Enhancing Retention in Clinical Trials of Psychosocial Treatments: Practical Strategies

Kathleen M. Carroll

There is increasing awareness, from both clinical and research perspectives, of the substantial methodological and statistical problems associated with the typically high rates of attrition in clinical trials (Howard et al. 1990; Kalton 1983; Lackin and Foulkes 1986; Lavori 1992). These issues are particularly critical for trials involving substance abusers (Howard et al. 1990; Sparr et al. 1993), where rates of attrition often range from 25 to 90 percent (Baekeland and Lundwall 1975; DeLeon 1991; Wickizer et al. 1994). Traditionally, attrition has been conceived as patient driven; that is, investigators have focused their efforts on searching for patient characteristics associated with poor retention, such as demographic characteristics, social instability, and low motivation (e.g., Agosti et al. 1991; Babst et al. 1971; Baekeland and Lundwall 1975; Swett and Noones 1989; Szapocznik and Ladner 1977).

That perspective is now shifting, and current efforts to reduce attrition in clinical trials reflect increasing awareness that retention reflects a combination of conditions and efforts contributed by therapists, investigators, and research staff, in addition to patients (DeLeon 1991; DiClemente 1993). This chapter describes practical strategies for retaining substance-abusing patients in clinical trials, particularly studies evaluating psychosocial treatments. Examples are drawn from the series of trials evaluating psychotherapies and pharmacotherapies for cocaine abusers at Yale (Carroll et al. 1991, 1994*c*), as well as the National Institute on Alcoholism and Alcohol Abuse (NIAAA)-funded Project MATCH (Project MATCH Research Group 1993), a multisite collaborative clinical trial evaluating patient treatment matching in alcoholics. In these studies, which evaluated manual-guided psychotherapeutic approaches in outpatient settings with a variety of substance-abusing populations, retention was given close attention because of the need for adequate statistical power, the need to expose patients to an adequate dose of study treatments, the need to retain a study sample that reflected the larger population from which it was drawn, and the need to avoid statistical problems associated with differential attrition. Thus, the author's research team used a number of strategies intended to enhance retention. Use

of these strategies reflects three assumptions about retention: retention reflects a good fit between patient, setting, provider and treatment; attrition typically occurs early in treatment; and retention is an outcome.

RETENTION REFLECTS GOOD FIT

In both clinical and research settings, patient heterogeneity has usually been met with treatment homogeneity. That is, regardless of patients' background and preferences, the nature or severity of their substance abuse and related problems, or the factors that precipitated seeking treatment, many treatment programs offer only a single type of treatment (which is usually poorly defined as to content, goals, approach, treatment provider, and duration). With this one-size-fits-all model, variations in retention and outcome have traditionally been ascribed to patient factors and characteristics (e.g., Agosti et al. 1991; Keil and Esters 1982; Swett and Noones 1989; Szapocznik and Ladner 1977). Thus, patients who are a good fit for a given approach are more likely to remain in treatment, and those who are less well suited are more likely to drop out.

Given this approach, the search for universal patient characteristics associated with retention has been no more successful than the search for the alcoholic personality, as patient characteristics associated with dropout in one treatment setting are usually not replicated in another setting with a vastly different treatment approach. A more recent, and potentially more fruitful, approach to evaluating retention is recognition that retention may have more to do with what investigators and treatment providers do than who the patients are. For example, Herceg-Baron and colleagues (1979) found that attrition patterns varied as a function of the type of treatment (pharmacotherapy or psychotherapy) patients received in a study of treatments for depression.

ATTRITION OCCURS EARLY

While there is little consistency across studies and treatment settings in terms of characteristics of patients who drop out of treatment, there is a good deal of consistency across studies suggesting that most attrition occurs early, with the majority of dropouts usually occurring during the first month of treatment (Baekeland and Lundwall 1975; DeLeon 1991; Silberfeld and Glaser 1978; Swett and Noones 1989).

Again, in treatment settings that offer only a single approach, it may not make sense to ask the patient what he or she needs, desires, or expects out of treatment, as if the patient wants something other than what the center provides; very often, there is little that staff can do. Moreover, treatment staff are often so vague in explaining to the patient what to expect in treatment that the patient typically has only an uncertain idea of what treatment will actually consist of until it begins. Thus, early attrition may reflect self-selection, where patients may find themselves in the wrong treatment setting, wrong group, with the wrong therapist, participating in a treatment geared to a stage other than the one they are in. It is thus not surprising that dropouts usually seek treatment again elsewhere (Peterson et al. 1994).

RETENTION IS AN OUTCOME

In substance abuse treatment, retention is more or less the outcome. Better retention tends to be associated with better outcomes in terms of reductions in substance abuse (Simpson and Sells 1982). Furthermore, the treatments for substance abuse are considered effective to the extent they demonstrate the ability to retain patients. Methadone maintenance, despite its drawbacks, is the most successful pharmacologic strategy for opioid dependence, in large part because of its power to retain patients over extended periods. On the other hand, naltrexone, which is an elegant, safe, long-acting, and theoretically perfect treatment, is infrequently used and often perceived as ineffective largely because of its poor track record of retention. Similarly, the combined voucher and community reinforcement approach (CRA) approach described by Higgins and colleagues (this volume) has generated a great deal of excitement because several trials evaluating this approach have shown high retention and abstinence rates among cocaine abusers.

To the extent that potent treatments can be developed that are responsive to patients' needs, it is likely that treatment retention, compliance, and outcome will be improved. Moreover, procedures and strategies that have been found to improve treatment compliance and retention in clinical areas other than substance abuse (Meichenbaum and Turk 1987) are likely to be applicable and effective in improving treatment retention among substance abusers as well.

STRATEGIES RELATED TO PATIENTS

Some, but clearly not all, variation in retention in clinical trials may have to do with the types of patients included in different trials. Because different types of patients may respond to different treatments, sample heterogeneity versus homogeneity may be one determinant of attrition patterns within a trial. The appropriate level of sample heterogeneity in a trial depends on its aims and goals. For example, in small, tightly controlled efficacy studies in which investigators attempt to attribute all variation in outcome to treatments evaluated (explanatory trials), variability in other factors, including patients, should be held to a minimum (Sackett and Gent 1979). Conversely, in a generalizability study, which evaluates the effectiveness of the study treatment in the broader population of individuals with the disorder, a more heterogeneous population would be desirable.

Restrict Sample Variability

One means of avoiding attrition in clinical trials is to narrow inclusion and exclusion criteria to patients who are likely to comply with, remain in, and benefit from study treatments. Thus such a study might exclude patients with high psychopathology, those who do not have stable social supports, those who live far from the treatment site, and those who are not motivated for treatment. With this type of strategy, however, the study sample is likely to be highly select and may have little resemblance to the larger population from which it was drawn. For example, in the Veterans Administration's (VA) Cooperative Disulfiram Study, the relatively restrictive set of inclusion-exclusion criteria used yielded only 600 subjects from a potential pool of over 6,000 (Fuller et al. 1986).

The effects of restricted sample variability on retention and outcome may be also illustrated by the series of studies evaluating the effectiveness of desipramine treatment of cocaine dependence. An early trial, led by Gawin and colleagues at Yale (1989), suggested the effectiveness of desipramine over lithium and placebo for retention and other outcomes, using a sample that was composed primarily of white, employed, intranasal users with comparatively low levels of psychopathology. Later desipramine trials, which included more heterogeneous samples that varied across several dimensions (e.g., race, severity, route of administration, and level of psychopathology), generally failed to find a desipramine effect on retention or cocaine use, or found an effect only for subsamples with

lower severity cocaine use (Carroll et al. 1994*c*) or for subjects without antisocial personality disorder (Arndt et al. 1994).

Increase Difficulty of Treatment Entry

Another method for reducing attrition is to make it more difficult for substance abusers to enter treatment in the first place. While not necessarily always conceived as such, many methadone programs routinely make use of this strategy. That is, treatment applicants are placed on waiting lists of up to 6 months and are asked to call every 2 weeks to confirm their interest in treatment or place on the waiting list, and patients who fail to call are dropped from the list. Thus, individuals who persist with contacting the clinic over an extended period of time, or survive the waiting list, may be more motivated or stable and hence more likely to remain in treatment once admitted.

Similarly, Craig (1985) described a set of procedures that reduced the rate of dropouts from an inpatient substance abuse treatment program from 70 to 20 percent. These procedures included requiring a 2-day preadmission evaluation or completion of a 30- to 60-day outpatient program prior to inpatient admission for patients who had histories of negative behavior. Once admitted, patients completed treatment contracts, and were required to meet with their group before leaving against medical advice (AMA). In addition, the program offered the availability of a counselor during evenings and weekends when the majority of AMA discharges tended to occur.

An example of this type of approach in clinical trials is the use of the run-in (Lang 1990), where potential subjects have an opportunity to practice study procedures (e.g., return questionnaires each week, take study medication according to schedule) and are selected for the study on the basis of their ability to conform to those procedures. This strategy is also seen in studies that require patients to demonstrate their ability to become abstinent or their motivation for treatment before program entry. In such studies, patients entering the trial are more likely to be retained, to be compliant, and to have better response to treatment; however, it is less likely that results will generalize to other settings or studies that do not make such stringent demands on patients prior to entering treatment.

Anticipate Heterogeneity

When patient heterogeneity is built in to a study, higher attrition is likely. For example, the author's cocaine studies and Project MATCH were intended to evaluate the types of patients who respond to different treatments, thus heterogeneous samples were recruited and inclusion and exclusion criteria were broad by design. It was found that within the boundaries of study treatments and the research protocol, anticipating and accommodating the needs of diverse patients may prevent practical and clinical problems and, ultimately, attrition. For example, in studies hoping to recruit and retain substantial numbers of women, the provision of child care while patients attend treatment and research appointments may be critical. For subjects who work, it may be impractical to ask them to come to sessions during regular office hours, so offering some evening appointments may help retain patients. Similarly, to retain socially unstable or homeless patients, providing transportation to the clinic and establishing links to social service agencies may be needed to help subjects develop at least a minimum level of social stability to support them while in outpatient treatments.

It should be noted, however, that some of the strategies described in this section and the next essentially change the nature of the treatments provided and thus their use in any given trial must be considered carefully and monitored closely.

Build Flexibility into Treatments and Treatment Manuals

Another problem associated with a broad range of patients in a clinical trial is that heterogeneity may increase the number of patients who are less than ideally suited to study treatments and therefore at risk of attrition. In studies of psychosocial treatments, investigators may address this issue by helping therapists strike an appropriate balance between the need to adhere to a structured treatment manual and meeting the needs of individual patients. For example, in psychotherapy studies conducted by the author's group, sessions typically begin with 15 to 20 minutes of less structured time (conducted within a framework consistent with the theoretical underpinnings of that treatment type), where major events since the last session are reviewed and the patient is given the opportunity to raise questions or concerns. For the remainder of the session, therapists attempt to work material raised by the patient into discussion of the manual-driven session topic for that week so as to

respond to the patient's immediate concerns and maximize each session's relevance.
Flexibility and the ability to treat several different types of patients within a single treatment approach also characterized the process of developing treatment manuals for Project MATCH. In the manuals (Kadden et al. 1992; Miller et al. 1992; Nowinski et al. 1992), guidelines were provided, for example, for treating patients at different settings, and with varied levels of severity and psychopathology. In addition, therapists' ability to be responsive to the needs of individual patients was built into the treatment manuals themselves. For example, both the cognitive-behavioral and 12-step facilitation manuals included a small set of core session topics that were considered essential to deliver for each patient to have received an adequate dose of that treatment, but each manual also included several elective sessions that addressed special issues or concerns (e.g., coping with depression, learning assertive responding). After covering the material in the essential core sessions, the therapist and patient could select additional elective topics in order to tailor the treatment for each patient (Carroll et al. 1994*a)*.

Also, to handle crises that might arise in a highly diverse sample, therapists in each condition were allowed to offer up to two emergency sessions. Emergency sessions were conducted within the frame of reference and using techniques consistent with each treatment type. For example, when problems and crises arose, cognitive-behavioral therapists modeled a problemsolving approach, 12-step facilitation therapists encouraged their patients to deepen their involvement in Alcoholics Anonymous (AA), and motivational enhancement therapy (MET) therapists invited their patients to explore and make use of resources already available to them (Carroll et al. 1994*a*).

Finally, investigators may make use of safety nets to protect patients who do not respond to study treatments. For example, most clinical trials specify a set of clinical deterioration criteria where patients who respond poorly to their assigned study treatment can be withdrawn and provided a more intensive level of care. Beyond preventing therapists from deviating from the treatment protocol with more difficult patients (as they know they will not be asked to persist indefinitely with a treatment that is not helpful to a patient), these procedures, if made explicit to patients, may prevent some patients from dropping out without giving treatment a reasonable try by reassuring them they will receive more intensive treatment if clinically indicated.

Involve Significant Others

Involvement of significant others in treatment has long been recommended as a technique to improve retention in general (Meichenbaum and Turk 1987) and has been shown to be beneficial in treatment of substance dependence (e.g., DeLeon 1991; Higgins et al. 1994; Sorenson et al. 1985). Thus, in the author's clinical trials, therapists are allowed to offer up to two significant-other sessions (which are closely monitored and analyzed as process variables). Guidelines for conducting these sessions are described in the respective treatment manuals, and are designed not as family therapy but rather an opportunity for family members to learn what the patient's treatment and involvement in the research encompasses, ask questions and express concerns, and participate in future treatment planning. Thus, by accommodating significant others and attempting to make them allies of the research team, the therapists seek to prevent sabotaging of treatment, which might be more likely to occur if significant others were excluded entirely.

STRATEGIES RELATED TO THERAPISTS

While investigators cannot necessarily select patients who will be retained, it may be possible to select study therapists who are more likely to hold on to patients. Some strategies are described below.

Careful Selection of Therapists

Investigators should strive to select therapists who are likely to be good fits for the treatment protocols and who can work well with a variety of patients. While specific therapist selection criteria vary across studies, therapist selection criteria typically include: completion of a terminal degree in the therapist's discipline (usually an M.D., Ph.D., or M.S.W.); several years of clinical experience with a population closely related to the study population; and experience in and commitment to the type of study treatment the therapist will be conducting in the trial (Carroll et al. 1994*b*; Chevron et al. 1983). Use of comparatively stringent criteria to promote a highly experienced therapist cohort is important. Therapists' training in clinical trials is typically (and necessarily) limited to helping them adjust their usual approach to fit manual guidelines; there is no opportunity to teach basic therapy skills to novice clinicians (Rounsaville et al. 1986).

In addition to meeting selection criteria, the author and colleagues typically require therapist candidates to submit a videotaped work sample. By viewing a therapist's actual work, researchers can appraise a number of key qualities that would be impossible to evaluate on the basis of a curriculum vitae alone. For example, Luborsky and colleagues (1985, this volume) identified several characteristics associated with retention and outcome of substance-abusing patients including the therapist's interest in helping, skill, and ability to form a good working relationship (alliance). Finally, requesting a videotaped work sample is a good introduction for the therapists to the increased scrutiny required in clinical trials of psychosocial treatments (e.g., videotaping of all sessions, frequent supervision, and process evaluation). Experience suggests that therapist candidates who refuse to submit work samples generally have good reason for doing so.

Moreover, with the growth of interest in patient-treatment matching studies and the resultant need to deliver highly distinct treatments with a minimum of overlap (Carroll et al. 1994*a*), it is important to ascertain that therapist candidates are competent practitioners of the treatment type to which they profess commitment. It is extremely difficult, for example, both to train and prevent overlap in behavioral therapists who profess to do dynamic therapy and in 12-step-oriented therapists who say their approach is cognitive-behavioral.

It is also important to recruit therapists who are open to working with substance abusers. Investigators should note that not all therapists are good at this work. Some very competent therapists who are experienced in working with other types of patients have strong opinions about the value (or lack thereof) in conducting psychotherapy with substance abusers. If such attitudes are not identified and addressed, therapists who have low expectations of patient success may convey these expectations in a number of ways (e.g., conveying a lack of optimism about the patient's chance for success, prematurely diagnosing their patients as having antisocial personality disorder) and undermine retention (Baekeland and Lundwall 1975).

Address Retention as Part of Therapist Training

Therapist training provides another important opportunity for heightening the importance of retention in the trial and selecting out therapists who are less likely to hold patients. For example, during initial didactic training seminars where the therapists are introduced to

the goals and aims of the trial and the treatment manuals are reviewed, it is helpful to underline the importance of retention and the expectation that the therapists will make special efforts to retain their patients. It may be helpful to highlight and discuss differences between being a therapist in research clinical trials versus regular clinical practice (Weissman et al. 1982), including random assignment, the short-term nature of treatment, and the high level of scrutiny around treatment delivery. Substantial attention also is devoted during training to working through issues of patient heterogeneity, that is, helping therapists develop strategies for successfully retaining patients who vary with respect to severity, psychopathology, motivation, and other characteristics within their treatment approach. Thus prepared, therapists may feel less tempted to borrow from other approaches or give up on patients when they confront difficult clinical issues during the study.

Training therapists for clinical trials designed to evaluate psychotherapeutic treatments also requires completion of several closely supervised practice cases; this is intended to help therapists gain experience adapting their usual approach to be consonant with the treatment manuals and research procedures. Supervision is also an opportunity to reinforce the importance of retention by attending to and addressing any missed sessions or dropouts. Again, while even experienced therapists can have some difficulty with training cases, it has been found that therapists whose patients frequently drop out during training are often those with poorer retention during the main phase of the trial.

Build in Therapist Incentives for Retention

In regular treatment clinics where therapists' caseloads are heavy, missed sessions are often experienced by the therapists as good fortune, giving them precious extra hours to catch up on paperwork and phone calls. Thus, there is little incentive to follow up on patients who miss sessions and attempt to shore up connections with treatment where resolve may be tenuous. By not following up on such patients, therapists can passively cull their caseload of patients they perceive as unmotivated, disagreeable, time consuming, or otherwise unappealing.

Conversely, in clinical trials, a great deal of time and many valuable resources are devoted to recruitment, screening, preparation, and assessment of each subject. Loss of a single subject is costly practically as well as statistically. To heighten therapists' awareness

of the importance of retention, it may be useful to build in incentives for retention. For example, rather than paying all or part of study therapists' salaries, therapists are paid on a per diem basis, where they receive an hourly fee for every hour of patient contact. Thus, as their earnings will be reduced if their patients leave treatment, there is incentive to attend to early problems in developing a relationship, and to call and follow through with patients who are late or no-shows.

Close Monitoring of Therapists

Close attention to the therapists' delivery of study treatments and level of competence may also improve retention. Video- or audiotaping all sessions, which is done primarily to facilitate process analyses and evaluation of treatment discriminability, may also increase the quality of treatment and possibly reduce attrition. For example, therapists who are aware that everything they say to a patient is being taped and evaluated may be more likely to be consistently diligent about delivering study treatments and perhaps to deliver better, higher quality treatments. Provided consistently and carefully, ongoing supervision itself may increase the quality of treatment and increase retention by providing support, bolstering morale, and broadening therapists' repertoire by working through issues raised by difficult patients. Supervisors should be particularly alert to attrition and explore with each therapist the process that may have led to patients leaving treatment and missing sessions. Ongoing attention to warning signs of attrition, especially missed appointments, also may be helpful.

Stability and Flexibility

Patients whose sessions are scheduled to occur at the same time each week tend to be more likely to complete treatment. While some variability in the structure of scheduling may be patient determined (e.g., patients who are using, with unstable work schedules or family life, are unlikely to come in the same time each week), it is important that therapists understand the need for consistency and the undesirability of varying the schedule of sessions and missing sessions.

Moreover, stability and flexibility can be improved through having a larger pool of trained study therapists. Besides reducing the likelihood of therapist effects (Crits-Christoph and Mintz 1991), having more therapists ready to deliver study treatments may prevent the need to interrupt treatment for therapist vacations and other absences. Furthermore, a larger therapist pool may increase flexibility in

accommodating the needs of individual patients such as patients with unusual schedules, patients who express a strong preference for a male or female therapist, and other considerations.

STRATEGIES RELATED TO INVESTIGATORS AND RESEARCH STAFF

Research staff can use many strategies to improve retention in clinical trials. Several have been recognized for many years and few are limited to the special needs of substance abusers. For example, the general principles recommended by Meichenbaum and Turk (1987) are applicable, including short referral times, involving the patient in the planning and implementation of the treatment program, using reminders, discussion of the reasons for previously missed appointments, patient education, fostering a collaborative relationship based on negotiation, involvement of significant others, being patient oriented, and reducing the level of complexity of the protocol.

As with the other strategies listed above, it is important to note that only some of the following have been evaluated empirically for their actual impact on retention. More studies specifically evaluating these strategies and others are clearly needed. Furthermore, as these strategies may have an effect on retention and outcome, it is important for investigators using these strategies to monitor that they are applied appropriately and consistently across study conditions.

Rapid Response and Assignment to Treatment

Patients may never be more motivated than the first time they call the clinic. Several studies have shown that by cutting down the time between application for treatment and first contact, retention can be improved significantly (Baekeland and Lundwall 1975; Leigh et al. 1984; Stark et al. 1990). Furthermore, research screening and assessment procedures, including medical evaluations and lengthy diagnostic interviews, can delay randomization and the start of treatment to up to 1 month. Rates of successfully starting patients in the protocols have increased as the author's group reduced the interval between first contact to first treatment session to less than 1 week. Alternatively, lengthening the pretreatment patient evaluation period is akin to a run-in period, which may reduce the number of

patients who enter the protocol, but may in turn produce a more compliant sample of patients more likely to be retained.

Subject Preparation and Inoculation

Building on the broader literature on the effectiveness of role-induction procedures for general psychotherapy patients as a strategy to improve retention (Hoehn-Saric et al. 1964), some investigators have found these procedures (including educating subjects regarding their role as drug abuse treatment patients or research subjects) helpful among substance abusers. For example, Stark and Kane (1985) found that a drug treatment-specific role induction procedure was more effective in increasing rates of return for second appointments than was a standard intake interview. Sutherland and colleagues (1985) reported that new subjects meeting with a research psychologist (who conducted a research interview that included extensive self-reports of substance abuse and a request to fill out a drinking diary) had significantly better rates of attendance at subsequent sessions than those who saw only a drug counselor (71 percent versus 43 percent). Brown and Miller (1993) found that two sessions of motivational interviewing significantly improved treatment involvement and outcome compared to no such preparation.

Thus, in the author's clinical trials, study staff spend on average at least 2 hours with each patient explaining the study, its procedures, the implications of random assignment, the roles of the treatment and research staff, the benefits and risks of study participation, the nature of the treatment that may be received, the likely duration of assessment sessions, the importance of collecting accurate data, and why videotaping of treatment sessions is done. Study staff also prepare handouts containing this information; the handouts are intended to clarify the treatment protocol, inoculate patients against disappointment or surprise, and help them prepare for their roles as patients and research subjects. Potential barriers to study participation such as transportation and child care problems, work schedules, vacations, meetings with probation officers, and court cases, are ferreted out and discussed in advance. For example, the study staff routinely review a calendar with the patient, pointing out days when the patient can expect to come to treatment sessions, assessment interviews, and followups, so patients can identify interruptions and problems and these can be worked through in advance or avoided.

Frequent Contact and Monitoring

Nirenberg and colleagues (1980) found that telephone or letter contact immediately after missed sessions significantly improved rates of return to treatment. The author's research colleagues assume the patient is in the study until the patient says this isn't so. Therefore, if a patient misses a treatment or assessment session, research staff call or write several times until the patient comes in or formally withdraws. Patients are not accustomed to this level of interest, and the clear message of concern about what happens to them can be very persuasive if a patient is ambivalent about continuing. Patients who choose to withdraw are asked about their reasons for doing so and staff try to address these if possible. Also, because most study therapists do not work at the research clinic and may be difficult to contact on short notice, a member of the research team is available by phone to answer questions, handle crises, or link the patient with the therapist if necessary.

User-Friendly Practices

Attending to the details of a clinical trial, which takes consistent effort and attention, conveys respect for the patient and may also improve retention (DelBoca and Mattson 1994). For example, if the assessment battery takes several hours to complete, the staff offers the patient frequent breaks and refreshments. Assessment forms are evaluated for grade level and ease of reading. Clean, legible copies of assessment instruments are used. Subjects are encouraged to complete self-report instruments at the clinic where a staff person is available if they have questions or problems. All staff, including the security guards and receptionists, are polite to the patients. Staff and therapists ask the patients whether they prefer to be called by their first or last name. Parking is close to the clinic and safe. Personalized letters are sent to remind patients about followup interviews. Summarizations of the major findings of the study are sent to the patients as a means of thanking them for their participation and maintaining contact.

STATISTICAL COPING STRATEGIES

Finally, despite investigators' best efforts, some attrition may be inevitable in any clinical trial (Lavori 1990). The statistical problems associated with missing data and the flaws of many frequently used approaches for coping with them are well known. For example,

traditional statistical models for analyzing clinical trial data, such as analysis of variance (ANOVA), are very vulnerable to missing data in that they typically result in either deletion of cases with any missing data or imputation of missing values. Furthermore, the practice of carrying forward endpoint ratings for patients who drop out of treatment has been severely criticized and is particularly vulnerable to bias when differential attrition occurs across groups (Lavori 1992).

Recently, however, sophisticated statistical models for evaluating treatment effects have become available that are less vulnerable to some problems associated with missing data. Random effects regression models permit a more flexible approach for studying change over time (Bryk and Raudenbush 1987; Hedeker, unpublished observations) by treating time as a random as well as a fixed effect, modeling an individual's behavior as a function of an individual growth trajectory and analyzing the individual change trajectories by treatment group. Furthermore, in contrast to repeated-measures ANOVA analyses which usually involve deleting subjects with missing data or imputing values for missing data points, random effects regression models allow use of all available data.

The potential value of these approaches has been demonstrated recently by applying random effects regression models to recent clinical trials. For example, the author and associates were able to follow 80 percent of patients randomized to the cocaine psychotherapy-pharmacotherapy study up to 1 year after they completed treatment, but could not successfully reach all patients for all followups. Analysis of the data using several different statistical models (cross-sectional, repeated measures MANOVA, and random regression) consistently pointed to continuing improvement, or sleeper effects, in the groups that received relapse prevention compared to supportive clinical management (Carroll et al. 1994*b*). However, it was also found that the more restrictive MANOVA models also indicated several spurious interaction effects related to imputation of missing values or analyses based on non-representative subgroups (Nich and Carroll, submitted).

SUMMARY

Given the close links between retention and outcome in substance abuse treatment, it is important to recognize that treatments are successful to the degree they retain patients. This chapter described

some practical strategies for improving retention in clinical trials of treatment for substance abuse. To summarize:

1. Retention can be conceived as an important treatment outcome that reflects good fit between patient, therapist, treatment, and setting. Procedures and practices that improve the quality of treatment are likely to also improve retention.

2. Attending to the problem of retention may help solve the problem. While trials are ongoing, investigators should monitor retention closely, attending to and addressing variations in retention that might be associated with setting, seasonal variations, therapist factors, and research procedure factors.

3. More data are needed on effective methods of enhancing retention in different treatment settings. It should be noted that the strategies presented here reflect common sense and are for the most part drawn from experience with several clinical trials. Few of them have been evaluated empirically. However, more data on effective retention strategies are likely to have broad clinical and research utility. For example, it would be possible to design studies that evaluate an adaptation of Higgins' voucher system (this volume) to specifically reinforce retention in treatments that have higher rates of attrition, different methods of rewarding clinicians with higher rates of retention, and the effect on retention of adding babysitting services, to mention but some areas where further research would be illuminating.

REFERENCES

Agosti, V.; Nunes, E.; Stewart, J.W.; and Quitkin, F.M. Patient factors related to early attrition from an outpatient cocaine research clinic: A preliminary report. *Int J Addict* 26:3227-334, 1991.

Arndt, I.O.; McLellan, A.T.; Dorozynsky, L.; Woody, G.E.; and O'Brien, C.P. Desipramine treatment for cocaine dependence: Role of antisocial personality disorder. *J Nerv Ment Dis* 182:151-156, 1994.

Babst, D.V.; Chambers, C.D.; and Warner, A. Patient characteristics associated with retention in a methadone maintenance program. *Br J Addict* 66:195-204, 1971.

Baekeland, F., and Lundwall, L. Dropping out of treatment: A critical review. *Psychol Bull* 82:783-738, 1975.

Brown, J.M., and Miller, W.R. Impact of motivational interviewing on participation and outcome in residential alcoholism treatment. *Psychol Addict Behav* 7:211-218, 1993.

Bryk, A.S., and Raudenbush, S.W. Application of hierarchical linear models to assessing change. *Psychol Bull* 101:147-158, 1987.

Carroll, K.M.; Kadden, R.; Donovan, D.; Zweben, A.; and Rounsaville, B.J. Implementing treatment and protecting the validity of the independent variable in treatment matching studies. Supplement. *J Stud Alcohol* 12:149-155, 1994*a.*

Carroll, K.M.; Rounsaville, B.J.; and Gawin, F.H. A comparative trial of psychotherapies for ambulatory cocaine abusers: Relapse Prevention and Interpersonal Psychotherapy. *Am J Drug Alcohol Ab* 17:229-247, 1991.

Carroll, K.M.; Rounsaville, B.J; Gordon, L.T.; Nich, C.; Jatlow, P.M.; Bisighini, R.M.; and Gawin, F.H. Psychotherapy and pharmacotherapy for ambulatory cocaine abusers. *Arch Gen Psych* 51:177-187, 1994*c*.

Carroll, K.M.; Rounsaville, B.J.; Nich, C.; Gordon, L.T.; Wirtz, P.W.; and Gawin, F.H. One year followup of psychotherapy and pharmacotherapy for cocaine dependence: Delayed emergence of psychotherapy effects. *Arch Gen Psych* 51:989-997, 1994*b*.

Chevron, E.S.; Rounsaville, B.J.; Rothblum, E.D.; and Weissman, M.M. Selecting psychotherapists to participate in psychotherapy outcome studies: Relationship between psychotherapist characteristics and assessment of clinical skills. *J Nerv Ment Dis* 171:348-353, 1983.

Craig, R.J. Reducing the treatment drop out rate in drug abuse programs. *J Subst Abuse Treat* 2:209-219, 1985.

Crits-Christoph, P., and Mintz, J. Implications of therapist effects for the design and analysis of comparative studies of psychotherapies. *J Consult Clin Psychol* 59:20-26, 1991.

DelBoca, F., and Mattson, M. "Improving Compliance in Matching Studies." In: Cushman, P., chair. *Project MATCH: A Therapy Matching Trial with Alcohol Dependent Clients*. Symposium presented at the 25th Annual Medical-Scientific Conference, American Society of Addiction Medicine, New York, April 16, 1994.

DeLeon, G. Retention in drug-free therapeutic communities. In: Pickens, R.W.; Leukefeld, C.G.; and Schuster, C.R., eds. *Improving Drug Abuse Treatment*. National Institute on Drug Abuse Research Monograph 106. DHHS Pub. No. (ADM)91-1754. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1991. pp. 218-244.

DiClemente, C.C. "Creating Compliance: An Interactive Process Between Patients and Providers." In: Mattson, M., and Krasnegor, N., chairs. *Behavioral Research in Clinical Trials: Addictive Diseases*. Symposium conducted at the National Institutes of Health Reunion Task Force Series, The Science of Compliance, Bethesda, MD, December 7, 1993.

Fuller, R.K.; Branchey, L.; and Brightwell, D.R. Disulfiram treatment for alcoholism: A Veterans Administration cooperative study. *JAMA* 256:1449-1455, 1986.

Gawin, F.H.; Kleber, H.D.; Byck, R.; Rounsaville, B.J.; Kosten, T.R.; Jatlow, P.I.; and Morgan, C.B. Desipramine facilitation of initial cocaine abstinence. *Arch Gen Psych* 46:117-121, 1989.

Gibbons, R.D.; Hedeker, D.; Elkin, I.; Waternaux, C.; Kraemer, H.C.; Greenhouse, J.B.; Shea, M.T.; Imber, S.D.; Sotksy, S.M.; and Watkins, J.T. Some conceptual and statistical issues in analyses of longitudinal psychiatric data. *Arch Gen Psych* 50:739-750, 1993.

Herceg-Baron, R.L.; Prusoff, B.A.; Weissman, M.M.; DiMascio, A.; Neu, C.; and Klerman, G.L. Pharmacotherapy and psychotherapy in acutely depressed patients: A study of attrition patterns in a clinical trial. *Comp Psych* 20:315-325, 1979.

Higgins, S.T.; Budney, A.J.; Bickel, W.K.; and Badger, G.J. Participation of significant others in outpatient behavioral treatment predicts greater cocaine abstinence. *Am J Drug Alcohol Abuse* 20:47-56, 1994.

Hoehn-Saric, R.; Frank, J.D.; Imber, S.D.; Nash, E.H.; Stone, A.R.; and Battle, C.C. Systematic preparation of patients for psychotherapy-I. Effects on therapy behavior and outcome. *J Psych Res* 2:267-281, 1964.

Howard, K.I.; Cox, W.M.; and Saunders, S.M. Attrition in substance abuse comparative treatment research: The illusion of randomization. In: Onken, L.S., and Blaine, J.D., eds. *Psychotherapy and Counseling in the Treatment of Drug Abuse*. National Institute on Drug Abuse Research Monograph 104. DHHS Pub. No. (ADM)91-1722. Washington, DC: Supt. of Docs., U.S. Govt. Print. Off., 1990. pp. 66-79.

Kadden, R.; Carroll, K.M.; Donovan, D.; Cooney, N.; Monti, P.; Abrams, D.; Litt, M.; and Hester, R. Cognitive-behavioral coping skills therapy manual: A clinical research guide for therapists treating individuals with alcohol abuse and dependence. NIAAA/Project MATCH Monograph 3.

DHHS Pub. No. (ADM)92-1895. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism, 1992.

Kalton, G. *Compensation for Missing Survey Data*. Ann Arbor, MI: Survey Research Center, 1983.

Keil, T.J., and Esters, R.A. Treatment dropouts: The effect of client and ecological variables. *Int J Addict* 17:95-108, 1982.

Lackin, J.M., and Foulkes, M.A. Evaluation of sample size and power for analyses of survival with allowance for nonuniform patient entry, losses to followup, noncompliance, and stratification. *Biometrics* 42:507-519, 1986.

Lang, J.M. The use of a run-in to enhance compliance. *Stat Med* 9:87-95, 1990.

Lavori, P.W. ANOVA, MANOVA, my black hen: Comments on repeated measures. *Arch Gen Psych* 47:775-778, 1990.

Lavori, P.W. Clinical trials in psychiatry: Should protocol deviation censor patient data? *Neuropsychopharmacology* 6:39-48, 1992.

Leigh, G.; Ogborne, A.C.; and Cleland, P. Factors associated with patient dropout from an outpatient alcoholism treatment service. *J Stud Alcohol* 45:359-362, 1984.

Luborsky, L.; McLellan, A.T.; Woody, G.E.; O'Brien, C.P.; and Auerbach, A. Therapist success and its determinants. *Arch Gen Psych* 42:602-611, 1985.

Meichenbaum, D., and Turk, D.C. *Facilitating Treatment Adherence: A Practitioner's Handbook.* New York: Plenum Press, 1987.

Miller, W.R.; Zweben, A.; DiClemente, C.C.; and Rychtarik, R.G. Motivational enhancement therapy manual: A clinical research guide for therapists treating individuals with alcohol abuse and dependence. NIAAA/Project MATCH Monograph 2. DHHS Pub. No. (ADM) 92-1894. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism, 1992.

Nich, C., and Carroll, K.M. "Now You See It, Now You Don't: A Practical Demonstration of Random Regression Versus Traditional ANOVA Models in the Analysis of Longitudinal Followup Data from a Clinical Trial." Manuscript submitted for publication.

Nirenberg, T.D.; Sobell, L.C.; and Sobel, M.B. Effective and inexpensive procedures for decreasing client attrition in an outpatient alcohol treatment program. *Am J Drug Alcohol Abuse* 7:73-82, 1980.

Nowinski, J.; Baker, S.; and Carroll, K.M. Twelve-step facilitation therapy manual: A clinical research guide for therapists treating individuals with alcohol abuse and dependence.

NIAAA/Project MATCH Monograph 1. DHHS Pub. No. (ADM)92-1893. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism, 1992.

Peterson, K.A.; Swindle, R.W.; Phibbs, C.S.; Recine, B.; and Moos, R.H. Determinants of readmission following inpatient substance abuse treatment: A national study of VA programs. *Med Care* 32:535-550, 1994.

Project MATCH Research Group. Project MATCH: Rationale and methods for a multisite clinical trial matching alcoholism patients to treatment. *Alcohol Clin Exp Res* 17:1130-1145, 1993.

Rounsaville, B.J.; Chevron, E.; Weissman, M.M.; Prusoff, B.A.; and Frank, E. Training therapists to perform interpersonal psychotherapy in clinical trials. *Comp Psych* 27:364-371, 1986.

Sackett, D.L., and Gent, M. Controversy in counting and attributing events in clinical trials. *New Engl J Med* 301:1410-1412, 1979.

Silberfeld, M., and Glaser, F.B. Use of the life table method in determining attrition from treatment. *J Stud Alcohol* 39:1582-1590, 1978.

Simpson, D.D., and Sells, S.D. Effectiveness of treatment for drug abuse: An overview of the DARP research program. *Adv Alcohol Subst Abuse* 2:7-29, 1982.

Sorenson, J.L.; Gibson, D.; Bernal, G.; and Deitch, D. Methadone applicant dropouts: Impact of requiring involvement of friends and family in treatment. *Int J Addict* 20:1273-1280, 1985.

Sparr, L.F.; Moffitt, M.D.; and Ward, M.F. Missed psychiatric appointments: Who returns and who stays away. *Am J Psych* 150:801-805, 1993.

Stark, M.J.; Campbell, B.K.; and Brinkerhoff, C.V. "Hello, may we help you?": A study of attrition prevention at the time of the first phone contact with substance-abusing clients. *Am J Drug Alcohol Abuse* 16:67-76, 1990.

Stark, M.J., and Kane, B.K. General and specific psychotherapy role induction with substance abusing clients. *Int J Addict* 20:1135-1141, 1985.

Sutherland, G.; Stockwell, T.; and Edwards, G. The impact of a research interview on clinical reattendance: A happy finding. *Br J Addict* 80:211-212, 1985.

Swett, C., and Noones, J. Factors associated with premature termination from outpatient treatment. *Hospital Commun Psych* 40:47-51, 1989.

Szapocznik, J., and Ladner, R. Factors related to successful retention in methadone maintenance: A review. *Int J Addict* 12:1067-1085, 1977.

Taylor, G.J.; Ryan, D.; and Bagby, R.M. Toward the development of a new self-report alexithymia scale. *Psychother Psychosomatics* 44:191-199, 1985.

Weissman, M.M.; Rounsaville, B.J.; and Chevron, E. Training psychotherapists to participate in psychotherapy outcome studies. *Am J Psych* 139:1442-1446, 1982.

Wickizer, T.; Maynard, C.; Atherly, A.; and Frederick, M. Completion rates of clients discharged from drug and alcohol treatment programs in Washington State. *Am J Pub Health* 84:215-221, 1994.

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AUTHOR

Kathleen M. Carroll, Ph.D.
Department of Psychiatry
Yale University School of Medicine
Substance Abuse Center/S208
34 Park Street
New Haven, CT 06519

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