Published in final edited form as:

Ment Health Subst Use. 2014 November ; 7(4): 381–390. doi:10.1080/17523281.2013.839574.

Risk factors for medication non-adherence among psychiatric patients with substance misuse histories

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Abstract

Medication non-adherence among psychiatric patients is known to be associated with poorer treatment outcomes. The study examined a comprehensive set of modifiable risk factors for non-adherence in a theoretical framework among a diverse, high risk sample of psychiatric patients with substance misuse histories (N=299). Medication side effects and excessive alcohol use were related to lower medication adherence and higher motivation for mental health treatment and recovery support were related to greater adherence. The results suggest that a multifaceted model for intervention to increase psychiatric medication adherence should be developed and tested.

Keywords

mental health; substance use; medication; adherence

Introduction

Medication non-adherence among psychiatric patients is known to be associated with poorer treatment outcomes, including lack of symptom stabilization, hospitalization, homelessness and lower quality of life (Julius, Novitsky, & Dubin, 2009; Magura, Laudet, Mahmood, Rosenblum, & Knight, 2002). A recent review indicated that non-adherence to various types of psychiatric medication ranges between 28% – 52% for major depressive disorder, 20% – 50% for bipolar disorder, 20% – 72% for schizophrenia; one study estimated it at 57% for anxiety disorders (Julius et al., 2009). Other reviews indicate non-adherence rates of 10% – 60% (median = 40%) for affective disorders, both uni-polar and bi-polar (Lingam & Scott, 2002); 50% – 75% for major depressive disorder (Trivedi, Lin, & Katon, 2007); and a mean of 26% for psychotic disorders (Nose, Barbui, & Tansella et al., 2003). A better understanding of the factors contributing to medication non-adherence can lead to more targeted strategies for increasing patient adherence. Although numerous studies have examined correlates of adherence to psychiatric medication, few have included a

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Conflict of Interest

The authors declare no conflicts of interest.

comprehensive set of risk factors (Lacro, Dunn, Dolder, Leckband, & Jeste, 2002); an exception is Zeber, Miller, Copeland, McCarthy, Zivin, Valenstein, Greenwald, and Kilbourne (2011). It is important to do so, since risk factors in different domains may interact in complex ways. For instance, substance misuse may influence other risk factors such as low commitment to treatment, but if substance misuse is not measured, low commitment to treatment cannot be understood and properly addressed.

In that regard, prior studies generally have not focused on psychiatric populations with a high risk of medication non-adherence due to substance abuse, although there are exceptions (Sowers & Golden, 1999; Weiss, 2004; Magura et al., 2002; Magura, Rosenblum, & Fong, 2011). The relative absence of such studies is surprising given the high prevalence of substance use comorbidity among psychiatric patients. The latest available data indicate there were 8.9 million adults in the U.S. with a mental illness and a substance use disorder (Substance Abuse and Mental Health Services Administration, 2012). Co-occurring mental health and substance use disorders are generally more severe, chronic, and less likely to result in positive treatment outcomes than single disorders (Kessler, 1995; Murphy, 1990; Rosenblum, Magura, Laudet, Vogel, 2011; Drake & Burnett, 1998). Low psychiatric medication adherence predicts relapse to substance use, re-hospitalization, homelessness and poorer quality of life (Julius et al., 2009; Magura et al., 2002; Offord, Lin, Mirski, & Wong, 2013). Several studies suggest an association between substance abuse and lower medication adherence among psychiatric patients (Sowers & Golden, 1999; Lacro et al., 2002; Weiss, Greenfield, Najavits, Soto, Wyner, Tohen, & Griffin, 1998), although few formal studies have been conducted to examine this association among psychiatric patients with substance misuse histories.

The current study is intended to add to our knowledge of medication non-adherence by examining a comprehensive set of risk factors in a theoretical framework for a diverse, high risk sample of psychiatric patients with substance misuse histories, which includes both patients who were and were not currently misusing substances. The study was also conducted as a cross-validation of a prior medication adherence study of psychiatric patients with substance misuse histories (author citation to be provided), with the advantage that the current study involves multiple clinics in two states with a much larger sample and thus is more likely to be generalizable.

Study Purpose and Hypotheses

The purpose of the study is to identify (modifiable factors associated with non- adherence to psychiatric medication in a diverse sample of psychiatric patients with substance misuse histories. The focus on malleable factors, rather than “fixed” background predictors such as demographics and social history, is intended to point to targets for intervention to increase adherence (e.g., Zeber et al., 2011; Magura et al., 2011). Julius et al.’s (2009) theoretical framework specifies three potentially malleable categories of factors to improve psychiatric medication adherence: medication-related risk factors, psychological risk factors, and social/ environmental risk factors. To that we add a fourth category particularly relevant to the population under study, behavioral risk factors. The study hypothesizes that higher risk in each category will be associated with lower psychiatric medication adherence.

Methods

Setting

The participants were recruited at eight mental health outpatient clinics, supported housing facilities with psychiatric care or mental health aftercare programs in New York City and Grand Rapids, Michigan in the U.S.A. This was a convenience sample of clinics/facilities.

Sample

Adult patients with a mental illness diagnosis and a lifetime history of substance misuse as identified by counselors were offered referral to the study. The study sample consists of those patients who had a current prescription for psychiatric medication ($n=299$).

Study Design and Procedures

This is a cross-sectional study of patients recruited in these clinics between January 2009 and January 2012. Patients were referred by counselors to a study research assistant for eligibility assessment. Patients were excluded from the study if they did not understand or speak English, appeared intoxicated on drugs or alcohol, or appeared unable to understand and give informed consent. The present analysis includes only those patients who had a prescription for psychiatric medication. All patients who agreed to participate in the study signed an informed consent. Participants received compensation of \$30 for a 90 minute in-person research interview. The study was approved by the Institutional Review Boards of Western Michigan University, National Development and Research Institutes, South Beach Psychiatric Center, and the Michigan Department of Community Health.

Measures

Sociodemographics and Psychiatric Diagnoses—These are the “fixed” variables: age, gender, race/ethnicity, education, public assistance, criminal record, and psychiatric diagnoses (Tables 1 and 2).

Psychiatric Medication Adherence—The Medication Adherence Rating Scale (MARS) (Thompson, Kulkarni, & Sergejew, 2000), designed for populations with serious mental illness, was modified by dropping Factor 3, consisting of two items (“medication makes me feel like a zombie; feel tired and sluggish”), to avoid overlap with the medication side-effects measure below. A further modification was to change the dichotomous response set (Yes/No) to a 4-point frequency scale (ranging from 1 “Never” to 4 “Always”) in order to better represent the range of non-adherent behaviors. The modified 8-item scale is labeled the MARS-8, e.g., items ask how often “forgot to take your medication” and “careless at times about taking your medication;” higher score = lower adherence. The original, somewhat anti-intuitive, directionality of the scoring is maintained to facilitate comparisons with other studies employing the MARS.

Medication-related Risk Factors for Non-adherence—Medication Side Effects were measured by presenting participants with a list of 16 items (e.g., sleep problems; shaking/tremors; restlessness/jitteriness) with responses that ranged from “not at all” to “very much;” higher score = more side effects.

Psychological Risk Factors for Non-adherence—Three such factors were measured; these were:

Self-Efficacy for Mental Health Recovery (Mental Health Confidence Scale) (Carpinello, Knight, & Markowitz, 2000). Sixteen items (e.g., How confident are you right now that you can: deal with symptoms related to your mental illness? face a bad day?); higher score = higher self-efficacy.

Self-Efficacy for Drug/Alcohol Avoidance (DASES) (Martin, Wilkinson, & Poulos, 1995). Seven items (e.g., imagine you are home alone, it's a dull weekend and you are bored. Would you give in to the urge to get stoned/loaded?); higher score = higher self-efficacy.

Readiness to Change Questionnaire (RCQ) (Rollnick, Heather, Gold, & Hall, 1992). This is a 12-item scale which is based on Prochaska and DiClemente's (1992) Trans-theoretical Model. Items for the RCQ are reworded to represent both drinking and drug use., e.g., "sometimes I think I should cut down on my drug use [or my drinking];" higher score = higher readiness.

Motivation for Mental Health Treatment. This is a 10-item scale adapted from the Circumstances, Motivation, Readiness, and Suitability (CMRS) scale (De Leon, Melnick, Kressel, & Jainchill, 1994)., e.g., "I feel I have to keep coming to treatment to really improve;" higher score = higher motivation.

Social/Environmental Risk Factors for Non-Adherence. Four such factors were measured; high scores on these scales indicate lower risk:

Recovery Support. This consists of six items adapted from the Social Support for Recovery scale (Laudet, Magura, Vogel, & Knight, 2000)., e.g., in the past month, how much support were your friends giving you in recovering: from mental illness? from drug/alcohol abuse? Higher score = more support.

Medical Support for Adherence. Six questions about participants' relation with his/her psychiatrist were asked., e.g., the psychiatrist answered all my questions about my psychiatric medications; at times, the psychiatrist was too rushed or busy to listen to me and answer all my questions about my psychiatric medications. Higher score = more support.

Financial Situation. How would you rate your financial situation right now? Visual analogue scale from "0 = awful" to "10 = great." Higher score = better financial situation.

Living Arrangement - Residential Treatment. This was coded as residential treatment = 1, other living arrangement = 0.

Behavioral Risk Factors for Non-Adherence—Five variables were measured, three relating to drugs/alcohol, one to current criminal justice involvement, and one to support group attendance.

Alcohol or Illicit Drug Use. Answered as "0" to "30" for the number of days used alcohol or illicit drugs in the past month.

Excessive Alcohol Use. Any “heavy drinking days” in the past month; none = 0, some = 1.

Urge to Use Drugs/Alcohol. Visual analogue scale from “0” (“no urge to use”) to “10” (“uncontrollable urge to use”) for the past week; higher score = greater urge.

Criminal Justice Involvement (Current). None= 0; probation, parole, case pending, etc. = 1, with involvement entailing higher risk.

AA/NA Attendance. Number of Alcoholics Anonymous (AA), Narcotics Anonymous (NA) or similar drug recovery-oriented meetings in the past six months. Lower score = higher risk. Although traditional 12-step self-help groups such as AA are associated with recovery from addiction, they typically do not provide support for (and in some cases discourage) medication adherence (Noordsy, Schwab, Fox, & Drake, 1996; Vogel, Knight, Laudet, & Magura, 1998).

Data Analysis

Analyses include descriptive statistics, bivariate correlations and multivariate linear regression. The level for statistical significance of independent variables was set at $p < .05$ (2-tailed). The Statistical Analysis System (SAS) software was used for all statistical analyses.

Bivariate correlations were calculated between each study variable and the MARS-8; Table 3 shows the statistically significant correlations. Then, a stepwise multiple regression analysis was done to determine the most parsimonious set of predictors of adherence (Table 4) Medication adherence was the dependent variable and sociodemographic characteristics, psychiatric diagnoses, and malleable risk factors for non-adherence were the independent variables. In the first step of the regression, all the sociodemographic and psychiatric diagnosis variables with significant bivariate correlations with adherence were entered simultaneously. In the second step, all the modifiable risk variables that had significant bivariate correlations with adherence were entered using a backwards elimination procedure. This involved starting with all risk variables, testing them individually for statistical significance, and deleting any that were not significant, until only statistically significant risk variables remained in the model. This analysis was intended to identify the risk variables that demonstrated the greatest total effects (i.e., direct plus indirect through other risk variables) on medication adherence.

Results

The majority of the sample was male and about one-half was from racial/ethnic minority groups, with an average age of 44 years. Over one-half had never married, less than one-half had graduated from high school, about one-half were supported by public assistance or disability and a large majority had a criminal record (Table 1). The most frequent psychiatric diagnoses were bipolar, major depression, and some type of schizophrenia (Table 2). The severity of the sample’s current mental disorders is indicated by the SCL-6 score (mean = 1.40, sd = 1.19), which may be relatively low because the patients were in treatment and receiving medication (Rosen, Drescher, Moos, Finney, Murphy, & Gusman, 2000).

Statistically significant correlations between study variables and the MARS-8 are shown in Table 3. Among the sociodemographics, only age was significant, the negative correlation indicating greater adherence with increasing age. Among psychiatric diagnoses, those with paranoid schizophrenia were more adherent and those with major depression or social phobia/anxiety were less adherent. The more medication side effects, the less adherence. Adherence was higher for those with high self-efficacy for either mental health recovery or drug/alcohol avoidance and higher for those with greater motivation for mental health treatment. Among the social environmental risk variables, adherence was higher for those with greater social supports for recovery, a better financial situation, and being in residential treatment. Among behavioral risk variables, presence of any substance abuse and urge to use were related to less adherence and current criminal justice involvement was related to less adherence.

The modifiable risk variables were also inter-correlated, which indicates the possibility of indirect as well as direct effects of individual variables on medication adherence. The risk variables with the largest total effects would be the most productive targets for intervention to increase medication adherence.

Step 1 of the regression analysis shows that subjects with a diagnosis of paranoid schizophrenia were more likely to be adherent and those with a diagnosis of depression were less likely to be adherent (Table 4) Age and a diagnosis of social phobia/anxiety were no longer significantly related to adherence.

The background variables that emerged as significant in Step 1 were maintained as control variables in the analysis for Step 2. The risk variables which survived are those that retained a significant effect on adherence based on both their direct and indirect effects on adherence. Medication side effects and excessive alcohol use were related to lower medication adherence and higher motivation for mental health treatment and recovery support were related to greater adherence (Table 4).

Further, a diagnosis of depression was associated with less adherence and a diagnosis of paranoid schizophrenia was associated with greater adherence. Because previous literature has not suggested any relation between diagnosis and adherence, a supplementary exploratory analysis was undertaken to try to understand this finding. This result appears to be attributable to differences in the use of depot injection in these two diagnostic groups. Among those diagnosed with paranoid schizophrenia, 52% reported receiving depot injection for at least one medication and among those with major depression, 8% reported it. Partial correlations computed between diagnosis and adherence controlling for depot injection were not statistically significant, indicating that the differential use of depot injection explains the relationships observed between these two diagnoses and medication adherence.

Discussion

The study was able to examine a relatively wide variety of risks for medication non-adherence among psychiatric patients with substance misuse histories, thus enabling the

most productive targets for intervention to be identified. Multivariate analysis assisted in reducing a large number of hypothesized risk factors to a manageable set of factors that were most strongly directly and indirectly related to medication non-adherence in a diagnostically heterogeneous sample of patients.

Because use of depot injection has only recently become common, previous medication adherence studies were not influenced by this practice; but it must be taken into account now (Lin, Wong, Offord, & Mirski, 2013). The current study found that apparent differences in adherence between patients with different diagnoses, particularly paranoid schizophrenia and major depression, could be accounted for by differential prescription of depot (long-acting) formulations of medication.

With respect to the modifiable risk factors, side effects of psychiatric medication were found to be important, which is a frequent finding in the literature. (Hoge, Appelbaum, Lawlor, Beck, Litman, Greer, Gutheil, & Kaplan, 1990; Perkins, Gu, Weiden, McEvoy, Hamer, & Lieberman, 2008; Ruscher, de Wit, & Mazmanian, 1997; Weiss et al., 1998). Patients should be encouraged to be proactive about describing medication side effects, not only with their psychiatrists but other medical personnel such as nurse practitioners and physician's assistants. Clearly there are many medication adjustments that can be helpful. But since it is sometimes impossible to eliminate all side effects, even with proper monitoring, rotation and titration of medications, patient education appears to be the key to ensuring adherence even in the presence of side effects. Patients should be guided in a realistic appraisal of the benefits of adherence versus the consequences of inconsistent medication or discontinuance. This can best be achieved in the context of adequate social support for mental health recovery (see below).

Current excessive alcohol use was associated with poorer adherence, which is consistent with previous literature that has usually found substance misuse of various types to be related to adherence (Lacro et al., 2002). The substance misuse variables in the study were highly inter-correlated. Drug use may well be a contributing factor in our sample, but apparently only insofar as drug use is associated with excessive alcohol use. Patients who are misusing substances clearly are in need of specialized treatment or intervention.

Greater social support for recovery was associated with higher adherence. Participation in self-help groups is often a good solution; however, self-help for alcoholism such as Alcoholics Anonymous is not suitable for discussing medication issues (Noordsy et al., 1996; Vogel et al., 1998), and mental health recovery groups such as Emotional Health Anonymous (2007) do not deal with substance misuse problems. For patients with both psychiatric illness and current substance misuse, a practical approach to increasing social support is to encourage participation in "dual focus" self-help groups that provide support for recovery from both problems. Recent research has shown that such dual focus group participation can reduce both substance misuse and increase adherence to psychiatric medication (Magura et al., 2002; Magura, Rosenblum, Villano, Vogel, Fong, & Betzler, 2008a; Magura, Villano, Rosenblum, Vogel, & Betzler, 2008b). Thus, participation in such groups should be encouraged by mental health and addiction treatment clinicians who work with patients with co-occurring disorders.

Motivation for mental health treatment was associated with greater adherence; such attitudes can be potentially reinforced. Application of basic motivational interviewing techniques when a patient first enters treatment in a given clinic or with a given practitioner could be useful in increasing treatment motivation (Miller & Rollnick, 2012). The objective is to help patients clarify in their own minds why they are in treatment, the anticipated benefits of treatment, and the consequences of not receiving adequate treatment, based on their personal experiences as well as what they have observed about others.

The study was conducted partly as a cross-validation of a less extensive study of medication adherence among psychiatric patients with substance misuse histories previously conducted by several of the authors (Magura et al., 2011). The results are generally consistent with that previous research, in particular the finding of the importance of informal social supports in encouraging adherence.

Study Limitations

The data are cross-sectional and therefore causal inferences must be made with caution. The study was conducted in a convenience sample of clinics; thus generalizability to all patients with both severe mental illness and substance misuse histories may be limited.

Directions for Future Research

The study suggests that a multifaceted model for intervention to increase psychiatric medication adherence should be developed and tested. Specifically, the model would include brief motivational interviewing at treatment entry to reinforce motivation for mental health treatment; explicit attention to potential medication side effects at every patient contact; and provision for dual-focus self-help group participation. The latter may require a clinic to take the initiative in helping patients establish such a group, since knowledge of this option is still limited and since patients may not be able to negotiate the logistics of setting up a group on their own. Once established, however, dual focus groups such as Double Trouble in Recovery have been shown to operate successfully according to standard 12-step principles (Magura et al., 2008a).

Acknowledgments

Funding

The study was funded by the National Institute on Drug Abuse (U.S.A.), grant no. R01 DA023119.

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Table 1Socio-demographic Variables ($n=299$)

Age in Years (mean, sd)	44, 11
Male	65%
White	46%
Black	33%
Hispanic	16%
Never Married	63%
Completed High School/GED	43%
Public Assistance/Disability	54%
Arrested as Adult	80%

Table 2Psychiatric Diagnoses ($n=299$)

Bipolar	51%
Major Depression	45%
Paranoid Schizophrenia	10%
Schizophrenia - Other	19%
Social Phobia/Anxiety	16%
Schizo-Affective	14%
Other Mood	9%
Psychotic-NOS	3%
Other	20%

Note: Total percent exceeds 100% because of multiple diagnoses.

Table 3

Significant Predictors of Medication (non)Adherence (MARS-8)

	Mean or <u>Proportion</u>	SD	Bivariate correlation <u>with MARS-8</u> *
MARS-8	1.47	0.39	
<i>Sociodemographics</i>			
Age	44	11	-.17**
<i>Psychiatric Diagnoses</i>			
Paranoid Schizophrenia	.10		-.16**
Major Depression	.45		.24***
Social Phobia/Anxiety	.16		.15**
<i>Medication-Related Risk</i>			
Medication Side Effects	3.3	3.1	.14*
<i>Psychological Risk</i>			
Self-Efficacy-Mental Health Recovery	3.0	0.6	-.21***
Self-Efficacy-Drug/Alcohol Avoidance	7.2	2.1	-.22***
Motivation-Mental Health Treatment	4.3	0.5	-.12*
<i>Social/Environmental Risk</i>			
Recovery Support	2.1	0.6	-.21***
Financial Situation	3.4	2.6	-.15*
Residential Treatment	.43		-.17**
<i>Behavioral Risk</i>			
Illicit Drug Use	2.1	6.4	.13*
Excessive Alcohol Use	.17		.22***
Alcohol or Illicit Drug Use	3.8	8.4	.19***
Urge to Use Drugs/Alcohol	2.9	3.3	.22***
Criminal Justice Involvement	.16		.14*

*
p<.05**
p<.01***
p<.001

Table 4**Stepwise Multivariate Linear Regression of Predictors on MARS-8**

	B	SE
<i>Step 1: Enter significant socio-demographic and psychiatric diagnosis variables</i>		
Age	-.0035*	.0017
Paranoid Schizophrenia	-.14*	.06
Major Depression	.13***	.04
Social Phobia/Anxiety	.058	.052
<i>Step 2: Add significant risk variables and conduct stepwise backwards elimination on the risk variables</i>		
Age	-.0023	.0017
Paranoid Schizophrenia	-.169**	.058
Major Depression	.102**	.038
Social Phobia/Anxiety	.038	.051
Medication Side Effects	.014*	.0057
Motivation-Mental Health Treatment	-.123**	.038
Recovery Support	-.082**	.032
Excessive Alcohol Use	.134**	.047

*
p<.05**
p<.01***
p<.001