, Compton W, Ben-Abdallah A, Horne M, Claverie D. Achieving a 96.6 percent follow-up rate in a longitudinal study of drug abusers. *Drug Alcohol Depend*. 1996; 41:209–217. [PubMed: 8842633]
24. Scott C. A replicable model for achieving over 90% follow-up rates in longitudinal studies of substance abusers. *Drug Alcohol Depend*. 2004; 74:21–36. [PubMed: 15072804]
25. Callaghan R, Hathaway A, Cunningham J, Vettese L, Wyatt S, Taylor L. Does stage-of-change predict dropout in a culturally diverse sample of adolescents admitted to inpatient substance abuse treatment? A test of the transtheoretical model. *Addict Behav*. 2005; 30:1834–1847. [PubMed: 16111832]
26. DiClemente C, Schlundt D, Gemmell L. Readiness and stages of change in addiction treatment. *Am J Addict*. 2004; 13(2):103–119. [PubMed: 15204662]
27. Dickert N, Grady C. What's the price of a research subject? Approaches to payment for research participation. *N Engl J Med*. 1999; 341(3):198–203. [PubMed: 10403861]
28. Fry C, Dwyer R. For love or money? An exploratory study of why injecting drug users participate in research. *Addiction*. 2001; 96:1319–1325. [PubMed: 11672496]
29. Koocher G. Questionable methods in alcoholism research. *J Consult Clin Psychol*. 1991; 59(2):246–248. [PubMed: 2030183]
30. McGee G. A piece of my mind. Subject to payment? *JAMA*. 1997; 278(3):199–200. [PubMed: 9218656]
31. McKeganey N. To pay or not to pay: respondents' motivation for participating in research. *Addiction*. 2001; 96:1237–1238. [PubMed: 11672486]
32. Shaner A, Eckman T, Robert L, et al. Disability income, cocaine use, and repeated hospitalization among schizophrenic cocaine abusers—a government sponsored revolving door? *N Engl J Med*. 1995; 333:777–783. [PubMed: 7643886]
33. Cunningham J, Sobell L, Chow V. What's in a label? The effects of substance types and labels on treatment considerations and stigma. *J Stud Alcohol*. 1993; 54(6):693–699. [PubMed: 8271805]
34. Mark T, Kranzler H, Poole V, Hagen C, McLeod C, Crosse S. Barriers to the use of medications to treat alcoholism. *Am J Addict*. 2003; 12(4):281–294. [PubMed: 14504021]
35. Anton R, O'Malley S, Ciraulo D, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence. The COMBINE Study: a randomized controlled trial. *JAMA*. 2006; 295:2003–2017. [PubMed: 16670409]
36. Desmond D, Maddux J, Johnson T, Confer B. Obtaining follow-up interviews for treatment evaluation. *J Subst Abuse Treat*. 1995; 12(2):95–102. [PubMed: 7623396]
37. McCrady B, Bux D. Ethical issues in informed consent with substance abusers. *J Clin Invest*. 1999; 67:186–193.
38. Grady C. Payment of clinical research subjects. *J Clin Invest*. 2005; 115:1681–1687. [PubMed: 16007244]
39. Amass L, Bickel W, Crean J, Higgins S, Badger G. Preferences for clinic privileges, retail items and social activities in an outpatient treatment program. *J Subst Abuse Treat*. 1996; 13(1):43–49. [PubMed: 8699542]
40. Kurlander J, Simon-Dack S, Gorelick D. Spending of remuneration by subjects in non-treatment drug abuse research studies. *Am J Drug Alcohol Abuse*. 2006; 32:527–540. [PubMed: 17127540]
41. Festinger D, Marlowe D, Croft J, et al. Do research payments precipitate drug use or coerce participation? *J Drug Alcohol Depend*. 2005; 78:275–281.
42. Miller, W. NIAAA Project MATCH Monograph Series. NIH Publication No. 96-4944. Vol. 5. Bethesda, MD: Department of Health and Human Services; 1996. Form 90: A Structured Assessment Interview for Drinking and Related Behaviors Test Manual.
43. Barrett, D.; Morse, P., editors. Handling Noncompliance. Bethesda, MD: Department of Health and Human Services; 1998.

44. Zweben, A.; Barrett, D.; Carty, K.; McRee, B.; Morse, P.; Rice, C., editors. NIAAA Project MATCH Monograph Series. NIH Publication No. 98-4144. Bethesda, MD: Department of Health and Human Services; 1998. Strategies for Facilitating Protocol Compliance in Alcoholism Treatment Research.
45. McRee, B., editor. Project MATCH: A Case Study. Bethesda, MD: Department of Health and Human Services; 1998.

TABLE 1

Tailoring the Retention Approach to Participant Risk Levels

Risk Level	Participant Indicators	Retention Strategies
Low	No problems scheduling appointments or completing assessment information	<ul style="list-style-type: none"> Express appreciation of participants' involvement and efforts (routine) Ensure confidentiality of Information provided (routine) Obtain and update contact information (routine) Allow for the flexible scheduling of appointments (routine) Discuss potential or anticipated barriers to attending appointments (routine) Provide payments for interviews (routine)
Medium	Concerns about the study medication, behavioral treatment, or procedures Concern that current condition or circumstances could interfere with fulfilling study requirements Reluctant to schedule follow-up appointments due to aforementioned concerns about treatments, circumstances, or conditions	<ul style="list-style-type: none"> Normalize and accept concerns about the study (routine) Employ a higher authority (physician or PI) to allay concerns about medications or behavioral treatment (routine) Remind participant about rationale for study involvement (routine) Remove aversive elements of the protocol (eg, blood draw) that may interfere with participation (nonroutine) Provide a range of options to facilitate involvement (eg, scale down study demands, postpone the next appointment) (nonroutine) Scale down demands of study requirements (eg, obtain partial data) (nonroutine)
High	Cancels appointments frequently without rebooking, regular no-show, and is unresponsive to contacts for rescheduling appointments Reveals a desire to drop out of the trial	<ul style="list-style-type: none"> Conduct an adherence assessment; that is, learn the participant's explanation for nonattendance or wish to drop out (nonroutine) Formulate a working hypothesis to explain nonadherence (nonroutine) Obtain consensus about risk factors associated with nonadherence (nonroutine) Establish priorities for attending to risk factors (nonroutine) Identify a range of options for addressing nonadherence (eg, see nonroutine strategies tailored to participants who are at medium risk for nonadherence) Send out strategic letters or emails to participants who are unresponsive to personal contact (nonroutine) Delay decision making about dropping out (nonroutine) Accept a "no" as temporary and obtain permission to recontact at a later time (nonroutine)

Adapted from Zweben A, Barrett D, Berger L, Murray K. Recruiting and retaining participant in a combined behavioral and pharmacological clinical trial. *J Stud Alcohol*. 2005;66(Suppl 15) S72–S81. Also see Barrett D, Morse P. Handling noncompliance. In Zweben A, Barrett D, Carty K, McRee B, Morse P, Rice C, eds. *Strategies for Facilitating Protocol Compliance in Alcoholism Treatment Research*. NIAAA Project MATCH Monograph No. 7. NIH Publication No. (ADM) 98-4144. Bethesda, MD: Department of Health and Human Services; 1995:33–64.