

## **EFFECT OF TELEPHONE OUTREACH COUNSELING ON PATIENTS' ADHERENCE TO ANTIDEPRESSANT MEDICATION**

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*ScriptAssist Medication Compliance Programs*

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Medication adherence is a major issue for all parts of the medical profession (Fawcett, 1995). More than 50% of all people prescribed medication for chronic conditions discontinue their treatment within the first year (Meichenbaum & Turk, 1987). This holds true for antidepressants, with an estimated 20% of patients never filling their initial prescription (Koop, 1985), and an additional 30% adhering to their medication regimen less than the minimum amount of time needed for acute treatment (Frank et al., 1990).

Major depression is a very common problem, with an estimated lifetime prevalence rate of 17% in the United States (Kessler et al., 1994). Antidepressant medication is a treatment of choice for major depression (Agency for Health Care Policy and Research [AHCPR], 1993). Patients who are not properly treated for depression, or who are treated for less than the minimum recommended length of time, risk a recurrence of depressive symptoms that may be even more intense and harder to treat than the initial episode (AHCPR, 1993). Given these facts and the high rate of nonadherence among depressed patients, an intervention to enhance antidepressant medication adherence has significant potential to enhance quality of life for a large number of individuals.

Psychosocial interventions are able to enhance adherence to a wide variety of medication regimens for chronic conditions, including treatments for hypertension, epilepsy, CHF, bipolar disorder, and schizophrenia. At the time this study was initiated, there were no published reports on interventions to improve antidepressant adherence. However, the literature indicated that psychosocial strategies

such as self-monitoring and feedback, cognitive restructuring, and the use of environmental cues were consistently helpful in improving adherence. A recent meta-analytic review of this literature (Cook, 1999) also demonstrated that interventions involving personal contact with a counselor were more helpful than interventions like unit-dose pill packaging or automatic reminders delivered by pager. Therefore, a telephone intervention was designed to enhance antidepressant medication adherence by providing patients with psychosocial counseling and support.

Development of this intervention began with an analysis of the most efficacious adherence-enhancing techniques described in the literature (Cook, 1999). Next, a team of psychiatrists with over 45 years of combined experience were consulted to identify key reasons for nonadherence with antidepressants and key times at which patients may require additional support to stay on the medication. These clinical experts' opinions were confirmed by a careful review of nonadherence patterns observed in published antidepressant drug trials (e.g., Frank et al., 1990). Finally, these findings were integrated by a clinical psychologist with experience in manualized therapies and outcomes research (the first author), to produce a final intervention manual with key questions for patients, a decision tree for clinical strategies, and instructions for implementing specialized clinical techniques.

In this intervention, patients received phone calls on a regular basis, beginning within 3 to 6 days after an antidepressant medication was first prescribed. Calls were made on a regular schedule (7 times over the course of 4 months), with more calls allowed if needed.

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After the start of this project, a report was published describing a very similar intervention for antidepressant compliance (Katzelnick et al., 2000). This study found that telephone outreach calls, together with mailed materials (taken from Pfizer's RHYTHMS program for patient education) were able to significantly increase antidepressant medication adherence relative to a treatment-as-usual control group. However, the intervention used by Katzelnick et al. differed from the present study's intervention in several important ways: First, Katzelnick et al.'s intervention seemed to rely mainly on reminders and support, a strategy that has been found relatively less efficacious in the literature (Cook, 1999). Second, this intervention was delivered by individuals with minimal training and experience, whereas the present study's intervention was developed for use by skilled behavioral health personnel. Finally, participants in Katzelnick et al.'s study also completed several lengthy telephone assessments during the course of treatment. Assessments of medication adherence tend to be highly reactive (e.g., Feinstein, 1990), and therefore it is possible that part of the improvement reported by Katzelnick et al. was due to the effects of repeated assessment.

Therefore, the experimental intervention described below represents a significant departure from previous work in this area, and has the potential to enhance medication adherence beyond rates seen in prior research. This study also used the least intrusive assessment methods possible, in order to be sure that any observed effects were truly the result of the intervention and not an artifact of the research methodology. Finally, given that antidepressant medications have rarely been targeted for adherence-enhancing interventions, this area could benefit from further research.

## Method

### *Participants*

*Setting.* Patients were recruited from staff-model clinics run by a managed behavioral health organization (PRO Behavioral Health [PRO]) at three different locations in Colorado

(Colorado Springs, Denver, and Westminster). All psychiatrists at these clinics ( $N = 14$ ) were informed about the project and agreed to have their new patients included in the study. These psychiatrists were asked to provide information about any patient who met inclusion criteria. Psychiatrists were asked not to engage in any additional screening of patients, and the psychiatrists' weekly schedules were examined to verify that all eligible patients had in fact been given the opportunity to participate.

*Inclusion/Exclusion Criteria.* Inclusion criteria for this study were as follows: (a) the patient had a documented psychiatric diagnosis of Major Depressive Disorder or Depression NOS; (b) the patient was given a new prescription (not a refill) for any antidepressant medication; (c) the patient was 18 years of age or older; and (d) the patient did not qualify for a diagnosis of substance abuse. Patients were not excluded on the basis of comorbid conditions, and depression did not have to be the patient's primary diagnosis. Patients with a diagnosis other than depression—including depressed patients with Bipolar Disorder, Dysthymia, or Adjustment Disorder with Depressed Mood—were excluded from the current study, even if they had been prescribed an antidepressant. Patients given other types of medication for depression (e.g., one patient given a benzodiazepine) were also excluded.

*Screening Results.* 101 new patients attended medication evaluations at PRO's clinics during the study period, and were screened for this study by their treating psychiatrist. 18 of these patients met the inclusion criteria, and all of these patients gave their informed consent for follow-up contact.

Other clinic patients were excluded from this study for the following reasons: no diagnosis of depression (43 patients), no new medication prescribed (16 patients), comorbid substance abuse (11 patients), patient met inclusion criteria but was not going to continue treatment at PRO Behavioral Health (4 patients), and patient under age 18 (9 patients).

*Patient Demographics.* Patients included in this study had the following demographic

characteristics: 83% (15/18) were female, and 17% (3/18) were male. Patients had completed an average 14.6 years of education, and 27% had a college degree. 56% of the patients included in the study were married. Patients in the study were receiving medication from an average of 1.5 doctors besides their psychiatrist, and used an average of just 1 pharmacy for all medications. Patients traveled an average of 30 minutes to reach the clinic.

*Current Medications.* Patients included in this study were prescribed a number of different antidepressant medications, including sertraline (Zoloft—6 patients), paroxetine (Paxil—2 patients), venlafaxine (Effexor—2 patients), mirtazapine (Remeron—2 patients), fluoxetine (Prozac—1 patient), bupropion (Wellbutrin—1 patient), citalopram (Celexa—1 patient), nortriptyline (Pamelor—1 patient), and other antidepressants (2 patients). In addition, one patient switched antidepressant medications on medical advice during the course of this study (from Paxil to Prozac), and one patient added a second antidepressant (Effexor added to Remeron). No between-group statistical comparisons were possible regarding type of medication ( $n < 5$  per cell); however, the pattern of this data does not suggest any systematic difference between the treatment and control groups in terms of the type of antidepressant prescribed.

Patients included in the study were receiving medication from a total of 6 psychiatrists, each of whom saw an average of 3 patients included in the study. Again, no statistical comparison is possible regarding the effect of treatment provider ( $n < 5$  per cell), but examination of the data does not suggest any systematic bias in this area. Psychiatrists who

saw more than one patient in this study generally had an equal mix of patients from the experimental and control groups.

*Prior Treatment Experiences.* 89% of the patients included in this study had prior experience with behavioral health treatment, and 82% had previous treatment experiences with psychotropic medication. 11% (2/18) of the patients in the study had previously been hospitalized for mental health issues.

Patients in the study had an average intake score of 2.4 (out of a possible 5) on a self-report scale that assessed their past history of adherence (Morisky, Green, & Levine, 1986). This indicates low to moderate past difficulties taking medication as it was prescribed.

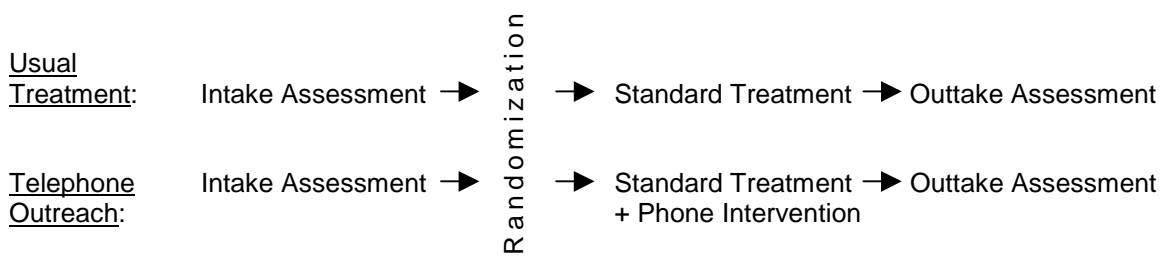
**Procedure**

The general methodology for this study is summarized in Figure 1.

*Recruitment Procedure.* All participants were informed about the experimental procedure at the time of intake. Before seeing a doctor, each patient was given intake forms by the clinic receptionist, along with consent forms for telephone contact and for data collection. Psychiatrists told all patients who qualified for the study that someone might be contacting them to check on how their new medication was working. At this time, patients could also ask their psychiatrist any questions they had about the follow-up procedure.

*Random Assignment to Groups.* At the time of intake, those patients who qualified for the study were randomly assigned to one of two groups: (a) psychiatric treatment as usual, or (b) treatment as usual plus telephone outreach counseling. Random assignment was

**Figure 1. Research Design**



accomplished using a computerized random number generator (“Statistica—1999 Edition” software package, StatSoft, Inc., 1999).

*Usual Treatment.* Patients in the usual-treatment group received antidepressant medication, as prescribed and supervised by their psychiatrist at one of PRO’s outpatient psychiatric clinics. These patients also had unlimited telephone access to both a staff nurse, who could answer medication questions, and a clinic-based, 24-hour telephone crisis intervention service.

*Experimental Intervention.* Patients in the telephone-outreach group received all of the above services, plus regular telephone calls from a staff member, who asked about their progress with their new medication. Telephone outreach calls followed a regular schedule starting from the date that a new antidepressant was first prescribed. Patients’ telephone numbers and prescription information were obtained directly from medical records. These records were also reviewed (by the first author) to verify patients’ eligibility for the study.

The telephone-outreach protocol used in this study was approved by PRO’s corporate medical director and was overseen by a multidisciplinary clinical team for both clinical and ethical considerations. A psychiatric nurse with 25 years of clinical experience was hired on a contract basis, and received 5 hours of training on how to deliver the manualized telephone intervention. This training included role-played telephone calls, and was conducted by the first author. About half of all patients in the experimental group received outreach calls from the nurse, and the other half received outreach calls from the first author. These two providers met weekly to discuss their experiences, in order to ensure standardized treatment delivery.

Patients in the telephone-outreach group received calls consistently from the same provider throughout the length of the study. Each patient in the experimental group

received between 5 and 8 telephone calls over the first three months of this study, with an average of 6.57 calls per patient.<sup>1</sup> On average, initial calls lasted 18 minutes, with subsequent calls taking about 8 minutes each. Each telephone call included the following three steps: (a) an assessment of the participant’s current level of adherence, (b) an assessment to identify any factors currently interfering with adherence, and (c) individualized feedback or suggestions to help the participant increase his or her level of adherence.

Most patients (63%) were also sent patient education materials by mail at some point during the study. These materials were targeted to address specific issues that came up during the telephone call, and were drawn from a specific set of materials designed to complement the intervention manual. Sample materials included an information sheet about side effects produced by a particular drug, a booklet on symptoms of depression, and a 1-page handout on “questions to ask your doctor.” The same materials were used by both individuals making outreach calls.

*Assessment Strategy.* It was considered important to minimize the number of times each patient was assessed, in order to rule out “white coat” monitoring effects (Feinstein, 1990; Roth, 1987) as a source of bias in the results. However, it was also important to obtain information about adherence from multiple informants using multiple methods, as each available way to assess adherence has its own possibilities for distortion (Fletcher, Pappius, & Harper, 1979; Roth, 1987).

Based on these considerations, information was collected from a number of sources at two different points in time. At intake, all patients completed several self-report measures before meeting with their psychiatrist. The treating psychiatrist also completed a brief form after the initial session, and other information was gathered from medical records.

No further data (other than ongoing process notes for patients in the experimental group)

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<sup>1</sup> This figure does not include the one patient who dropped out of our study in month #2 (see “Attrition,” below). That patient received only two outreach calls before she left the intervention group.

were collected until the time of an outtake assessment, approximately 3 months after patients began treatment. This time frame was selected based on the average recommended length of acute-phase antidepressant treatment (AHCPR, 1993), which is 3 to 4 months. It was felt that a longer assessment period would produce confusing results, as some patients would have finished treatment by that point.

At the time of outtake, each patient (in both the experimental and control groups) was contacted by telephone and asked a series of questions about his or her medication adherence over the course of the study. These questions were asked in a standardized format, by a clinical psychologist (the second author) who was familiar with the hypotheses of this study, but who was blind to individual participants' group assignment. After this telephone interview, each patient was mailed a final packet of self-report forms, along with a postage-paid return envelope. If patients completed the outtake telephone assessment and returned the self-report forms, they were sent a \$10 check for their time.

### **Measures**

*Intake Self-Report Form.* At intake, patients completed a self-report packet that asked them for the following demographic information: number of doctors currently seen; number of pharmacies currently used; number of times per day pills are currently taken; years of formal education; travel time from home to clinic (in minutes); past history of psychiatric hospitalization; marital/relationship status; and perceived social support ("how much can you count on your family and friends for help with a problem," scored on a 7-point Likert-type scale, ranging from 1—"not much" to 7—"very much"). These items are theoretically related to medication nonadherence (Col, Fanale, & Kronholm, 1990; Cramer, 1995; Rodríguez, Díaz, Colón, & Santiago-Delpín, 1991).

*Self-Reported Medication-Taking Scale (SRMTS).* The SRMTS (Morisky, Green, & Levine, 1986) was included in the packet of forms that patients completed at intake. This scale, originally using a True/False format, was

modified for the current study to use a 5-point Likert-type scale (ranging from 1—"never true" to 5—"always true"). Two items were added to the four original items to tap additional theoretically-relevant dimensions of medication adherence (unhelpful beliefs and difficulty communicating with one's doctor). The scale's four original items assess forgetting to take medication, carelessness about taking medication, discontinuing medication when one feels better, and discontinuing medication when one experiences negative side effects.

Although all self-reports of medication adherence are likely to provide overestimates (Roth, 1987), this scale is the best-validated self-report adherence measure available. The original version of the SRMTS demonstrated adequate internal consistency (Cronbach alpha = 0.61) and was moderately correlated with physiological outcome (high blood pressure) for antihypertensive medication ( $r = 0.43$ ,  $p < 0.01$ ) (Morisky, Green, & Levine, 1986). The SRMTS was re-administered at outtake, to test for treatment effects on self-reported medication adherence. It should be noted that SRMTS scores at intake refer to past experiences with medication in general, while SRMTS scores at outtake refer to experiences with the prescribed antidepressant in particular.

*Multidimensional Health-Related Locus of Control Scales (MHLOC).* Locus of control for health-related behaviors is another factor that is theoretically related to medication adherence (e.g., Williams, Rodin, Ryan, Grolnick, & Deci, 1998). Individuals may attribute health outcomes to their own behavior, to external factors or powerful others, or to chance. The MHLOC (Wallston, Wallston, & DeVellis, 1978) assesses patients' attributions in each of these areas, with three conceptually and statistically distinct measurement scales. The MHLOC includes 18 items, each answered on a 7-point Likert-type scale ranging from 1—"strongly disagree" to 5—"strongly agree." Sample items are: "I am in control of my health" (internal scale), "regarding my health, I can only do what my doctor tells me to do" (external scale), and "my good health is largely a matter of good fortune" (chance scale).

The MHLOC scales have shown adequate internal consistency (alphas ranging from 0.67 to 0.86), and are relatively uncorrelated with measures of social desirability. The MHLOC was included in the intake self-report packet, and was administered again at outtake.

*Marlowe-Crowne Social Desirability Scale (MCSDS)—Short Form C.* The MCSDS short form (Reynolds, 1982) was developed as a brief measure of individuals' tendency to exaggerate or distort information in order to make a positive social impression. This scale is useful as a validity check for many types of self-report information, including the adherence information gathered in this study.

Short Form C of the MCSDS has demonstrated adequate internal consistency ( $r_{KR-20} = 0.76$ ), and is highly correlated with the original 33-item Social Desirability Scale (Crowne & Marlowe, 1960). This short form consists of 13 True-False items, such as "I'm always polite, even to people I don't like," that most people will answer in a consistent way. Some items are reverse-scored to minimize a simple response set. The MCSDS was administered as part of the intake packet.

*Behavior and Symptom Identification Scale (BASIS-32).* The BASIS-32 (Eisen, Dill, & Grob, 1994) was developed as a short self-report outcome measure on psychiatric symptoms and life functioning. This scale's 32 items ask patients "to what extent are you experiencing difficulty in the area of..." various life domains, and requires a response on a 5-point bubble-fill scale ranging from "no difficulty" to "extreme difficulty." The total score calculated using all BASIS-32 items correlates well with interview measures of psychiatric distress (Eisen, 1995). The BASIS-32 total score has demonstrated adequate internal consistency ( $\alpha = 0.89$ ) and retest reliability ( $r = 0.85$ ) (Eisen et al., 1994).

Participants completed the BASIS-32 as part of PRO's standard intake paperwork, prior to being screened for this study. Data for this original administration were collected from participants' clinical charts. Patients were mailed a second BASIS-32 form as part of the

outtake self-report packet, to test for changes in psychiatric severity due to the intervention.

*Psychiatrist Intake Form.* At intake, each participant's psychiatrist completed a 1-page form to verify the patient's eligibility for the study (appropriate diagnosis, new antidepressant prescription, and no substance abuse diagnosis). Four additional items asked whether the patient was provided with samples of the medication (YES/NO), whether the patient was given written material about the drug and its effects (YES/NO), the psychiatrist's name, and the date of intake.

*Information from Medical Records.* The first author completed a medical records review for each patient included in the study. Patients' charts were checked to confirm that they were appropriate for inclusion in the study. Then, the following information was gathered: the participant's address, telephone number, and contact information (best times to call, OK to call at home or work, OK to leave message, etc.); the type and dose of medication prescribed; the participant's date of birth; and the participant's DSM-IV diagnosis and Global Assessment of Functioning (GAF) score (American Psychiatric Association, 1994), as documented by the treating psychiatrist at the time of intake. Charts were again reviewed at the time of outtake, and any additional GAF scores or diagnoses that the patient's psychiatrist had recorded during the course of the study were also noted.

*Outtake Telephone Assessment.* After three months of either usual treatment or usual treatment plus outreach calls, all participants received a telephone call to assess their adherence with antidepressant medication over the course of the study. These calls were conducted by an experienced clinical psychologist (the second author), using a structured interview format. The interviewer was blind to participants' group assignment, and had no contact with any participant prior to the outtake assessment call. The assessment began with a nonjudgmental statement about medication adherence ("some people find it difficult to take medication as prescribed"), and an open-ended question about adherence ("are

you still taking that medication? Have you had any difficulties taking the medication as prescribed?”). More specific follow-up questions (e.g., “last week, what percentage of the time were you able to take the medication as prescribed?”) were used based on the participant’s initial response. Finally, the participant was asked to give a 0% to 100% rating of his or her own adherence since the time the medication was first prescribed.

This interview yielded three separate pieces of data: (a) the participant’s numeric rating of his or her own adherence (0%-100%), (b) the interviewer’s rating of the participant’s adherence (again, 0%-100%—the interviewer was permitted to use all available clinical information in making this decision, in addition to the participant’s self-rating), and (c) any qualitative information provided by the participant about the reasons for his or her nonadherence. After this information was collected, the interviewer asked whether the participant had received outreach calls, and if so, whether he or she wanted to offer any feedback about these calls.

Independent interviews of this type are in many ways the “gold standard” measure for medication adherence: They correlate well with physiological and self-report measures (e.g., Fletcher, Pappius, & Harper, 1979; Hilbert, 1985), they are relatively easy to administer (Fletcher, Pappius, & Harper, 1979), and they seem to produce less patient exaggeration of adherence than other assessment methods (Haynes et al., 1980). In one study (Haynes et al., 1980), an independent, nonjudgmental interviewing format produced ratings that were highly correlated ( $r = 0.74$ ) with a pill count made during a surprise visit at patient’s homes.

*Pill Count.* Finally, an attempt was made to validate interviewer ratings of adherence by asking patients to perform a pill count during the outtake interview. Patients were asked to provide information on the date of their most recent prescription, the number of pills they should be taking each day, and the number of pills remaining in the pill bottle at the time of the outtake telephone call. Unfortunately, pill count information proved too difficult to

obtain. Even among adherent patients, participants were often unsure whether they had started taking their current refill on exactly the date it was issued by the pharmacy, when their doctor had told them to change dosages, whether they had removed pills to put in other bottles, etc. Therefore, pill count data are not included in the results reported below.

## Results

### *Power Analysis*

Because this was a small- $N$  study, it was important to know how much statistical power was available to detect an effect of the expected size. A prior meta-analysis (Cook, 1999) found the average effect size for adherence-enhancing counseling to be around  $r = 0.45$ . However, power analysis indicated that with 18 patients and  $\alpha = 0.05$ , power to detect an effect of this size would be only 0.47. This was not considered sufficient for a pilot study, in which Type II error was of greater concern than Type I error. Relaxing the significance criterion somewhat, to  $\alpha = 0.20$ , provided power = 0.77 to detect an effect size of  $r = 0.45$  or larger. This was considered adequate power for our current study design.

### *Attrition Rate*

As of this writing (3 out of 4 months planned for the intervention), one out of 8 patients assigned to the telephone intervention had dropped out of treatment at PRO. This woman decided to discontinue psychiatric treatment (against medical advice) due to general dissatisfaction with the psychiatric services she was receiving, not because she was dissatisfied with the telephone outreach intervention itself. Outtake data for this participant *are* included in the results presented below.

### *Contact Rate for Outtake Interview*

Not all patients could be contacted for telephone interviews at outtake. In the group that received the outreach intervention, 71% (5/7) of all patients provided data for the telephone outtake assessment. However, recent clinical notes were available on the two

patients who could not be contacted by telephone, allowing for a relatively accurate assessment of their adherence even without the outtake interview data. The contact rate was 70% (7/10) for outtake interviews among control group participants. Of those individuals who could not be contacted for follow-up in the control group, two had disconnected telephone numbers, and one could not be reached and did not return messages after numerous attempts at contact. Chart information was used to infer adherence for as long as these patients were receiving prescriptions. When no new prescription was issued, nonadherence was not assumed; rather, patients were dropped from analyses.

### ***Representativeness of Patient Sample***

Overall, the patients included in this study seem to be representative of the total population seen for medication evaluations in PRO's staff-model clinics. Patients in the treatment and control groups were similar to the general clinic population in terms of the following variables: level of education, age, self-reported level of social support, marital status, past history of psychiatric hospitalization, level of psychological distress at intake, distance traveled from home to the clinic, GAF score at intake, past history of psychiatric treatment, past use of psychotropic medications, need for social approval, number of pharmacies used, and doses of medication taken per day (all  $ps > 0.12$ ). All patients included in the study had a primary DSM-IV diagnosis of Major Depressive Disorder; one patient in the control group had a secondary diagnosis of Generalized Anxiety Disorder. In the treatment group, one patient had a secondary diagnosis of Anxiety NOS, and one patient probably met criteria for a somatoform disorder in addition to depression.

However, patients included in the study were slightly more likely to be female,  $\chi^2(1, N = 99) = 6.59, p = 0.01$ , to use multiple doctors,  $t(54) = 2.08, p = 0.04$ , and to report marginally higher baseline levels of nonadherence,  $t(54) = 1.67, p = 0.10$ , than patients not included in the study.

Furthermore, although patients included in the study had health beliefs about self-efficacy and chance that were representative of the general population ( $ps > 0.20$ ), patients included in the study were slightly less likely to express faith in doctors on the MHLOC scale,  $t(50) = 2.16, p = 0.04$ . Finally, patients included in the study were by definition less likely to have comorbid substance abuse than those in the general clinic population. These differences may limit the generalizability of any findings, and must be taken into account in interpreting these results.

### ***Comparability of Study Groups***

On average, patients in the treatment and control groups of this study were similar in terms of the following variables: past history of psychiatric hospitalization, past history of behavioral health treatment, age, level of education, self-reported level of social support, level of psychological distress at intake, marital status, health-related beliefs, need for social approval, number of doctors used, number of pharmacies used, doses of medication taken per day, GAF score at intake, past history of treatment with psychotropic medication, distance from home to the clinic, and presence of comorbid diagnoses (all  $ps > 0.12$ ).

Furthermore, patients' intake scores on the Self-Reported Medication-Taking Scale were not significantly different between the treatment and control groups,  $t(9) = 0.86, p = 0.41$ , indicating a similar baseline level of medication adherence across the two groups.

### ***Effect of Intervention on Nonadherence***

For purposes of outcome assessment, "adherence with the prescribed antidepressant medication" was operationally defined as the patient taking a dose between 80% and 120% of the recommended dose, on at least 80% of days since the prescription was first given, unless there had been a psychiatrist-approved change in the patient's medication regimen since that time. For those patients whose doctors had changed their medication regimens ( $n = 2$ ), adherence was defined as taking 80%-120% of the prescribed dose of the *new* medication on 80% of days since the change.

**Table 1. Adherence Rates Over Time, vs. Predicted Adherence Over Time**

Time	Adherence Rate Based on Literature	Adherence Rate for Control Group	Adherence Rate for Experimental Group
Initial Prescription	80%	90% (9/10)	100% (8/8)
End of Month #1	72%	77% (7/9)	88% (7/8)
End of Month #2	64%	71% (5/7)	88% (7/8)
End of Month #3	62%	57% (4/7)	88% (7/8)

**Note.** “Adherence Rate Based on Literature” was predicted using a hypothetical attrition curve obtained from findings in published studies of adherence and clinical trials with imipramine, a tricyclic antidepressant medication (Fawcett, 1995; Frank et al., 1990; Koop, 1985).

Generally, patients’ responses to the outcome interview suggested one of two patterns: Either the patient was still taking the medication at the prescribed dose almost all of the time, or else the patient gave some reason for having discontinued the medication and was no longer taking it at all. All patients who discontinued treatment cited either (a) side effects of medication or (b) side effects and “feeling better” as their rationale for doing so. Patients did not generally seem to be mis-dosing or taking medication inconsistently, which suggests that most nonadherence in this particular population was intentional. Only one patient was refilling prescriptions but not taking the medication correctly; in all other cases, nonadherent patients simply dropped out of treatment. This tended to occur very early in treatment, with nonadherent patients filling an average of only 1 prescription.

Based on the general finding that 60% of all nonadherence happens within the first 2-3 months of treatment (Fawcett, 1995), it was expected that approximately 38% of the control patients would be nonadherent by the end of month #3. In fact, there was a nonadherence rate of 43% among participants receiving usual care. The rate of nonadherence was only 12% in the telephone-outreach group, which was a significant improvement over the nonadherence rate for the group receiving usual care,  $\chi^2(1, N = 15) = 3.04, p = 0.08$ . This difference was significant not only at the required 0.20 level, but also at the more stringent 0.10 level. Therefore, even with the small sample size

used in this pilot study, it is possible to have confidence in the stability of these results.

Additional confidence in the interview findings is provided by the improvement seen on a second, independent measure of medication compliance. The Self-Reported Medication-Taking Scale gives patients’ own views on their level of compliance. In the control group, patients’ self-reported medication compliance deteriorated slightly over time in the control group (an average drop of 1.06 points on a 5-point scale), while patients in the experimental group reported a slight increase in compliance over time (an average increase of 0.22 points on a 5-point scale). The difference in patients’ self-reports about compliance approached conventional levels of statistical significance,  $t(4) = 2.36, p = 0.08$ , even with small sample size. This finding serves to confirm the interview data based on a different type of measure (no shared method variance) and a second perspective (patient rather than clinician) on compliance.

See Table 1 for a comparison of control and experimental group adherence rates over time, versus predicted adherence over time. Interestingly, adherence rates for the control group were slightly higher initially than what would have been predicted based on the published literature. This is potentially due to the relatively high level of initial distress seen in a psychiatric clinic as opposed to in a university research setting. Alternatively, this finding might be due to the fact that the “predicted rate” figures were based on clinical

trials for imipramine, a tricyclic antidepressant, while control group figures were based primarily on patients' experiences with selective serotonin reuptake inhibitor (SSRI) antidepressants, which are known to have fewer side effects.

Regardless of this finding, it is noteworthy that the control group's adherence by the end of this study was actually *below* the predicted rate. Furthermore, the intervention group had improved adherence relative to the control group at *every* individual point in time.

Interview data suggest that those patients who received outreach calls found this service to be helpful. All patients who received calls indicated that they appreciated the ongoing contact, and there were no negative comments about this service. Positive comments expressed appreciation for ongoing contact, for someone taking time to listen, for a sense that someone cared, for the chance to discuss side effects (particularly sexual side effects) as normal experiences, and for the chance to receive information about medications and about effective communication with doctors. Patients also said the outreach calls were helpful for continuity of care when they had to switch physicians due to insurance changes and other external circumstances. Illustrative comments include "people cared," and "I felt like I had a link."

### **Discussion**

This study was designed to test an experimental telephone outreach intervention, which used evidence-based techniques to support patients' adherence to treatment with antidepressant medication. Those patients who received telephone outreach counseling in addition to standard psychiatric services were 54% more likely to be adherent to their prescribed medication regimen after three months than were other patients who did not receive this additional service. The difference between the experimental and control groups was statistically significant, and suggests that this type of telephone outreach counseling is

able to produce reliable improvement in patients' adherence to antidepressant treatment.

Participants' comments about the service suggest that they did not experience the outreach service as intrusive, and that in fact they appreciated both the information they were given and the interpersonal contact with their outreach counselor.

### ***Validity of the Current Results***

Before each participant's first meeting with a psychiatrist (which was also prior to random group assignment), patients provided information on a number of demographic and clinical variables that are theoretically related to medication adherence. Randomly selected treatment and control groups in this study seem to have been comparable in terms of all relevant pre-treatment variables, including their baseline level of medication adherence. This finding allows us to be confident that between-group differences in medication adherence were the result of the experimental procedure.

### ***Generalizability of the Current Results***

Patients selected for this study seem to have been representative of the general population seen at this staff-model behavioral healthcare organization's outpatient medication clinics. Although there were some differences between the experimental sample and the larger population (notably sex ratio, number of physicians used, comorbid substance abuse, and faith in doctors), the current results are probably generalizable to outpatient psychiatric clients in general. Those patients sampled for this study actually reported higher baseline levels of medication nonadherence than others in the total clinic population. Therefore, the current intervention seems to have been targeted to a group of patients who were particularly in need of assistance with medication adherence.

### ***Limitations/Directions for Further Research***

One important limitation of this study is its small sample size. Concern about this problem is somewhat alleviated by the dramatic findings

shown in Table 1, which demonstrate that this study's experimental intervention produced results sharply different from the results obtained under usual psychiatric care as well as from the nonadherence rates expected based on previously published clinical trials. However, replication of this finding is still required to verify the current results. In addition, a larger sample size would have permitted us to examine other questions of interest, such as whether this intervention produced benefits in terms of decreased symptoms of depression, increased patient satisfaction with treatment, etc. Further study is necessary to investigate the magnitude of our intervention's effect on these important clinical variables.

Further research is also needed to determine whether the current intervention can be modified to improve adherence with other types of medication, or in settings other than an outpatient, staff-model managed behavioral healthcare clinic. In particular, it would be of interest to determine whether the present findings can be replicated when medications are prescribed by Primary Care Physicians (PCPs), who are responsible for supervising the vast majority of individuals on antidepressant medication. It seems likely that nonadherence in PCP practices would be even higher than the current rates, which were obtained among patients seen in a specialty psychiatric practice.

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