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The Clinical Utility of the Medication Adherence Questionnaire (Maq) in an Alcohol Pharmacotherapy Trial

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Abstract

Background—Medication nonadherence is a ubiquitous problem in pharmacology treatment for alcohol use disorders. Unintentional and purposeful nonadherence as measured by the Medication Adherence Questionnaire (MAQ) has been shown to predict problems with medication adherence; however, feedback from the MAQ has never been incorporated into a behavioral intervention to facilitate medication adherence. We assessed the integration of the MAQ into Medical Management (MM), a counseling approach frequently employed in conjunction with alcohol pharmacotherapy, to determine whether prior patterns of nonadherence could be addressed effectively to promote medication adherence.

Methods—We conducted a post-hoc analysis of data from 131 alcohol dependent smokers who participated in a double blind, placebo controlled study of varenicline for the treatment of alcohol dependence. At baseline, participants completed a single administration of the MAQ, which asks 2 questions about unintentional nonadherence (e.g., forgetting) and 2 questions about purposeful nonadherence (e.g., stopping because feeling good or feeling bad). Based on these responses, participants were divided into 1 of 3 three categories. Adherent (n=60), Unintentional **or** Purposeful Nonadherent (n=50) and Unintentional and Purposeful Nonadherent (n=21). Over the course of the 16-week treatment period, patients were expected to participate in 12 Medical Management (MM) sessions; a brief psychosocial treatment. Feedback based on the MAQ responses was integrated into the MM sessions to facilitate medication and treatment adherence.

Results—The 3 adherence groups were compared on baseline characteristics, medication adherence, treatment attendance and end-of-treatment patient ratings of treatment helpfulness. Baseline demographics and characteristics were not significantly different among the three categories. We found no statistically significant differences among the three groups with respect to pill adherence, treatment attendance, and treatment satisfaction ratings.

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Conclusions—The findings suggest that the incorporation of MAQ feedback into the MM approach could be effective in mitigating risks associated with prior patterns of nonadherence suggesting that further testing of the integrated behavioral approach is warranted.

Keywords

varenicline; alcohol pharmacotherapy; medication adherence; medication adherence questionnaire; medical management

1. Introduction

Medication nonadherence is well documented as an ongoing problem in pharmacological treatment for chronic conditions. Patients receiving medications for chronic illnesses such as diabetes, asthma and heart disease have notably high rates of nonadherence ranging from 25 to 40% with similar rates reported for alcohol use disorders (AUDs) (McLellan, 2000; DiMatteo, 2004; Weiss, 2007).

Within the past decade a substantial amount of research has demonstrated the efficacy of medications in treating alcohol use disorders. The success of the treatment is often dependent upon patients taking the drug as prescribed. Individuals who are adherent to the medication report greater reductions in drinking as compared to those who are nonadherent (Volpicelli et al., 1997; Chick et al., 2000; Pettinati, 2006; Baros et al., 2007; Weiss, 2004, Zweben et al., 2008; Gueorguieva et al., 2013). These findings highlight the need to develop innovative techniques that are effective in reducing the risk of nonadherence in alcohol pharmacological treatment.

Concerns about medication nonadherence also have implications in conducting pharmacological trials for alcohol treatment. Patient nonadherence can skew the interpretation of results by introducing bias, type II error, and reducing statistical power (Haynes & Dantes, 1987; Vander, 1991; Boudes, 1998; Kastrissios & Blaschke, 1997). Also, undetected nonadherence can lead to safety issues, e.g., unanticipated side effects and overprescribing doses (Serenbruany et al. 2015; Farmer et al 1999). Again, this underscores the importance of addressing and improving medication adherence in pharmacological treatment.

1.1 Unintentional and Purposeful Nonadherence

There are multiple reasons for why a patient may not be adherent to the prescribed medication regimen. These reasons can be divided into two distinct categories: unintentional and purposeful. Unintentional nonadherence describes a behavior in which a patient may inadvertently not follow the regimen by being forgetful or careless with regard to taking proper doses. Some individuals lead very busy lives or have memory difficulties and are unable to manage a medical regimen, especially if the pills are taken several times a day. Most adherence interventions are designed to address this form of nonadherence (e.g., reminder systems, setting up a routine).

In contrast, a patient who is purposefully nonadherent may make the conscious decision not to follow the regimen for a specific reason. One of the circumstances in which the patient

would deliberately alter or stop the medication is in response to a change in the way he or she feels since starting the therapeutic drug (Morisky et al., 1986). This change could be feeling worse (i.e., side effects) or feeling better (i.e., achieving treatment goal). Additionally, a patient may perceive the drug not to be working as intended and consequently decide not to adhere to the prescribed medication regime. Overall, nonadherence is multi-faceted in nature and addressing it requires a measure that will identify specific behaviors within the broad spectrum of nonadherence.

1.2 Medication Adherence Questionnaire (MAQ)

The Medication Adherence Questionnaire (MAQ; Morisky et al., 1986), is a widely-used device to identify distinct patterns of adherence and to predict future adherence behavior (Čulig & Leppée, 2014). The questionnaire is brief (4 items), easy to administer and to score, and can be readily applied in a wide variety of medical and social service settings.

Since the original publication, the MAQ has been used to establish validity in treatment studies of patients with various diagnoses in diverse settings. In the past decade, research has used the questionnaire (or modified versions of) in studies of hypertension (Islam et al., 2008; Fernandez et al., 2008; Morisky et al., 2008; Van de Steeg et al., 2009; Krousel-Wood et al., 2009; Berni et al., 2011; Lee et al., 2013), cigarette smoking (Toll et al., 2007; Catz et al., 2011), psychiatric illness (Fialko et al., 2008; Kikkert et al., 2008; Adewuya et al., 2009), HIV (Simoni et al., 2006; Sodergard et al., 2006; Cha et al., 2008) among others.

However, the MAQ has not been employed in the context of behavioral intervention to facilitate medication adherence. More specifically, responses to the items on the MAQ have not been linked with particular intervention strategies to forestall adherence problems and at the same time, strengthen a commitment to the medication regime. Integrating the information acquired from the MAQ into a behavioral intervention would create an opportunity, early on, to identify and address patient-specific adherence concerns and provide ongoing personalized feedback to prevent or minimize the risks associated with nonadherence to the medication.

1.3 Aim/Objectives

The aim of the current paper is to examine the integration of the MAQ into a behavioral intervention to achieve high medication adherence. We describe specific methods and strategies associated with using MAQ as a component of the behavioral intervention. We evaluate this model by assessing medication adherence, treatment attendance, and treatment satisfaction ratings. It is expected that our findings will inform approaches to improving medication-assisted alcohol treatment and future pharmacotherapy trials that include a behavioral platform aimed at achieving and sustaining high medication adherence rates.

2. Materials and Methods

2.1 Advance Study

This investigation is part of the larger study, named the ADVANCE Study, which was aimed at testing the efficacy of varenicline in treating alcohol use disorders in heavy drinking

smokers (O'Malley & Zweben, 2016). Varenicline, a partial nicotinic acetylcholine agonist, has been shown to be effective for smoking cessation and considered to play a role in modifying the rewarding effects of both nicotine and alcohol (Davis & de Fiebre, 2006; Schlaepfer, Hoft, et al., 2008; Soderplam, Loft, et al., 2009). In this trial, both alcohol and smoking outcomes were investigated. All protocols were reviewed and approved by the Institutional Review Boards of Columbia University and Yale University as well as a study Data and Safety Monitoring Board.

2.1.1 Behavioral Intervention Platform—In the ADVANCE Study, medical management (MM) was utilized as the behavioral platform. MM was originally created by a cohort of experts in the alcohol treatment field for the COMBINE study (Anton et al., 2006), an NIAAA supported, multisite national study that investigated combinations of medications and behavioral interventions in 1,383 patients to improve treatment outcome for alcohol dependence. In this approach, the MM practitioner orients the individual to the study medication, addresses medication adherence issues and provides ongoing support for abstinence. The MM intervention is particularly geared toward primary care settings and does not require extensive training (Pettinati & Mattson, 2010).

2.1.1.1 Infusing the MAQ and Motivational Interviewing (MI) into Medical Management: The original MM manual (Pettinati & Mattson, 2010) was adapted for use in the ADVANCE study. It was decided that the original manual could be improved by incorporating feedback on the MAQ. At the same time, motivational interviewing (MI) strategies could be used to respond to issues or concerns raised in the MAQ. In a recent meta-analysis, MI was found to be significantly more effective than comparative approaches in enhancing medication adherence among adults receiving medication for chronic diseases (Zomahoun, et al., 2016).

Consequently, the MM manual was modified to include MI strategies and vignettes that could be used in reducing obstacles to adherence. In line with the MI approach, greater emphasis was placed on the benefits of changing drinking behavior (i.e., improved relationships, enhanced quality of life) rather than on the risks associated with not changing the drinking behavior (i.e., elevated liver enzymes, legal issues). MI techniques such as reflective listening, normalizing, promoting optimism, focusing, and evoking change talk were incorporated into the manual to attend to obstacles related to adherence and to strengthen a patient's commitment to the medication regime (Hettema, et al., 2005; Miller & Rollnick, 2013; Rollnick & Miller,1995).

To illustrate, in the initial session feedback on the MAQ was provided to help the patient develop a medication adherence plan. The plan outlines where and when to take the medication along with detailed reminders specific to the patient's lifestyle. MI strategies were used in helping to resolve situations or conditions where the patient may be ambivalent about taking the medication (see section 2.5.). These methods helped to reduce potential obstacles in facilitating and sustaining adherence to the medication regime.

2.2 Procedures

A total of 131 patients were randomized (70% men; 30% women) to one of two conditions: 2 mg varenicline or matching placebo. Patients were expected to attend 12 MM sessions over a 16-week treatment period and were followed up at various intervals up to 52 weeks following randomization. The goal of the first four visits was to orient patients to the study medication and to address medication nonadherence issues such as side effects to the study medication. Issues pertaining to drinking goals and strategies were not introduced until the fourth visit.

At the initial appointment, the MM practitioner reviews the results from the intake evaluation and addresses any medical concerns. He or she explains the diagnosis and informs the patient that while varenicline is currently prescribed as a smoking cessation drug, the rationale for use of the medication in this trial is to address alcohol use. The practitioner explains how the medication is non-addicting and different from disulfiram and other medications that are used for detoxification. He or she reviews directions for dosing, explains the blister card packaging, and discusses the potential side effects resulting from the medication. This is followed by the development of a medication adherence plan. (See section 2.5). At the end of the session, the practitioner summarizes what was covered and addresses any questions or concerns the patient may have about his or her involvement in the study. The patient then takes his or her first dose of varenicline. The initial session is approximately 60 minutes long.

For the rest of the sessions, which last from 15 to 20 minutes, patients receive 2 blister packets each containing a week's worth of medication. Patients are asked to return with blister packets at every appointment to review for missed doses. Smoking cessation is not discussed during treatment, but a referral to the state Tobacco Telephone Quitline is offered at the final session.

2.3 Eligibility Criteria

To be eligible for inclusion in the study, patients had to be between ages of 18 to 70 years old, meet DSM-IV criteria for alcohol dependence, report heavy drinking at least 2 times a week, have no more than 7 consecutive days of abstinence for the past 90 days at baseline and to be help-seeking for alcohol problems. Patients also had to be currently smoking at least 2 times per week with a urinary cotinine level > 30ng/ml. and report smoking at least 100 cigarettes over lifetime. Exclusion criteria included current, clinically significant physical abnormality based on medical history and examination; a diagnosis of a serious psychiatric illness; current suicidal ideation or lifetime history of suicidal behavior; a current diagnosis of drug dependence other than nicotine and marijuana. Marijuana abuse and/or dependence was not an exclusion criterion in order to expand the pool of potentially eligible participants and at same time, enhance the generalizability of the study findings. Patients could not be at risk of an alcohol withdrawal syndrome or have used any medication to reduce alcohol or tobacco use in the past 90 days.

2.4 Measures

Medication Adherence Questionnaire (MAQ; Morisky, et al., 1986): The MAQ is a 4-item self-report measure in which respondents are asked about past experience in taking medications. The responses are in 'yes' or 'no' format and each item is scored 1(yes) or 0 (no). The questions are as follows: Item 1: Do you ever forget to take your medication? Item 2: Are you careless at times about taking your medicine? Item 3: When you feel better, do you sometimes stop taking your medication? Item 4: Sometimes if you feel worse when you take the medicine, do you stop taking it? The MAQ yields two factors: unintentional (Items 1 & 2) and purposeful nonadherence (Items 3 & 4) (Toll et al., 2007). At the initial in-person screening visit, all potential patients completed a single administration of the MAQ.

Medication Adherence: Daily medication adherence was monitored at each appointment using a combination of pill counts based on returned blister packets and self-reported medication compliance using the timeline follow-back procedures similar to the COMBINE study (Zweben et al., 2008).

Treatment Session Attendance: Treatment session attendance was determined by the number of counseling sessions patients attended during the intervention phase of the study. As indicated earlier, patients were expected to attend 12 sessions over a 16-week treatment period.

Termination Rating Form (TRF): At the final treatment appointment, patients rated their perceptions of effectiveness and helpfulness of the different treatment components in addressing alcohol problems and adherence to medication. For the purposes of this paper, we examined the degree to which the patients rated the helpfulness (i.e., very helpful, somewhat helpful, or not at all helpful) of the counseling in learning to remember to take the study medication.

2.5 Intervention Strategies

The intervention emphasized the importance of medication adherence to clinical benefit and provided feedback from the MAQ. The information acquired from the MAQ was used as a framework from which other nonadherence issues could be addressed that are not covered specifically in the MAQ items.

In the first session, feedback provided on the MAQ was used to raise participants' awareness of potential adherence problems and convey to them the importance of adhering to the medication regime. Taking into account this information, an individualized medication adherence plan was developed for each day of the upcoming week. The goal was to anticipate problems that might come up (e.g., travel) and to plan for a variety of contingencies. In discussions with the patient, information from the MAQ was used to reinforce good adherence and to identify and forestall potential problems with nonadherence related to unintentional and purposeful nonadherence.

A general approach to feedback from the Medication Adherence Questionnaire was as follows: 1) Review patient's responses on the MAQ and why they are important; 2) Ask

them about an example related to their response; 3) Consider how this might manifest itself in the current study, and 4) How this information could be used to strengthen their adherence. Wherever possible solutions were elicited from the individual rather than the practitioner. The practitioner affirmed these answers and incorporated them into the medication adherence plans.

Specific strategies to address the three factors of adherence as identified by the MAQ: Adherent, Unintentional Nonadherence, and Purposeful Nonadherence are illustrated below.

2.5.1 Adherent strategies—If patients endorse 'no' to all items on the MAQ, the practitioners affirms and reinforces the individual's commitment by reviewing the benefits of the medication (i.e., improved health) and offers supportive statements (e.g., "*you are ready to stick with the treatment plan."*) The practitioners ask adherent patients what strategies they used in the past that led them to be able to perform so well in taking medication. This is followed-up by asking the patients to consider incorporating these methods into their approach to taking the study medications. However, because not all medications are prescribed the same way, this also requires patients to brainstorm additional strategies to remember when to take and where to keep the medication. For example, a patient may only have had good adherence experiences with taking one pill a day, yet varenicline is prescribed twice a day. Therefore, the patient is encouraged to think of effective methods to remember to take the second dosage.

2.5.2 Unintentional nonadherence strategies—If patients endorse 'yes' to either forgetfulness or carelessness (item 1 or item 2) the practitioner explores patient-specific issues related to unplanned nonadherence. MI techniques such as open-end questioning, reflective listening, and affirming are employed. For example, if patients endorse forgetfulness due to a busy travel schedule, the practitioner states the following: *"It sounds like your travel schedule can vary from time to time which can result in forgetting to take your pills." "How do you usually plan to take your medications when you travel?" or "What strategies have been successful?"* These questions allow patients to consider strategies that work within their schedules as opposed to the practitioner suggesting methods that may not be concordant with an individual's lifestyle.

This approach is applied to many situations that might have posed as an unintended hurdle to taking the medication regularly (e.g., unexpected overnight plans). The rationale is that patients are committed to the medication regime, but external circumstances or conditions serve as barriers to carrying out the commitment. Thus, once the problem is identified, a revised plan can be generated.

2.5.3 Purposeful nonadherence strategies

2.5.3.1 Purposeful Nonadherence Related to "Feeling Better": The MI technique of normalizing is used in situations in which patients desire to discontinue the medication due to feeling better (item 3). The practitioner informs patients that this feeling is not unusual in the context of treatment and attempts to evoke further change talk to encourage patients to see the medication regimen through. For example, the practitioner could pose these questions: *"How has the medication helped?" and "How can you sustain such*

improvement?" In these interactions, patients are inclined to understand that continuing the medication would maximize benefits and forestall setbacks.

2.5.3.2 Purposeful Nonadherence Related to "Feeling Worse": One of the most common reasons patients purposefully stop taking the medication is due to side effects. If baseline MAQ responses indicated this history, the prior situation was reviewed. Sometimes patients, for example, report they are reluctant to contact their provider with concerns about side effects and so stopped on their own. In response, patients are encouraged to call if they experienced troublesome problems or if they were worried about something. The practitioner reassures their patients that they will work with them to find a solution.

When addressing side effects experienced while on the study medication, the practitioner considers whether the side effects are caused by the medication or by other factors. Many of the effects of abstinence from alcohol resemble the medication side effects (e.g., sleep problems). Patients are informed that most adverse effects of the medication are transient and diminish over time. For symptoms that can easily be treated, over the counter medication is recommended (e.g., anti-nausea medication). If a patient reports more persistent side effects, the dosage is reduced. Management of adverse events is proactive and rapid as adverse events contribute to early drop out from treatment (Gueorguieva et al. 2013). For more severe side effects, patients are withdrawn from the medication and are continued with only the behavioral intervention.

For situations in which patients are at risk of stopping the medication because they feel that it is not helping them reach their drinking goal (item 4), strategies of normalizing, information sharing (i.e., feedback), eliciting concerns, and evoking, responding to, and supporting change statements made by the patients are employed. The following example illustrates information sharing and evoking change statements: "*Data show that the effects of the medication do not necessarily have immediate benefits. In many cases, it may take a while before the medication can have impact on the drinking. In the meantime, are there things that you can do to improve your situation?*" Another MI technique that could be employed is enhancing self-efficacy. The aim is to encourage the patient's belief in his or her own ability to change drinking habits and not to rely exclusively on the medication alone (i.e., "magic pill"). This helps to reduce misunderstandings and negative expectations about the medication.

3. Results

Table 1 reports on the frequency distribution of MAQ responses. Consistent with prior smoking cessation studies (Toll et al., 2007), data on the 131 patients showed that a higher percentage of patients endorsed past purposeful nonadherent behavior. Of the total sample, 6% of the patients answered "yes" to only unintentional nonadherence items (i.e. forgetfulness or carelessness) on the MAQ while 32% of the patients responded affirmatively to only purposeful nonadherence items (i.e. stopping due to feeling better or feeling worse) on the MAQ.

To conduct further analysis on the MAQ, we classified participants into 3 MAQ categories: (1) Adherent (2) Unintentional **or** Purposeful Nonadherent and (3) Unintentional and Purposeful Nonadherent. These categories were based on the varying risk levels for medication nonadherence. Consequently, individuals who answered 'no' to all 4 MAQ items were categorized as "Adherent" (N=60) and considered to be at low-risk for medication nonadherence. Individuals who answered "yes" to either of the items associated with unintentional nonadherence (i.e., forgetfulness or carelessness) (n = 8) or to either of the items associated with purposeful nonadherence (i.e., stopping due to feeling better or feeling worse) (n = 42) were considered to be at *moderate risk* for medication nonadherence and were categorized as "Unintentional **or** Purposeful Nonadherent" (N=50). Finally, individuals who answered "yes" to both purposeful and unintentional items on the MAQ were categorized as "Unintentional and Purposeful Nonadherent" (N=21) and considered to be at *high risk* for medication nonadherence.

Table 2 compares baseline characteristics of the study population across the three MAQ categories. Overall, there were no significant differences in patient characteristics across the three categories. The average age of all the patients was 43 years. The percentage of Caucasians ranged from 32% to 43%, African-Americans ranged from 52 to 54% and those who identified as 'other' ranged from 5% to 14%. The percentage of Hispanics in the entire study population ranged from 5 to 14% across the three groups. The mean number of percent heavy drinking days (5 or more standard drinks for men; 4 or more standard drinks for women) in the 90 days prior to entering the study was 67.2 in the Adherent group; 63.4 in the Unintentional **or** Purposeful Nonadherent group; and 66.0 in the Unintentional and Purposeful Nonadherent group. The mean number of cigarettes smoked per day was 11.75, 10.98 and 12.09 in the Adherent group, Unintentional **or** Purposeful Nonadherent group and Unintentional and Purposeful Nonadherent group, respectively.

Table 3 compares medication adherence and treatment attendance across the three MAQ categories. Medication adherence was computed from pill count records for the 131 patients randomized to either of the two conditions (active medication or placebo). For purposes of the current paper, we used the number and percentage of pills taken out of the prescribed dosage as the measure of medication adherence. We decided to use the prescribed dosage rather than targeted dosage (i.e., 2 mgs per day (4 tablets)) since dosage reductions were used as an adherence strategy for patients who were experiencing adverse effects.

Medication adherent was defined as taking at least 80% of the total medication prescribed. An 80% cut-off point for medication adherence has been employed in several alcohol medication trials (Zweben et al, 2008; Baros et al., 2007; Chick et al., 2000; Osterberg & Blaschke, 2005; Pettinati et al., 2000).

In general, the data show that medication adherence rates are consistent across the MAQ categories with no significant differences between the categories. In each of the three groups, over 90% of the patients were adherent to the medication regimen. The average percentage of prescribed pills that were taken was over 90% for all three groups.

Treatment attendance, as assessed by the number of treatment sessions that were utilized by the patients, was not significantly different for the three groups (Table 3). Out of the total of 12 sessions, the Adherent group attended an average of 9.93 sessions; Unintentional **or** Purposeful Nonadherent group attended an average of 9.80 sessions; the Unintentional and Purposeful Nonadherent group attended an average of 10.05 sessions.

Table 4 compares responses on the Termination Rating Form (TRF) by adherence category. In the Adherent group, 89.36% rated the MM intervention as “very helpful” or “somewhat helpful”. Similarly, 84.45% of the Unintentional **or** Purposeful group rated that intervention as “very helpful” or “somewhat helpful”. And 94.44% of the Unintentional and Purposeful Adherent group rated the intervention as “very helpful” or “somewhat helpful”. Again, there were no significant differences across the three groups.

Our results show that despite reporting different levels of risk for nonadherence at baseline, there were no significant differences between the three groups in medication adherence, treatment attendance and treatment satisfaction ratings. Individuals who were categorized as high risk for medication nonadherence performed equally well as those categorized as low risk for medication adherence.

4. Discussion

This paper presents an approach that may have benefits in facilitating adherence to an effective medication in a highly vulnerable population. The percentage of patients who were adherent in each group was exceptionally high for an alcohol pharmacotherapy trial. Depending on the definition of medication adherence, rates of medication adherence range from a low of 20% to a high of 80% (Lohit, 2016); results of the current study show a medication adherence rate of over 90%.

Almost half of the 131 patients endorsed a history of *both* types of purposeful nonadherence (48%)–i.e., stopping medication when feeling better and stopping when feeling worse—on the MAQ. These findings suggest that strategies typically used to remedy medication nonadherence such as calendars, alarms and other reminder systems would not be sufficient for this group. In fact, only 6% reported past nonadherence due exclusively to carelessness or forgetting that are the target of reminder systems. The current integrated approach offered practitioners an opportunity to address patient-specific misunderstandings of and negative expectations about the alcohol medication, uncertainties about having an AUD, pros and cons of medication taking, and other related factors (Resnicow et al., 2002).

Patients not only became more aware of the adherence problems, but also learned how to address them thereby achieving and sustaining a commitment to the medical regime. Overall, participants with the highest risk of nonadherence due to a past history of unintentional and purposeful nonadherence maintained a medication adherence rate that was only 3 percentage points less than those who did not endorse past nonadherence.

The majority of patients rated MM as somewhat or very helpful. The high ratings suggest that the methods and strategies offered in MM are relevant to experiences and concerns of

these patients which in turn may have helped to maintain positive ties between the practitioner and patient.

MM sessions were regularly attended by patients. There was no group in which treatment attendance was substantially better than the others. The MM manual recommends that practitioners have ongoing problem-solving discussions on attendance issues (e.g., missed appointments, no-shows, and tardiness). This may have helped to reduce the potential for any significant gap in treatment attendance and pill-taking between those who were at low risk and those who were at medium or high risk of nonadherence.

An important innovation in this study was the introduction of a “preparation stage” for the first four visits. Most alcohol medication trials begin addressing drinking related problems in the first session and continue throughout the entire course of treatment. Unlike most alcohol pharmacotherapy trials, drinking goals or strategies for reduction or quitting were not actively discussed until the fourth visit. Rather, in this preparatory phase we focused on evaluating and managing drug tolerability using the SAFTEE (Johnson et al., 2005), examining potential medication adherence issues and developing a medication plan. This period afforded the practitioner a better opportunity to deal with questions and concerns about the study medication and at the same time address uncertainties and ambivalences of patients about undertaking the medication regime. It was also hypothesized that participants receiving varenicline would experience less rewarding effects from alcohol (Ericson et al., 2009; Fucito et al., 2011) during this preparatory period that would ultimately make it easier for them to actively change their drinking after the first month.

MI strategies that were introduced in the preparation stage were revisited in the context of the patients' response to ongoing treatment. Real and potential obstacles to the medication plan were also examined from a MI framework. This typically required forging a partnership between practitioners and patients in reviewing potential options if a medication adherence plan was not working. The practitioner also reinforced and affirmed a patient's commitment to the medication adherence plan in each of the sessions.

Although we did not have a comparison group that received traditional MM, it appears that integrating the MAQ in the MM manual might have helped to forestall medication nonadherence. Unlike prior studies in which purposeful nonadherence measured with the MAQ predicted poorer medication adherence during treatment (Toll et al., 2007; Catz et al., 2011), participants who reported past nonadherence on the MAQ in the current study had similar high rates of medication and treatment adherence compared to patients without past adherence problems on the MAQ. The majority of individuals in each group who attended the termination session found that the counseling was somewhat or very helpful in helping them learn to remember to take their medications and the groups did not differ on this outcome.

4.1 Limitations

The primary limitation in this assessment is that there was no control group that did not receive the MAQ feedback with which to compare to those who did receive the feedback.

This limits our ability to conclusively say that MAQ feedback is effective at improving adherence rates in the patients.

Another limitation is the lack of a self-report measure that specifically questions whether receiving MAQ feedback facilitated a change in pill-taking behavior. However, we did have a measure on the helpfulness of the counseling for remembering to take the medication which did have a bearing on the utility of the study intervention.

4.2 Clinical Implications

The intervention model could be readily incorporated into primary care settings which suggest that the current model could be useful for health providers including nurses, social workers, physicians and other health care providers working in these settings. It would help to foster greater attention to adherence issues among health care professionals many of whom have few tools and strategies to address adherence problems beyond simple advice about reminders to take the particular medication. In short, the intervention model provides preliminary evidence of its applicability to real world settings and could eventually lead to improving treatment outcomes.

5. Conclusions

Pharmacotherapy has been shown to be more effective when patients adhere to the prescribed medication regime; however, medication nonadherence remains a troublesome issue in pharmacological research and treatment. Evidence has shown that it is possible to identify potential medication adherence problems early in treatment (Toll, et al. 2007). Effective tools are needed to screen patients at risk for adherence lapses and develop strategies to improve medication adherence. To address problems with nonadherence the Medication Adherence Questionnaire (MAQ) was integrated into medical management (MM), the behavioral platform for the ADVANCE study. These efforts appeared to raise both patients' and practitioners' awareness of the importance of dealing with medication adherence problems and consequently patients were helped not only to resolve medication adherence difficulties but strengthened their commitment to the medication regime as well. Future research should test the efficacy of the revised MM manual in treating AUD in a randomized control trial and to determine the mechanisms of action associated with this intervention approach.

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Highlights

- The integration of an adherence measure with a behavioral intervention in pharmacotherapy could help achieve and maintain high medication adherence rates in medication-assisted alcohol treatment and alcohol pharmacotherapy trials.
- Patients receiving the integrated approach performing equally well with respect to medication adherence and treatment attendance rates and levels of treatment satisfaction despite having different levels of nonadherence at baseline.
- Future research should consider testing the integrated approach in a randomized control trial that would include examining the mechanisms of action associated with the approach.

Table 1
Frequency Distribution of MAQ Responses (Total n=131)

MAQ Measures	Frequency	Percentage
Unintentional nonadherence items		
MAQ1: Forgetfulness	25	19.08
MAQ2: Carelessness	12	9.16
Purposeful nonadherence items		
MAQ3: Stop when feeling better	31	23.66
MAQ4: Stop when feeling worse	54	41.22
Adherent (no to all 4 items)	60	45.80
Unintentional[a] **or** purposeful[b] nonadherence	50	38.1
Only unintentional nonadherence[a]	8	6.11
Only purposeful nonadherence[b]	42	32.06
Unintentional and purposeful nonadherence[c]	21	16.03

Note: MAQ = Medication Adherence Questionnaire

[a]Yes to item 1 and/or 2 but no to items 3 and 4

[b]Yes to item 3 and/or 4 but no to items 1 and 2

[c]Yes to item 1 and/or item 2 and yes to item 3 and/or 4

Table 2

Baseline Characteristics (*n*=131)

Characteristic	Adherent (*n*=60)	Unintentional or purposeful nonadherent (*n*=50)	Unintentional and purposeful nonadherent (*n*=21)	*p-value*
Gender, *n* (%)				
Male	42 (70.0)	37 (74.0)	13 (61.9)	0.60
Female	18 (30.0)	13 (26.0)	8 (38.1)	
Age in years, mean (SD)	42.8 (11.75)	42 (12.62)	43.8 (9.43)	0.83
Race, *n* (%)				
White	25 (41.7)	16 (32.0)	9 (42.9)	
Black	31 (51.7)	27 (54.0)	11 (52.4)	0.63[+]
Other	4 (6.7)	7 (14.0)	1 (4.8)	
Hispanic, *n* (%)				
Yes	7 (11.7)	7 (14.0)	1 (4.76)	0.54
No	53 (88.3)	43 (86.0)	20 (95.24)	
Percent heavy drinking days, mean (SD)	67.2 (23.95)	63.4 (27.30)	66.0 (25.74)	0.73
Cigarettes per day, mean (SD)	11.8 (8.71)	11.0 (5.83)	12.1 (6.26)	0.80

Note: Heavy drinking day ≥4 standard drinks for women; ≥5 standard drinks for men

[+]Fisher's Exact Test

Table 3
Medication Adherence and Retention (Total *n*=124)

Outcome	Adherent (n=57)	Unintentional or purposeful nonadherent (n=47)	Unintentional and purposeful nonadherent (n=20)	*p*-value
≥80% prescribed pills taken, n (%)	56 (98.3)	43 (91.5)	19 (95.0)	0.26[+]
Percentage of prescribed pills taken, mean (SD)	94.8 (6.87)	93.5 (12.26)	91.4 (12.44)	0.43
Number of sessions attended, mean (SD)	9.9 (3.23)	9.8 (3.60)	10.1 (3.17)	0.96

[+]Fisher's Exact Test

Based on Available Data

Table 4

Termination Rating Form (Total *n*=101)

	Adherent (*n*=47)	Unintentional or purposeful nonadherent (*n*=36)	Unintentional and purposeful nonadherent (*n*=18)	*p*-value
Helpfulness, *n* (%)				
Not at all	5 (10.6)	2 (5.6)	1 (5.6)	
Somewhat	15 (31.9)	10 (27.8)	8 (44.4)	0.71[+]
Very	27 (57.5)	24 (66.7)	9 (50.0)	

Note. TRF = Termination Rating Form Question “Please rate the helpfulness of these aspects of the counseling in learning to remember to take the medication.”

[+] Fisher's Exact Test

Based on available data