Rehabilitation Psychology
2014, Vol. 59, No. 2, 136–146

DOI: 10.1037/a0036322

Telephone Counseling and Home Telehealth Monitoring to Improve Medication Adherence: Results of a Pilot Trial Among Individuals With Multiple Sclerosis

Aaron P. Turner
VA Puget Sound Health Care System, Seattle, Washington, VA MS Center of Excellence West, Seattle, Washington, VA Center of Excellence in Substance Abuse Treatment and Education, Seattle, Washington, and University of Washington

Alicia P. Sloan
VA Puget Sound Health Care System, Seattle, Washington and VA MS Center of Excellence West, Seattle, Washington

Daniel R. Kivlahan
VA Puget Sound Health Care System, Seattle, Washington, VA Center of Excellence in Substance Abuse Treatment and Education, Seattle, Washington, and University of Washington

Jodie K. Haselkorn
VA Puget Sound Health Care System, Seattle, Washington, VA MS Center of Excellence West, Seattle, Washington, and University of Washington

Objective: To evaluate the impact upon medication adherence of brief telephone-based counseling using principles of motivational interviewing and telehealth home monitoring. ***Design:*** Randomized controlled pilot trial of 19 veterans with multiple sclerosis (MS) currently prescribed disease modifying therapy (DMT) who endorsed missing doses. Follow-up was conducted at 1, 3, and 6 months. ***Results:*** Participants in the intervention condition reported better adherence relative to controls at 6-month follow-up [*M* (*SD*) = 1.3 (2.1) vs. 8.2 (12.3) past month missed doses]. All participants in the intervention condition completed all 3 telephone counseling sessions and 90% or greater rated the program as highly successful. ***Conclusion:*** Brief telephone counseling represents a promising mechanism for improving medication adherence. The primary components, motivational interviewing and home telehealth monitoring, provided complementary mechanisms for initiating and sustaining behavior change over time. The intervention was well tolerated and provided an opportunity to extend access and reduce barriers to care by bringing it into the homes of participants.

Keywords: multiple sclerosis, medication adherence, motivational interviewing, self-management, telehealth

Impact and Implications

- Preliminary evidence suggests that brief telephone counseling based upon motivational interviewing is an effective means of promoting self-management and health behavior change.
- The flexibility of telephone-based counseling has considerable potential to extend the reach of psychological interventions outside of traditional practice settings.
- There is considerable opportunity to incorporate telephone-based counseling and self-management into both chronic illness management and rehabilitation care.

Introduction

Medication adherence represents a significant challenge to the efficacy and cost-effectiveness of health care. Problems with medication adherence are well documented in many common conditions, including hypertension, chronic obstructive pulmonary disease, depression, and diabetes. Existing literature suggests that typical rates of adherence are often as low as 50% (Haynes,

This article was published Online First April 7, 2014.

Aaron P. Turner, VA Puget Sound Health Care System, Seattle, Washington, VA MS Center of Excellence West, Seattle, Washington, VA Center of Excellence in Substance Abuse Treatment and Education, Seattle, Washington, and Department of Rehabilitation Medicine, University of Washington; Alicia P. Sloan, VA Puget Sound Health Care System and VA MS Center of Excellence West; Daniel R. Kivlahan, VA Puget Sound Health Care System, VA Center of Excellence in Substance Abuse Treatment and Education, and Department of Psychiatry and Behavioral Sciences, University of Washington; and Jodie K. Haselkorn, VA Puget Sound Health Care System, VA MS Center of Excellence West, Department of Rehabilitation Medicine and Department of Epidemiology, University of Washington.

This research was supported by Department of Veterans Affairs Rehabilitation Research and Development Service Career Development Awards (B3319VA) and (B4927W) to Aaron P. Turner. Additional support was provided by the VA MS Center of Excellence West and the VA Center of Excellence in Substance Abuse Treatment and Education. Trial Registration clinicaltrials.gov Identifier: NCT00118547.

Correspondence concerning this article should be addressed to Aaron P. Turner, PhD, VA Puget Sound Health Care System, Rehabilitation Care Service, S-117-RCS, 1660 S. Columbian Way, Seattle, WA 98108. E-mail: Aaron.Turner@med.va.gov

McKibbon, & Kanani, 1997; Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Haynes, McDonald, & Garg, 2002; R. B. Haynes, McKibbon, & Kanani, 1996) significantly impacting the delivery of care as it was originally prescribed. Recognition of this fact has led many authors including the World Health Organization to argue that in coming years, increasing the effectiveness of adherence interventions may have a greater impact on long term health than improvements in specific medical treatments (Haynes et al., 2000; World Health Organization, 2003).

Individuals with multiple sclerosis (MS) face similar challenges to adherence. MS is a chronic degenerative demyelinating disorder of the central nervous system. It is associated with a host of disabling and sometimes unpredictable symptoms that may include sensory, motor, and balance impairment, fatigue, pain, cognitive impairment, and depression (Goodkin, 1992; Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000; R. Williams et al., 2005). These symptoms often have a considerable impact upon quality of life (Aronson, 1997; Gottberg et al., 2006; Rao, Leo, Bernardin, & Unverzagt, 1991). Several medications effectively reduce acute exacerbation and disability associated with MS. Despite the wide availability of these disease modifying therapies (DMT), close to one half of individuals who begin an appropriate course of DMT discontinue use at some time (Fraser, Hadjimichael, & Vollmer, 2003; Hadjimichael & Vollmer, 1999) and less than two thirds remain on medication without a prescription lapse (Tremlett & Oger, 2003). Most recently, in a study of over 2,600 individuals with MS in 22 countries, participants reported adherence rates in the past month of 75% (Devonshire et al., 2011). Evidence suggests that psychosocial factors such as health beliefs, emotions, social support, and self-efficacy figure prominently in the initiation and maintenance of this important health behavior (Mohr, Boudewyn, Likosky, Levine, & Goodkin, 2001; Mohr, Cox, & Merluzzi, 2005; Mohr et al., 1997; Mohr et al., 1996; Siegel, Turner, & Haselkorn, 2008; Turner, Kivlahan, Sloan, & Haselkorn, 2007; Turner, Williams, Sloan, & Haselkorn, 2009).

There is increasing recognition that chronic illness management should be viewed as a collaborative process and that coordinated approaches to problems such as medication adherence improve outcomes (Bodenheimer, Wagner, & Grumbach, 2002a, 2002b; Clark & Gong, 2000; Wagner, 2000; Wagner, Austin, & Von Korff, 1996). Individuals with MS and their providers must work together to define problems, engage in solutions, and monitor and respond to changes in physical and mental health (Von Korff, Gruman, Schaefer, Curry, & Wagner, 1997). These illness management skills require self-direction, motivation, and self-efficacy, but also can be learned over time. Interventions should provide a variety of self-management training strategies, and management should include sustained follow-up (Clark & Gong, 2000; Von Korff et al., 1997). Although providers play an essential role in the recommendation to initiate therapies, ultimately the success of self-management strategies such as medication adherence will depend upon the actions of persons with the disease and the ability of health care providers to support and sustain their behavior change.

One form of intervention that is particularly promising for facilitating chronic illness care and promoting self-management behaviors such as medication adherence is motivational interviewing. *Motivational interviewing* is a "person-centered form of guiding to elicit and strengthen motivation for change."(Miller & Rollnick, 2009) Motivational interviewing encourages behavior change by contrasting current behavior (such as poor medication adherence) to desired goals and values (such as good self care, health, and quality of life), while simultaneously providing empathy and promoting self-efficacy in a manner that is supportive, evocative, and collaborative (Miller & Rollnick, 2002). It is informed by the transtheoretical model that recognizes individuals are often ambivalent about changing behavior, and may be in different stages of willingness to do so (Prochaska & DiClemente, 1983). As a result, the content of counseling is titrated to a person's readiness to change and implemented with the goal of minimizing resistance and maximizing engagement. Motivational interviewing is often used in conjunction with other self-management behavioral strategies, such as targeted goal setting and problem solving and has been shown to improve medication adherence in a variety of contexts including treatment for asthma (Halterman et al., 2011), hypertension (Ogedegbe et al., 2008), alcohol dependence (Heffner et al., 2010; Reid, Teesson, Sannibale, Matsuda, & Haber, 2005), and HIV (DiIorio et al., 2008; Ingersoll et al., 2011), though in most cases evidence has been preliminary.

Motivational interviewing and self-management support are well suited to delivery by telephone and home telehealth monitoring. Interventions using these modalities are consistently well tolerated, effective across a variety of chronic illnesses (Bell et al., 2003; Bell et al., 2005; Bombardier et al., 2009; Bombardier et al., 2008; Bombardier et al., 2013; Dellifraine & Dansky, 2008; Pare, Jaana, & Sicotte, 2007; Pare, Moqadem, Pineau, & St-Hilaire, 2010), and provide important opportunities to deliver care to those who may not otherwise receive it (Hatzakis, Haselkorn, Williams, Turner, & Nichol, 2003). Several studies have used telephone-based motivational interviewing as an adjunct to in-person sessions to improve medication adherence in asthma (Halterman et al., 2011) and HIV (DiIorio et al., 2008).

Only one educational program to date has used telephone-based intervention to improve medication adherence among individuals with MS (Stockl et al., 2010). It did not specifically target adherence, but rather provided monthly calls, provided by nurses and pharmacists, on 12 MS-related topics, one of which was adherence. The program included goal setting but was also largely didactic in nature.

The purpose of the current study was to investigate the feasibility and efficacy of a brief intervention combining telephone counseling based upon principles of motivational interviewing and home telehealth monitoring to improve adherence to DMT for people with MS. The intent was to create a counseling-based intervention that was brief in duration, focused on a specific goal, and flexible so that it could be adapted to the differing needs of participants. If successful, it could stand alone or serve as a component of a larger self-management intervention.

Methods

Design

This study is a randomized controlled pilot trial of a brief intervention combining telephone counseling and home telehealth monitoring to improve adherence to MS disease modifying therapies (DMT). The primary outcome, adherence, was examined at

baseline prior to randomization, and then at 1, 3, and 6 months (following the telephone counseling but during ongoing home telehealth monitoring). Participants received either the telephone-based counseling intervention or care as usual.

Participants

Participants were recruited from veterans receiving outpatient services for MS at a VA regional medical center as part of a larger project examining DMT adherence in MS. Inclusion criteria for the original study included a diagnosis of MS, current use of one of four injectable DMTs to slow disease progression available at the time of the intervention (inteferon beta-1a [Avonex], interferon beta-1a [Rebif], interferon beta-1b [Betaseron], or glatiramer acetate [Copaxone]), and active participation in medication administration. Individuals who received their injections primarily from an injection clinic nurse or a caregiver were excluded. The study consisted of two parts. Participants of the original study were first enrolled into a longitudinal cohort by a coordinator during a regularly scheduled clinic visit, or in response to a mailing. Medication adherence of individuals participating in the original study was obtained during monthly follow-up assessments for a period of 6 months. Individuals who endorsed difficulties with adherence (missed doses during the study period) were invited to participate in the intervention trial after the completion of this 6-month period.

Of 89 original participants, 36 individuals were alive, still taking DMT medication, and reported missing doses during the original study. Of the 36, 19 (52.8%) enrolled in the brief intervention trial. Among those who did not enroll, five (13.9%) declined and 11 (30.6%) were not available or did not respond to enrollment queries within the recruitment time frame. One individual consented, but then moved out of state prior to completion of baseline (please see Figure 1). All 19 individuals who were enrolled in the trial completed the entire study; no individuals dropped out or were lost to follow-up. All 19 individuals were active users of DMTs during the entire study period. No individual switched to a different DMT during the study period.

Procedure

As part of the original study, potential participants' medical records were prescreened to confirm that they were currently taking a DMT. Additional screening was conducted to verify that the individual was primarily responsible for administering his or

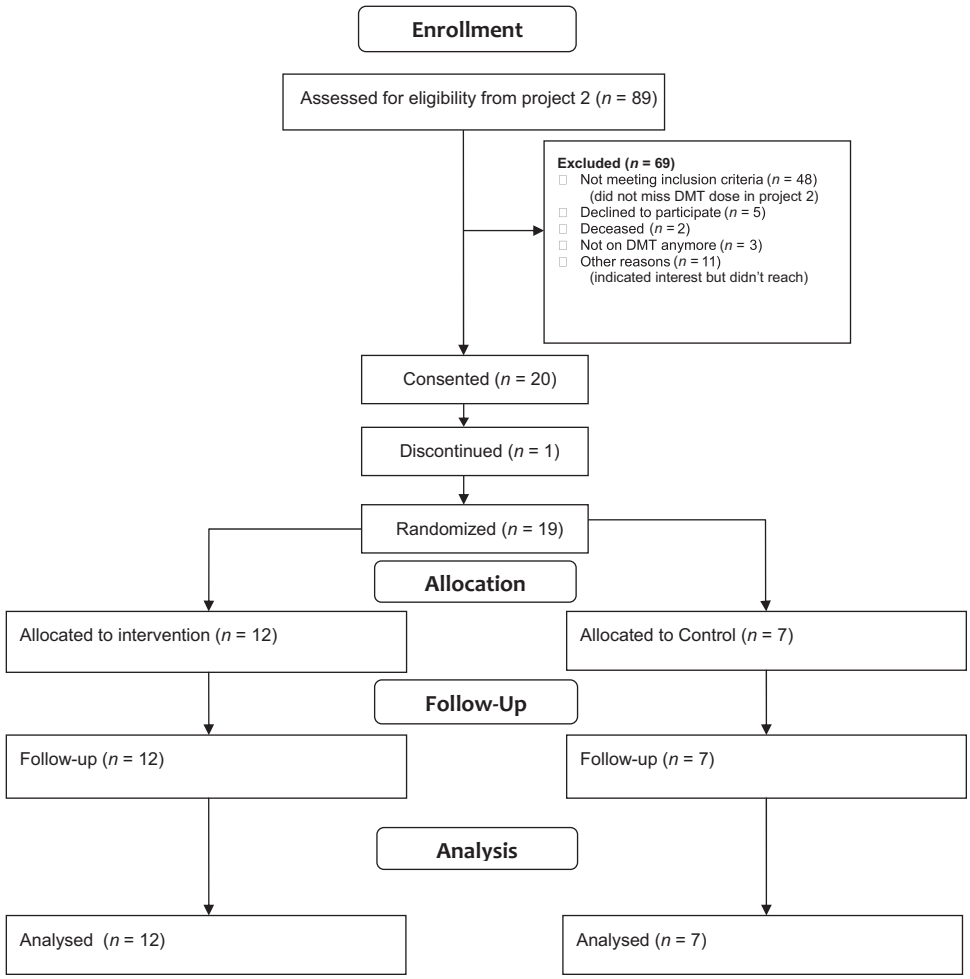

Figure 1. Consort diagram.

her own DMT, and that there was a telephone number where the person could be reached.

For this study, individuals were approached by the study coordinator and asked if they would be willing to participate in a study examining a brief telephone-based intervention to improve adherence. Participants were required to meet criteria for Veterans Health Administration (VHA) home telehealth programs and be willing to agree to the installation of a brief telehealth home monitor in their primary residence.

Participants completed a telephone interview that included questionnaires addressing adherence behavior over the past month including DMT missed doses, adherence self-efficacy, and side effects and reasons for missed doses. Baseline demographic information (e.g., age, gender, education) and disease information (e.g., years with MS, mobility disability, fatigue, depression, cognitive functioning) were obtained from information obtained in the original study.

Following completion of baseline, individuals were individually randomized via computer algorithm to the intervention or the control condition. Prior to assignment, treatment condition was unknown to the project coordinator to ensure concealment of allocation.

Individuals assigned to the treatment condition participated in a combination of brief telephone counseling and home telehealth monitoring to promote improved DMT adherence. The telephone sessions were scheduled at a time and place of the participant's choosing (usually the veteran's home and at various times of the day and evening). Individuals assigned to the control condition received treatment as usual and were offered telephone counseling and monitoring only after the completion of the final follow-up time point (waitlist control). All participants completed follow-up telephone interviews at Months 1, 3, and 6. Treatment condition was concealed from the telephone interviewer for all outcome assessments. All study procedures were approved by the local institutional review board.

Measures

Demographic information. Age, gender, race (White vs. non-White), marital status (currently married vs. all other) and education level (in years) were all obtained from single-titem queries.

Disease information. Years with ms was obtained from a single item query. Medical comorbidity was measured using the Seattle Index of Comorbidity (SIC; (Fan et al., 2002) a weighted composite of medical conditions (e.g., cancer, diabetes) combined with age and current smoking status into a single score reflecting total medical comorbidity. The SIC has been shown to predict rates of mortality and hospitalization (Fan et al., 2002). The presence of medical conditions was obtained from a review of the medical record.

Mobility disability and upper extremity disability were obtained from subscale scores from the North American Research Committee on Multiple Sclerosis (NARCOMS) survey. Disability in each of these two areas was assessed with a single self-report item with possible scores ranging from 0 (*normal*) to 6 (*total gait disability*) for mobility and 0 (*normal*) to 5 (*total hand disability*), respectively. These subscales have demonstrated excellent test–retest reliability (Schwartz, Vollmer, & Lee, 1999) and the mobility scale is highly correlated with the Expanded Disability Status Scale (Kurtzke, 1983), a widely used and extensively validated physician-rating tool that estimates disease-related impairment in persons with MS.

Fatigue was measured with the Modified Fatigue Impact Scale Short Form (MFIS-5). The original MFIS assesses the impact of fatigue in physical, cognitive, and psychosocial domains (Fischer et al., 1999). Participants rate the frequency of impact upon daily life in the past month using values ranging from 0 (*never*) to 4 (*almost always*). The MFIS-5 consists of the five items (representing all domains) that correlate most highly with the full scale total score. Values range from 0 to 20. The MFIS has established validity (Fischer et al., 1999) and internal consistency in the current sample was good ($\alpha = .90$).

Depression was evaluated using the nine-item depression module from the Patient Health Questionnaire (PHQ-9; (Kroenke, Spitzer, & Williams, 2001). The PHQ-9 is a brief screening instrument designed to identify depressive symptoms consistent with criteria of the *Diagnostic and Statistical Manual for Mental Disorders*, 4th ed. (American Psychiatric Association, 1994). Participants rate the degree to which they experienced each of 9 symptoms of depression over the last 2 weeks from 0 (*not at all*) to 3 (*nearly every day*). The PHQ-9 has shown utility in estimating the level of depressive severity in medical patients using the sum of scores on each of the 9 items (Spitzer, Kroenke, & Williams, 1999). Internal consistency in the current sample was good ($\alpha = .88$).

Cognitive functioning was measured using a series of brief screening measures administered during the telephone interview. Verbal memory was examined using the short delay recall task from the Screening Examination for Cognitive Impairment (Beatty et al., 1995). Attention was examined using the digit span task from the Wechsler Adult Intelligence Scale–III (Wechsler, 1997). Verbal fluency/executive functioning was examined using the Controlled Oral Word Association Task (FAS version; (Strauss, Sherman, & Spreen, 2006). All three measures have been used extensively and have well established psychometric properties (Beatty et al., 1995; Strauss et al., 2006; Wechsler, 1997),. The use of telephone-based cognitive assessment has been used in multiple trials of psychotherapy interventions in individuals with MS (Mohr, Hart et al., 2005) and telephone administration of functionally similar measures have been shown to be valid and reliable in other samples (Debanne et al., 1997; Unverzagt et al., 2007).

Medication Information

Adherence to DMT medications was assessed with a single self-report question adapted from HIV adherence literature.(Stone, 2001) Participants were asked, "People often have difficulty taking their medications for one reason or another. How many times have you missed taking your DMT in the past month?" DMT medications are taken at different frequencies ranging from once per week (interferon beta-1a [Avonex]) to once per day (glatiramer acetate). As a result, it was necessary to create a common metric for missed doses across medications. Standard weightings corresponding to a 30-day month were computed for each medication. A missed dose of once per week interferon beta-1a (Avonex) was given a weight of 7.5 such that total nonadherence (4 doses) $\times$ 7.5 = 30. A missed dose of daily glatiramer acetate was given a weight of 1 such that

total nonadherence (30 doses) × 1 = 30 as well. Self-report of adherence to DMT has been shown to be very highly correlated with multiple measurement modalities including medication diaries and Medication Event Monitoring System data (Bruce, Hancock, & Lynch, 2010). This specific missed dose measure is highly correlated with other self-reported indicators of adherence and the cross-medication missed dose common metric has been used in previous literature on adherence to DMT in MS (Siegel et al., 2008; Turner et al., 2007; Turner et al., 2009).

Current DMT type was extracted from participants' medical records. Because of limited sample size, DMT type was dichotomized for analyses to reflect the use of an interferon based medication (inteferon beta-1a [Avonex], interferon beta-1a [Rebif], interferon beta-1b [Betaseron]), or glatiramer acetate (Copaxone).

Length of time on current DMT medication was obtained from a single item query in the interview. Side effects of current DMT medication were measured using a six-item scale created for this study. Item selection was based upon published information regarding frequent side effects of DMT medications and included items such as "injection pain, red spot or rash at injection site," "flu-like symptoms (increased fatigue, fever, chills, sweating, muscle aches)," and "shortness of breath, strong heartbeat, chest pain, flushing." Participants were asked to rate the frequency of occurrence of side effects with response options ranging from 1 (*never*) to 5 (*always*).

Adherence self-efficacy was measured using a single-uitem adapted from previous research on medication adherence in MS (Mohr et al., 2001; Mohr, Cox, Epstein, & Boudewyn, 2002). The item asks participants "How confident are you that you will be taking your prescribed DMT one month from now?" with response options ranging from 1 (*not at all*) to 5 (*extremely*).

Treatment acceptability was measured using the four credibility items adapted from the Reaction to Treatment Questionnaire (Holt & Heimberg, 1990). The items ask participants to rate confidence the program would help with adherence, the success of the program, confidence in recommending the program to a friend, and how logical the program was using a Likert-type scale ranging from 1 to 10. For purposes of this study, responses were dichotomized and scores of 7 out of 10 or higher were considered positive (confident, successful, recommended, logical).

Intervention

The treatment intervention consisted of two primary components: telephone counseling and home-based telehealth monitoring. Telephone counseling was based upon principles of motivational interviewing and was intended to increase motivation and confidence in medication adherence. Telehealth monitoring was based upon principles of self-management and intended to support sustained medication adherence over time.

Telephone Counseling

Telephone counseling consisted of three sessions. Session 1 included the following components: (a) a discussion with the participant about his or her experiences coping with the challenges of MS, as well as hopes for life with the illness over time; (b) identification of participants' perceptions of the pros and cons for DMT use; (c) personalized graphic feedback summarizing the scientific evidence supporting the benefits of the specific medication taken by each participant (delayed progression of disability, reduced proliferation of MRI lesions, sustained cognitive ability) and individual performance on a brief cognitive screening battery; and (d) a review of each participants' recent missed doses and medication adherence. The overall purpose of the early session components was to facilitate readiness to change by increasing the salience of adherence benefits and developing discrepancies between actual behavior (missed doses) and desired behavior (effective self-care that promoted health and well being with chronic illness). At the end of Session 1, when appropriate, participants created a change plan that identified desired improvements in medication adherence, personal reasons to reduce missed doses, specific steps to make these changes, and ways to elicit support and reduce barriers. The purpose of this final exercise was to elicit and articulate commitment to medication adherence as well as begin the process of problem solving sustained adherence.

Session 2 consisted primarily of skills training. The counselor and participants reviewed strategies for reducing medication side effects, rotating injections, interacting with providers and pharmacies, and creating a sustainable medication schedule. Participants were asked to identify personal high-risk situations that increased the likelihood of a missed dose, engage in a behavioral chain analysis of a recent missed dose, and problem solving coping strategies to intervene at various points along the path of the circumstances leading to a missed dose. Session 2 also included an orientation to the telehealth home monitor, including set-up and introduction to functions.

Session 3 was a booster session. The counselor engaged in problem solving around missed doses, adherence skills, additional motivational interviewing, and trouble-shooting difficulties with home telehealth monitors depending upon the needs of individual participants. Each of the three sessions ranged from 45 to 75 min in length.

Telehealth Home Monitoring

Between telephone counseling Sessions 2 and 3, each participant received a home monitoring unit that connected to ordinary telephone lines that could deliver customized text messages using store and forward technology. Monitors were programmed to participants' individual medication administration schedules and provided reminder alarms if desired. Participants were asked after every programmed dose interval, "Did you take your DMT dose as prescribed?" Individuals who answered yes received encouraging statements. Individuals who answered no received a follow up question examining why the dose was missed. All responses were transmitted to the project coordinator who viewed responses via a web-based graphical interface that was color coded to allow quick daily review of all study participants (green = adherent, red = not adherent, blue = did not respond when expected to do so). Individuals who were nonadherent, or did not respond to the question when expected to do so, received a follow-up telephone call for additional counseling and problem solving as necessary. This process allowed for flexible follow-up of participants that could be titrated to their specific needs.

Intervention Training and Treatment Fidelity

Treatment fidelity is the extent to which an intervention is delivered as intended. The study therapist (Alicia P. Sloan) received training from the study principal investigator who has significant experience with motivational interviewing. The therapist also participated in an additional multiday training in motivational interviewing conducted by an independent motivational interviewing trainer. Prior to study initiation, the study therapist participated in experiential and role play exercises as well as case-consultation exercises utilizing core MI skills, and also completed training cases. All telephone counseling sessions were audio taped. Immediately following each session, the study therapist completed a fidelity checklist of behaviors consistent with the spirit of motivational interviewing (e.g., open ended questions, affirmation, reflection, summary) and inconsistent with motivational interviewing (e.g., closed questions, arguing, giving advice without permission). Overall ratings of counselor style were obtained in the areas of warmth, understanding, and egalitarianism, as was an overall rating of participant resistance. During the course of the study, the study therapist participated in supervision with the principal investigator in which recorded intervention sessions were reviewed in detail, including a focus on the behavioral and style ratings previously mentioned. Supervision meetings were held weekly and tapered to biweekly over the course of the study.

Data Analytic Strategy

Our primary aim was to test the hypothesis that participation in a brief telephone-based intervention in combination with home telehealth-monitoring would improve adherence to DMT compared to a treatment as usual control group. We first examined the adequacy of randomization by comparing baseline differences in demographic, disease, and medication-related variables. Means and frequencies for continuous and categorical variables were compared using *t* tests and chi-square tests, respectively. To test our primary aim, we conducted three separate analysis of covariance (ANCOVA) analyses (one for each of our three follow-up time points). We compared differences in adherence to DMT in the control and intervention conditions at each time point adjusting for baseline adherence. This particular strategy was selected because of its favorable ability to detect group differences (Vickers, 2001). All participants completed the entire study and completed all assessment time points (except one participant at Month 3). For this reason, individuals were considered "analyzed as randomized" and results were considered based upon an intent-to-treat sample. No additional completers subanalyses were conducted (in a follow-up analysis, imputing the one missing data element by carrying the last observation forward did not alter the overall significance of the results).

Results

Sample Characteristics at Baseline

Participants were largely male (84.2%), Caucasian (84.2%), and married (57.9%), with a mean age of 52.4 ($SD = 7.4$) years and a mean education level of 15.0 ($SD = 2.2$) years. Overall, the sample population was highly representative of the larger population of VHA veterans with MS (Vollmer, Hadjimichael, Preiningerova, Ni, & Buenconsejo, 2002).

Participants reported they had been diagnosed with MS for a mean of 14.1 ($SD = 10.2$) years and reported moderate levels of MS disease severity for Performance Scale Mobility Subscale, M (SD) = 3.0 (1.8) and Performance Scale Hand Function Subscale, M (SD) = 1.7 (1.5). They reported taking their current DMT medication for a mean of 2.6 ($SD = 2.7$) years. All four injectable medications available at the time of the study were represented in the sample with 15.8% taking inteferon beta-1a (Avonex), 10.5% taking interferon beta-1a (Rebif), 31.6% taking interferon beta-1b (Betaseron), and 42.1% taking glatiramer acetate (Copaxone). No participant changed DMT during the study period.

Adequacy of Randomization

Twelve individuals were assigned to the intervention condition and 7 individuals to the control condition. To examine randomization adequacy we compared the intervention and control conditions at baseline on demographics, disease-related variables, and medication-related variables. There were no significant differences between groups for any of these variables (see Tables 1 and 2).

Intervention Integrity

All participants in the intervention condition received mailed graphic feedback and participated in all three telephone counseling sessions. All participants were successful in enrolling in VA telehealth, installing telehealth monitors in their homes, and making use of the home telemonitoring question set. In addition to the prescribed telephone counseling sessions, during the study period, the study therapist provided an average of 11.2 additional telephone follow-up attempts resulting in an average of 4.0 support telephone calls for each participant (range 1 to 9) over 6 months. The average call duration was 9.3 min (range 2 to 60) and the average total time in calls per participant was 44.2 min (range 5 to 125). The primary reason for calls was to follow-up about missing data when telehealth monitors did not transmit data accurately within the expected timeframe.

Primary Outcome: Medication Adherence

Following the brief telephone-based counseling, and during ongoing telehealth home monitoring, participants in the intervention condition reported missing fewer doses of DMT in the prior month compared to the control group at all time points including 1-month follow-up, M (SD) = 3.9 (8.4) versus 7.3 (11.5); 3-month follow-up, M (SD) = 0.8 (1.0) versus 5.7 (12.0); and 6-month follow-up, M (SD) = 1.3 (2.1) versus 8.2 (12.1) (see Figure 2). These differences corresponded to moderate effect sizes for follow-up at 1 month ($d = .4$), and large effect sizes for 3 months ($d = .7$) and 6 months ($d = .9$). Using ANCOVA to examine differences in adherence by treatment condition adjusting for baseline adherence, the effect of treatment condition was not significant at 1 month, $F(1, 16) = .67$, $p < .40$; approached significance at 3 months, $F(1, 15) = 1.77$, $p < .20$;; and was significant at 6 months, $F(1, 16) = 4.79$, $p < .05$. Overall, differences between the intervention and control arms were consistent and large, but significance was limited in part by small baseline differences favoring

Table 1
Baseline Characteristics of the Study Sample

Characteristic	Condition		Significance
	Control	Telephone counseling	
Demographics			
Age	55.29 (4.92)	50.75 (8.18)	*ns*
Gender (male)	85.71%	83.3%	*ns*
Race (White)	85.71%	83.3%	*ns*
Married	57.14%	58.3%	*ns*
Education (years)	15.21 (2.94)	14.79 (1.71)	*ns*
Global perceived social support	0.19 (0.49)	0.11 (0.43)	*ns*
Disease variables			
Years with multiple sclerosis	10.00 (7.44)	16.05 (11.07)	*ns*
Mobility disability	2.57 (2.15)	3.17 (1.64)	*ns*
Upper extremity disability	1.57 (1.81)	1.83 (1.40)	*ns*
Medical comorbidity	3.00 (1.92)	3.67 (2.64)	*ns*
Fatigue	11.29 (4.57)	12.08 (3.85)	*ns*
Depression	7.43 (4.89)	10.25 (7.33)	*ns*
Verbal recall	6.57 (1.51)	4.25 (2.96)	*ns*
Simple attention	16.71 (3.20)	15.67 (4.19)	*ns*
Fluency	30.71 (9.34)	31.75 (11.99)	*ns*
Medication variables			
Time on current disease modifying therapy	1.43 (1.71)	3.25 (3.02)	*ns*
Side effects	1.28 (0.40)	1.87 (0.96)	*ns*
Medication type (interferon)	71.4%	50.0%	*ns*
Adherence self-efficacy	4.86 (0.38)	4.75 (0.45)	*ns*

Note. $N = 19$. Global perceived social support = Stress and Support Scale; Medical comorbidity = Seattle Index of Comorbidity; Fatigue = Modified Fatigue Impact Scale (five-item); Depression = Patient Health Questionnaire-9; Verbal recall = Repeatable Battery for the Assessment of Neuropsychological Status List Recall; Simple attention = WAIS-III Digit Span total score; Fluency = Controlled Oral Word Association Task. Mobility and Upper Extremity Disability from Disability subscales of the NARCOMS survey.

the intervention condition, M (SD) = 5.2 (8.9) versus M (SD) = 6.9 (11.8), and more notably by the study's small sample size. Differences between the intervention and control condition increased over time (see Figure 2).

Secondary Outcome: Adherence Self-Efficacy

Adherence self-efficacy improved in the intervention condition relative to the control condition. However, using ANCOVA controlling for baseline values, these results only approached statistical significance, for example, at 6-month follow-up, M (SD) = 5.00 (0.01) versus 4.29 (1.50), $F(1, 16) = 2.87$, $p = .10$.

Treatment Acceptability

On the reaction to treatment questionnaire, 91.6% of participants viewed the intervention as logical and 91.6% stated that they were confident the program would help them maintain improved adherence. One hundred percent of participants rated the program as highly successful and 100% said they would recommend the program to a friend.

Satisfaction With Home Telehealth Monitoring Data

Overall, home telehealth monitoring was well tolerated: 83.3% of participants were "quite a bit" or "extremely" satisfied with home telehealth monitoring, 100% "agreed" or "strongly agreed" that the monitor was useful as a medication reminder, and 91.6% "agreed" or "strongly agreed" the monitor was easy to use.

Table 2
Adherence Rates by Treatment Condition Across Study Duration

Condition	Baseline M (SD)	Month 1 M (SD)	Month 3 M (SD)	Month 6 M (SD)
Control	6.86 (11.77)	7.29 (11.47)	5.67 (12.03)	8.23 (12.13)
Intervention	5.17 (8.85)	3.92 (8.43)	0.79 (1.03)	1.33 (2.10)

Note. $N = 19$. M (SD) = Unadjusted mean and standard deviation of standardized missed doses during past month at each time point by condition.

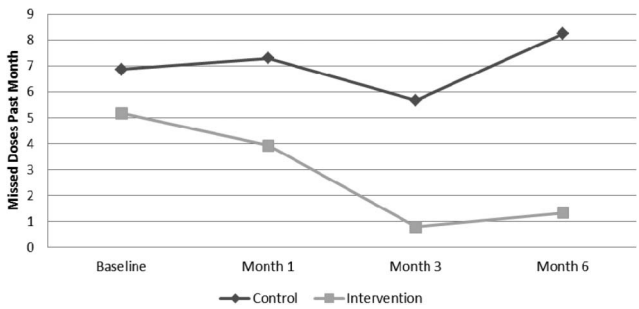

Figure 2. Adherence by condition across time.

Discussion

Results of this pilot trial provide preliminary evidence that brief telephone counseling combined with telehealth home monitoring improves adherence to DMT among individuals with MS. By 6-month follow-up, individuals in the intervention group had improved their past month adherence by an average of 6.9 standardized doses. Individuals participating in counseling and monitoring were essentially adherent with their medication one week per month more than individuals in the treatment as usual control condition. Two-thirds of intervention condition participants reported missing one dose or less.

Findings from this study confirm the feasibility and acceptability of telephone-based motivational interviewing to encourage health promotion, and specifically demonstrate its value in supporting medication adherence among individuals identifying improved adherence as a goal. This is consistent with much if not all of the limited available literature (Cook, Emiliozzi, & McCabe, 2007; Cook, Emiliozzi, Waters, & El Hajj, 2008; Cook, McCabe, Emiliozzi, & Pointer, 2009; DiIorio et al., 2008; Halterman et al., 2011; Solomon et al., 2012; A. Williams, Manias, Walker, & Gorelik, 2012) and is promising for a number of reasons. First, there is increasing evidence that sustained adherence to DMT is associated with better health outcomes for individuals with MS including reduced relapses and fewer hospitalizations (Steinberg, Faris, Chang, Chan, & Tankersley, 2010; Tan, Cai, Agarwal, Stephenson, & Kamat, 2011), suggesting a favorable cost/benefit ratio for a psychosocial intervention that typically involved three provider encounters and an average of 44 min of follow-up over 6 months. Second, telephone administration of the counseling intervention improves access to care by reducing the need for appointments, travel, and physical space within a medical facility. This is consistent with the philosophy of rehabilitation to match treatment with the abilities and limitations of the person served and the vision of the VHA to make the home and local community into the preferred place of care whenever possible and practicable (Department of Veterans Affairs, 2013).

It is not uncommon for the effects of treatment interventions such as motivational interviewing to decrease over time. The maintenance of gains over time in this study well past the period of initial counseling in the first month suggest that telehealth home monitoring provided additional value to participants and supported the ongoing practice of self-management to sustain behavior change. Home monitoring, when appropriately implemented (i.e., goals are specific, measurable, achievable, and timely follow-up is available) is also extremely promising as it allows for flexible care that can be scaled up or down to the needs of a specific individual. It also allowed for the efficient delivery of care, as individuals who were doing well continued to receive close monitoring without unneeded additional visits. On the other hand, individuals who experienced an adherence lapse could be identified quickly for additional support.

Overall, the intervention was both well accepted and feasible with all participants considering it to be successful and willing to recommend it to a friend. Over 80% were satisfied with the home telehealth monitors and over 90% found them useful and easy to use. All study participants completed all three telephone counseling sessions and successfully used home monitoring. The primary threat to feasibility appeared to be that home monitors would occasionally malfunction and that each successful telephone contact required approximately three attempts, even when the study therapist had invested considerable energy establishing the best times to contact participants.

This study has several limitations worthy of mention. Most immediate is the small sample size, which detracts from the ability of randomization to provide equal allocation of known and unknown influences upon the primary outcome, to all study conditions. Compounding this, small sample size also increases the likelihood, as seen in this trial, that pure randomization will lead to unequal allocation of participants to conditions (we had 63% randomization to the intervention condition). This phenomenon also increases the likelihood of unequal allocation of variables that may influence our adherence outcome and places additional burden on the examination of baseline differences in treatment groups. Also, our sample was limited to veterans with MS, who are typically older, male, and more disabled (Vollmer et al., 2002). The adherence variable used in this study was based upon self-report, which may be subject to bias because of social desirability or errors in recall, although as previously noted self-report of DMT adherence is highly correlated with other adherence measurement modalities (Bruce, Hancock et al., 2010), and there is no reason to suspect differential bias in the report of adherence between our randomized treatment arms given that follow-up assessment was independent of the intervention staff and blinded to condition. There was a small baseline difference in adherence favoring the intervention condition ($d < .2$), though baseline values were controlled in our ANCOVA model. It is also possible that limited sample size masked important pretreatment demographic differences between treatment arms, though the majority of current literature has typically failed to find consistent associations between demographic variables and DMT adherence (Turner et al., 2007) and medication adherence more generally (Haynes et al., 2002). In instances in our study where there was a difference (though still small and still nonsignificant) between conditions that has been shown in prior studies to be related to adherence (such as depression and verbal recall) (Bruce, Bruce, Hancock, & Lynch, 2010) differences favored the control condition. Although the difference, again, was not significant, there was also a higher proportion of individuals on medications taken less frequently in the intervention condition. To alleviate the concern the behavior of taking medication weekly versus taking medication daily was qualitatively different and may have differed in the treatment arms, we created a "possible dose" variable based on the specific medication of each participant. There was no significant difference between the conditions in the number of doses that could potentially be missed. Since the completion of this study, new oral disease-modifying therapies that do not require injection have been introduced to market and several others are in development. It is not clear that results of this study will translate to these noninjectable medications, although in the largest available survey, the two most common reasons for missing doses—forgettin' and being-'tired of taking a medication—are likely universal (Devonshire et al., 2011).

This study also has considerable strengths worth briefly reviewing. It is a randomized, controlled pilot trial. Threats to validity were minimized by concealment of treatment allocation and blinding of outcome assessment. There was no attrition in either study arm and all participants received the full prescribed intervention

(three counseling sessions and participation in home telemonitoring). Results were analyzed as randomized and can be considered to be based upon an intent-to-treat sample. Treatment fidelity was monitored throughout the course of the study. The 6-month study duration provided adequate time to examine short-term intervention efficacy. Stakeholder (participant) feedback was elicited and was overwhelmingly positive.

The next logical step would be to establish the efficacy of this intervention in a larger definitive trial that would provide better power and could establish more definitively the generalizability of our findings as well as better alleviate concerns of baseline differences in treatment conditions inherent in small trials. Such a study would include newer classes of oral DMT medications and would allow for examination of individual and medication-related factors that may moderate treatment outcome. Future studies would also benefit from more extensive evaluation of the fidelity of the intervention by an outside rater and the ability to examine individual components of treatment (e.g., counseling vs. counseling with additional monitoring).

References

Aronson, K. J. (1997). Quality of life among persons with multiple sclerosis and their caregivers. *Neurology, 48,* 74–80. doi:10.1212/WNL.48.1.74

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition Ed.)*. Washington DC: Author.

Beatty, W. W., Paul, R. H., Wilbanks, S. L., Hames, K. A., Blanco, C. R., & Goodkin, D. E. (1995). Identifying multiple sclerosis patients with mild or global cognitive impairment using the Screening Examination for Cognitive Impairment (SEFCI). *Neurology, 45,* 718–723. doi:10.1212/WNL.45.4.718

Bell, K. R., Esselman, P., Garner, M. D., Doctor, J., Bombardier, C., & Johnson, K. (2003). The use of a World Wide Web-based consultation site to provide support to telephone staff in a traumatic brain injury demonstration project. *Journal of Head Trauma Rehabilitation, 18,* 504–511. doi:10.1097/00001199-200311000-00004

Bell, K. R., Temkin, N. R., Esselman, P. C., Doctor, J. N., Bombardier, C. H., & Fraser, R. T. (2005). The effect of a scheduled telephone intervention on outcome after moderate to severe traumatic brain injury: A randomized trial. *Archives of Physical Medicine and Rehabilitation, 86,* 851–856.

Bodenheimer, T., Wagner, E. H., & Grumbach, K. (2002a). Improving primary care for patients with chronic illness. *Journal of the American Medical Association, 288,* 1775–1779.

Bodenheimer, T., Wagner, E. H., & Grumbach, K. (2002b). Improving primary care for patients with chronic illness: The chronic care model, Pt. 2. *Journal of the American Medical Association, 288,* 1909–1914.

Bombardier, C. H., Bell, K. R., Temkin, N. R., Fann, J. R., Hoffman, J., & Dikmen, S. (2009). The efficacy of a scheduled telephone intervention for ameliorating depressive symptoms during the first year after traumatic brain injury. *Journal of Head Trauma Rehabilitation, 24,* 230–238. doi:10.1097/HTR.0b013e3181ad65f0[pii]

Bombardier, C. H., Cunniffe, M., Wadhwani, R., Gibbons, L. E., Blake, K. D., & Kraft, G. H. (2008). The efficacy of telephone counseling for health promotion in people with multiple sclerosis: A randomized controlled trial. *Archives of Physical Medicine and Rehabilitation, 89,* 1849–1856.

Bombardier, C. H., Ehde, D. M., Gibbons, L. E., Wadhwani, R., Sullivan, M. D., & Rosenberg, D. E. (2013). Telephone-based physical activity counseling for major depression in people with multiple sclerosis. *Journal of Consulting and Clinical Psychology, 81,* 89–99.

Bruce, J. M., Bruce, A. S., Hancock, L., & Lynch, S. (2010). Self-reported memory problems in multiple sclerosis: Influence of psychiatric status and normative dissociative experiences. *Archives of Clinical Neuropsychology, 25,* 39–48.

Bruce, J. M., Hancock, L. M., & Lynch, S. G. (2010). Objective adherence monitoring in multiple sclerosis: Initial validation and association with self-report. *Multiple Sclerosis, 16,* 112–120.

Clark, N. M., & Gong, M. (2000). Management of chronic disease by practitioners and patients: Are we teaching the wrong things? *British Medical Journal, 320,* 572–575. doi:10.1136/bmj.320.7234.572

Cook, P. F., Emiliozzi, S., & McCabe, M. M. (2007). Telephone counseling to improve osteoporosis treatment adherence: An effectiveness study in community practice settings. *American Journal of Medicine Quality, 22,* 445–456.

Cook, P. F., Emiliozzi, S., Waters, C., & El Hajj, D. (2008). Effects of telephone counseling on antipsychotic adherence and emergency department utilization. *American Journal of Managed Care, 14,* 841–846.

Cook, P. F., McCabe, M. M., Emiliozzi, S., & Pointer, L. (2009). Telephone nurse counseling improves HIV medication adherence: An effectiveness study. *Journal of the Association of Nurses in AIDS Care, 20,* 316–325.

Debanne, S. M., Patterson, M. B., Dick, R., Riedel, T. M., Schnell, A., & Rowland, D. Y. (1997). Validation of a telephone cognitive assessment battery. *Journal of the American Geriatrics Society, 45,* 1352–1359.

Dellifraine, J. L., & Dansky, K. H. (2008). Home-based telehealth: A review and meta-analysis. *Journal of Telemedicine and Telecare, 14,* 62–66. doi:10.1258/jtt.2007.070709

Department of Veterans Affairs. (Producer). (2013, April 16). *VHA telehealth services*. Retrieved from http://vaww.telehealth.va.gov/index.asp

Devonshire, V., Lapierre, Y., Macdonell, R., Ramo-Tello, C., Patti, F., & Fontoura, P. (2011). The Global Adherence Project (GAP): A multicenter observational study on adherence to disease-modifying therapies in patients with relapsing-remitting multiple sclerosis. *European Journal of Neurology, 18,* 69–77.

DiIorio, C., McCarty, F., Resnicow, K., McDonnell Holstad, M., Soet, J., & Yeager, K. (2008). Using motivational interviewing to promote adherence to antiretroviral medications: A randomized controlled study. *AIDS Care, 20,* 273–283.

Fan, V. S., Au, D., Heagerty, P., Deyo, R. A., McDonell, M. B., & Fihn, S. D. (2002). Validation of case-mix measures derived from self-reports of diagnoses and health. *Journal of Clinical Epidemiology, 55,* 371–380.

Fischer, J. S., LaRocca, N. G., Miller, D. M., Ritvo, P. G., Andrews, H., & Paty, D. (1999). Recent developments in the assessment of quality of life in multiple sclerosis (MS). *Multiple Sclerosis, 5,* 251–259.

Fraser, C., Hadjimichael, O., & Vollmer, T. (2003). Predictors of adherence to glatiramer acetate therapy in individuals with self-reported progressive forms of multiple sclerosis. *Journal of Neuroscience Nursing, 35,* 163–170. doi:10.1097/01376517-200306000-00006

Goodkin, D. E. (1992). *The natural history of multiple sclerosis*. New York, NY: Springer-Verlag.

Gottberg, K., Einarsson, U., Ytterberg, C., de Pedro Cuesta, J., Fredrikson, S., & von Koch, L. (2006). Health-related quality of life in a population-based sample of people with multiple sclerosis in Stockholm County. *Multiple Sclerosis, 12,* 605–612. doi:10.1177/1352458505070660

Hadjimichael, O., & Vollmer, T. (1999). Adherence to injection therapy in multiple sclerosis: Patients survey. *Neurology, 52*(Suppl. 2), A549.

Halterman, J. S., Riekert, K., Bayer, A., Fagnano, M., Tremblay, P., & Blaakman, S. (2011). A pilot study to enhance preventive asthma care among urban adolescents with asthma. *Journal of Asthma, 48,* 523–530. doi:10.3109/02770903.2011.576741

Hatzakis, M., Jr., Haselkorn, J., Williams, R., Turner, A., & Nichol, P. (2003). Telemedicine and the delivery of health services to veterans with multiple sclerosis. *Journal of Rehabilitation Research and Development, 40,* 265–282.

Haynes, R. B., Ackloo, E., Sahota, N., McDonald, H. P., & Yao, X. (2008). Interventions for enhancing medication adherence. *Cochrane Database*

of Systematic Reviews, (2), CD000011. doi:10.1002/14651858.CD000011.pub3

Haynes, R. B., McDonald, H. P., & Garg, A. X. (2002). Helping patients follow prescribed treatment: Clinical applications. *Journal of the American Medical Association, 288,* 2880–2883.

Haynes, R. B., McKibbon, K. A., & Kanani, R. (1996). Systematic review of randomised trials of interventions to assist patients to follow prescriptions for medications. *Lancet, 348*(9024), 383–386.

Haynes, R. B., McKibbon, K., & Kanani, R. (1997). Systematic review of randomized trials of interventions to assist patients to follow prescriptions for medications. *Lancet, 348,* 383–386. doi:10.1016/S0140-6736(96)01073-2

Haynes, R. B., Montague, P., Oliver, T., McKibbon, K. A., Brouwers, M. C., & Kanani, R. (2000). Interventions for helping patients to follow prescriptions for medications. *Cochrane Database of Systematic Reviews, (2),* CD000011.

Heffner, J. L., Tran, G. Q., Johnson, C. S., Barrett, S. W., Blom, T. J., & Thompson, R. D. (2010). Combining motivational interviewing with compliance enhancement therapy (MI-CET): development and preliminary evaluation of a new, manual-guided psychosocial adjunct to alcohol-dependence pharmacotherapy. *Journal of Studies on Alcohol and Drugs, 71,* 61–70.

Holt, C. S., & Heimberg, R. G. (1990). The Reaction to Treatment Questionnaire: Measuring treatment credibility and outcome expectancies. *The Behavior Therapist, 13,* 213–214, 222.

Ingersoll, K. S., Farrell-Carnahan, L., Cohen-Filipic, J., Heckman, C. J., Ceperich, S. D., & Hettema, J. (2011). A pilot randomized clinical trial of two medication adherence and drug use interventions for HIV+ crack cocaine users. *Drug and Alcohol Dependence, 116,* 177–187.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine, 16,* 606–613.

Kurtzke, J. F. (1983). Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). *Neurology, 33,* 1444–1452. doi:10.1212/WNL.33.11.1444

Miller, W. R., & Rollnick, S. (2002). *Motivational interviewing: Preparing people for change* (2nd ed.). New York, NY: The Guilford Press.

Miller, W. R., & Rollnick, S. (2009). Ten things that motivational interviewing is not. *Behavioural and Cognitive Psychotherapy, 37,* 129–140.

Mohr, D. C., Boudewyn, A. C., Likosky, W., Levine, E., & Goodkin, D. E. (2001). Injectable medication for the treatment of multiple sclerosis: The influence of self-efficacy expectations and injection anxiety on adherence and ability to self-inject. *Annals of Behavioral Medicine, 23,* 125–132. doi:10.1207/S15324796ABM2302_7

Mohr, D. C., Cox, D., Epstein, L., & Boudewyn, A. (2002). Teaching patients to self-inject: Pilot study of a treatment for injection anxiety and phobia in multiple sclerosis patients prescribed injectable medications. *Journal of Behavior Therapy and Experimental Psychiatry, 33,* 39–47. doi:10.1016/S0005-7916(02)00011-3

Mohr, D. C., Cox, D., & Merluzzi, N. (2005). Self-injection anxiety training: A treatment for patients unable to self-inject injectable medications. *Multiple Sclerosis, 11,* 182–185. doi:10.1191/1352458505ms1146oa

Mohr, D. C., Goodkin, D. E., Likosky, W., Gatto, N., Baumann, K. A., & Rudick, R. A. (1997). Treatment of depression improves adherence to interferon beta-1b therapy for multiple sclerosis. *Archives of Neurology, 5,* 531–533. doi:10.1001/archneur.1997.00550170015009

Mohr, D. C., Goodkin, D. E., Likosky, W., Gatto, N., Neilley, L. K., & Griffin, C. (1996). Therapeutic expectations of patients with multiple sclerosis upon initiating interferon beta-1b: Relationship to adherence to treatment. *Multiple Sclerosis, 2,* 222–226.

Mohr, D. C., Hart, S. L., Julian, L., Catledge, C., Honos-Webb, L., & Vella, L. (2005). Telephone-administered psychotherapy for depression. *Archives of General Psychiatry, 62,* 1007–1014.

Noseworthy, J. H., Lucchinetti, C., Rodriguez, M., & Weinshenker, B. G. (2000). Multiple sclerosis. *New England Journal of Medicine, 343,* 938–952. doi:10.1056/NEJM200009283431307

Ogedegbe, G., Chaplin, W., Schoenthaler, A., Statman, D., Berger, D., & Richardson, T. (2008). A practice-based trial of motivational interviewing and adherence in hypertensive African Americans. *American Journal of Hypertension, 21,* 1137–1143.

Pare, G., Jaana, M., & Sicotte, C. (2007). Systematic review of home telemonitoring for chronic diseases: The evidence base. *Journal of the American Medical Informatics Association, 14,* 269–277.

Pare, G., Moqadem, K., Pineau, G., & St-Hilaire, C. (2010). Clinical effects of home telemonitoring in the context of diabetes, asthma, heart failure and hypertension: A systematic review. *Journal of Medicine Internet Res, 12,* e21.

Prochaska, J. O., & DiClemente, C. C. (1983). Stages and processes of self-change of smoking: Toward an integrative model of change. *Journal of Consulting and Clinical Psychology, 51,* 390–395. doi:10.1037/0022-006X.51.3.390

Rao, S. M., Leo, G. J., Bernardin, L., & Unverzagt, F. (1991). Cognitive dysfunction in multiple sclerosis. I. Frequency, patterns, and prediction. *Neurology, 41,* 685–691. doi:10.1212/WNL.41.5.685

Reid, S. C., Teesson, M., Sannibale, C., Matsuda, M., & Haber, P. S. (2005). The efficacy of compliance therapy in pharmacotherapy for alcohol dependence: A randomized controlled trial. *Journal of Studies on Alcohol, 66,* 833–841.

Schwartz, C. E., Vollmer, T., & Lee, H. (1999). Reliability and validity of two self-report measures of impairment and disability for MS. *Neurology, 52,* 63–70. doi:10.1212/WNL.52.1.63

Siegel, S., Turner, A., & Haselkorn, J. K. (2008). Adherence to disease-modifying therapies in multiple sclerosis: Does caregiver social support matter? *Rehabilitation Psychology, 53,* 73–79. doi:10.1037/0090-5550.53.1.73

Solomon, D. H., Iversen, M. D., Avorn, J., Gleeson, T., Brookhart, M. A., & Patrick, A. R. (2012). Osteoporosis telephonic intervention to improve medication regimen adherence: A large, pragmatic, randomized controlled trial. *Archives of Internal Medicine, 172,* 477–483.

Spitzer, R. L., Kroenke, K., & Williams, J. B. (1999). Validation and utility of a self-report version of PRIME-MD: The PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. *Journal of the American Medical Association, 282,* 1737–1744.

Steinberg, S. C., Faris, R. J., Chang, C. F., Chan, A., & Tankersley, M. A. (2010). Impact of adherence to interferons in the treatment of multiple sclerosis: A non-experimental, retrospective, cohort study. *Clinical Drug Investigation, 30,* 89–100.

Stockl, K. M., Shin, J. S., Gong, S., Harada, A. S., Solow, B. K., & Lew, H. C. (2010). Improving patient self-management of multiple sclerosis through a disease therapy management program. *Am J Manag Care, 16,* 139–144.

Stone, V. E. (2001). Strategies for optimizing adherence to highly active antiretroviral therapy: Lessons from research and clinical practice. *Clinical Infectious Diseases, 33,* 865–872. doi:10.1086/322698

Strauss, E., Sherman, E. S., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary*. New York, NY: Oxford University Press.

Tan, H., Cai, Q., Agarwal, S., Stephenson, J. J., & Kamat, S. (2011). Impact of adherence to disease-modifying therapies on clinical and economic outcomes among patients with multiple sclerosis. *Advances in Therapy, 28,* 51–61. doi:10.1007/s12325-010-0093-7

Tremlett, H. L., & Oger, J. (2003). Interrupted therapy: Stopping and switching of the beta-interferons prescribed for MS. *Neurology, 61,* 551–554. doi:10.1212/01.WNL.0000078885.05053.7D

Turner, A. P., Kivlahan, D. R., Sloan, A. P., & Haselkorn, J. K. (2007). Predicting ongoing adherence to disease modifying therapies in multiple

sclerosis: Utility of the health beliefs model. *Multiple Sclerosis, 13,* 1146–1152.

Turner, A. P., Williams, R. M., Sloan, A. P., & Haselkorn, J. K. (2009). Injection anxiety remains a long-term barrier to medication adherence in multiple sclerosis. *Rehabilitation Psychology, 54,* 116–121. doi:10.1037/a0014460

Unverzagt, F. W., Monahan, P. O., Moser, L. R., Zhao, Q., Carpenter, J. S., & Sledge, G. W., Jr. (2007). The Indiana University telephone-based assessment of neuropsychological status: A new method for large scale neuropsychological assessment. *Journal of the International Neuropsychological Society, 13,* 799–806.

Vickers, A. J. (2001). The use of percentage change from baseline as an outcome in a controlled trial is statistically inefficient: A simulation study. *BMC Medical Research Methodology, 1,* 6. doi:10.1186/1471-2288-1-6

Vollmer, T., Hadjimichael, O., Preiningerova, J., Ni, W., & Buenconsejo, J. (2002). Disability and treatment patterns of multiple sclerosis patients in United States: A comparison of veterans and non veterans. *Journal of Rehabilitation Research and Development, 39,* 163–174.

Von Korff, M., Gruman, J., Schaefer, J., Curry, S. J., & Wagner, E. H. (1997). Collaborative management of chronic illness. *Annals of Internal Medicine, 127,* 1097–1102. doi:10.7326/0003-4819-127-12-199712150-00008

Wagner, E. H. (2000). The role of patient care teams in chronic disease management. *British Medical Journal, 320,* 569–572. doi:10.1136/bmj.320.7234.569

Wagner, E. H., Austin, B. T., & Von Korff, M. (1996). Organizing care for patients with chronic illness. *Milbank Quarterly, 74,* 511–544. doi:10.2307/3350391

Wechsler, D. (1997). *Wechsler Adult Intelligence Scale*. San Antonio, TX: Harcourt Assessment.

Williams, A., Manias, E., Walker, R., & Gorelik, A. (2012). A multifactorial intervention to improve blood pressure control in co-existing diabetes and kidney disease: A feasibility randomized controlled trial. *Journal of Advanced Nursing, 68,* 2515–2525. doi:10.1111/j.1365-2648.2012.05950.x

Williams, R., Turner, A., Hatzakis, M., Bowen, J., Rodriquez, A., & Haselkorn, J. (2005). Prevalence and correlates of depression among veterans with multiple sclerosis. *Neurology, 64,* 75–80. doi:10.1212/01.WNL.0000148480.31424.2A

World Health Organization. (2003). *Adherence to long term therapies: Evidence for action*. Geneva, Switzerland: Author.

Received May 10, 2013
Revision received November 4, 2013
Accepted November 8, 2013 ■