The effects of antidepressant medication adherence as well as psychosocial and clinical factors on depression outcome among older adults

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SUMMARY

Objective To examine the contribution of medication adherence to 12-month depression scores in the context of other psychosocial and clinical predictors of depression in a sample of older adults treated for depression.

Methods Secondary analysis of a prospective cohort study involving 241 older patients undergoing depression treatment using a standardized algorithm. Depression was measured at baseline and 12-months post-baseline. Baseline predictor variables included antidepressant adherence, barriers to antidepressant adherence, four domains of social support, basic and instrumental activities of daily living (BADLs and IADLs), and clinical factors including past history of depression and medical comorbidities.

Results Nearly 28% of patients reported being nonadherent with their antidepressant medication. In bivariate analyses, greater antidepressant medication nonadherence, more medication barriers, poorer subjective social support, less non-family interaction, greater BADL and IADL limitations, poor self-rated health, higher baseline depression scores, and not having diabetes were related to higher 12-month depression scores. In multivariable analyses, greater medication nonadherence, not having diabetes, poorer subjective social support, greater BADL limitations, and higher baseline depression scores were related to higher 12-month depression scores.

Conclusion Interventions should be directed toward improving antidepressant adherence and modifiable psychosocial variables. Copyright © 2007 John Wiley & Sons, Ltd.

INTRODUCTION

Although research has identified psychosocial and clinical predictors of greater depression severity in the elderly (Paykel et al., 1996; Hays et al., 1997; Bosworth et al., 2002a; Blazer, 2003), few studies have examined the role of medication adherence (Berman et al., 1997). Among the few studies that have examined depression medication adherence, 20% to 80% of patients who are prescribed antidepressant medications fail to adhere to the prescription at one month (Katon, 1992; Maddox et al., 1994; Lin et al., 1995; Hotopf et al., 1997; Pevler et al., 1999; Demyttenaere and Haddad, 2000; Lingam and Scott, 2002). This wide range of adherence rates includes data from various types of studies. For instance, adherence is generally higher in clinical trials than community care (Blackwell, 1992). Naturalistic clinical studies, which aim to be ecologically valid with respect to clinical practice, may bridge some of the differences between

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standardized, single-agent treatment trials and community-based outcomes. Although there is less research on medication adherence in naturalistic studies, a better understanding of the role of medication adherence in a flexible, yet well-examined treatment context may yield findings to reduce adverse treatment outcomes in community samples.

The current study examines the role of medication adherence on depression severity while considering the underlying influence of both psychosocial and clinical factors on depression severity. To identify important constructs that are potentially important in explaining the effects of depression medication adherence on depression scores, we used a framework that identifies important patient characteristics (e.g., physical disabilities, comorbidities), as well as social and cultural environment factors (e.g., social support), and medical environment (e.g., barriers to care) (Bosworth, 2006).

Research indicates that several psychosocial characteristics, such as physical function, social support, and stress, may affect depression severity (Kaplan et al., 1987; Hays et al., 1997; Bosworth et al., 2003; Niiranen et al., 2006). Depression severity is associated with clinical characteristics as well, such as comorbid illness, history of depression, and prior use of ECT. Because the underlying cause of depression severity may be multifactorial and complex, an increased understanding of how these factors contribute to depression severity will enhance our ability to reduce the all-too-frequent chronic course of this condition.

METHODS

This secondary data analysis of a prospective cohort study included participants from the National Institute of Mental Health Clinical Research Center (MHCRC) for the Study of Depression in Later Life, located at Duke University. All patients met DSM-IV criteria for unipolar major depression at enrollment. The MHCRC operates in a guideline-based treatment milieu, using an algorithm established by the Duke Affective Disorders Program rather than a standardized treatment protocol (Steffens et al., 2002).

Inpatients and outpatients of the Duke University Psychiatric Service presenting with clinically significant depressive symptoms or previous diagnosis of a mood disorder were screened with the Center for Epidemiologic Studies-Depression Scale (CES-D) (Radloff, 1977). Eligibility was limited to patients aged 60 years or older. See Bosworth et al. (2002b) for more details regarding study exclusion criteria.

Procedure

At baseline, the purpose of the MHCRC and its procedures were explained, and those who provided written informed consent were enrolled. A trained interviewer administered the Duke Depression Evaluation Schedule (DDES) which includes sections of the NIMH Diagnostic Interview Schedule (DIS) (Robins et al., 1981) depression tool as well as assessment of physical health, stress, and social support. DSM-IV major depression diagnoses were established by MHCRC geriatric psychiatrists via clinical interviews and were confirmed by responses on the DIS. Patients also received a battery of standardized clinical assessments, including the Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). Patients were administered the DDES annually and a study psychiatrist administered the MADRS at every clinical visit, at least quarterly. Some time during the study, a medication adherence measure was administered to 241 of the 403 enrolled patients. The 241 participants in the current study did not differ from those not included in terms of demographic or clinical factors. Thus, for the current analyses, the baseline was defined as the date of adherence assessment. The average length of time participants had been followed prior to baseline was 758 days (~2 years; SD = 794 days).

Dependent measure

The MADRS is a ten-item, clinician-based interview that assesses depression severity. It is designed to be sensitive to change resulting from treatment (Montgomery and Asberg, 1979; Davidson et al., 1986) and has adequate psychometric qualities (Maier and Philipp, 1985; Maier et al., 1988). The possible range is 0–60 with higher scores representing greater depression severity (Snaith et al., 1986; Bosworth et al., 2002). The measure has been found to have high inter-rater reliability ranging from 0.89 to 0.97 (Maier and Philipp, 1985), and intraclass coefficients from 0.66 to 0.82 (Maier et al., 1988). The MADRS was administered at baseline and approximately 12 months later ($r = 0.04, p = 0.53$).

Independent measures

Demographic measures. Patients responded to a financial resources question asking: (1) how well the amount of money they have takes care of their needs; and (2) whether they have enough financial resources to meet emergencies. Patients also reported...
their race, employment status, age, amount of education, and marital status.

**Psychosocial measures.** The DDES includes four social support subscales, derived from the 35-item Duke Social Support Index (DSSI) (George et al., 1989; Landerman et al., 1989). These include: (1) social network size (four items: number of family members, co-workers, and friends, household size); (2) social interaction (four items: family proximity, in-person and telephone contact with friends and family, group affiliations); (3) availability of instrumental aid (13 items: for sick care, errands, chores, finances, transportation, etc.); and (4) subjective social support (ten items: feeling useful, listened to, satisfied with relationships, etc.: $\alpha = 0.79$) Social support variables were utilized in their interval-level format.

**BADL.** Basic activities of daily living (BADL) were assessed by seven items derived from epidemiological studies (Katz et al., 1970; Nagi, 1976; Branch et al., 1984). Instrumental activities of daily living (IADL) were assessed by nine items (Rosow and Breslau, 1966; Fillenbaum, 1985). Composite measures were constructed separately for BADL and IADL by summing the scores for all items within their respective domain (Alexopoulos et al., 1996). Higher numbers represented more disability. Frequency and severity of stressful life events (positive, negative, and total level of stress) during the year preceding the interview was assessed by a 19-item life-events checklist (George et al., 1989). Self-rated health was assessed using a four-level question. However, given the distribution of responses, poor or fair health were combined, and good and excellent health were combined.

**Clinical variables.** Clinical variables were obtained from both patient self-report on the DDES and from medical records recorded by patients’ psychiatrists. These variables included baseline MADRS, history of prior electroconvulsive therapy, presence of self-reported diabetes, heart disease, and hypertension, age at first depressive episode, and number of depressive episodes prior to study entry. To be consistent with prior work and because age at first episode and prior number of depressive episodes (0–50) were skewed, we dichotomized these variables ($\geq 6 \text{ vs } \leq 59$ years, $\geq 4 \text{ vs } \leq 3$ prior episodes) (Bosworth et al., 2002).

**Adherence.** Self-rated adherence was assessed using the Morisky Self-reported Medication-Taking Scale (Morisky et al., 1986), which is composed of four yes/no items. The possible range is 0–4, with 0 representing adherence and 4 representing nonadherence on all four items. Individuals were categorized as adherent or non-adherent based on whether they reported that they were non-adherent on any of the four items. The theory underlying this measure is that depression medication nonadherence could occur in any or all of several ways: forgetting, carelessness, stopping the drug when feeling better, or starting the drug when feeling worse (Lowry et al., 2005). We chose the Morisky scale because the measure had been previously shown to have reasonable operating characteristics; in a prior study, the scale had sensitivity (72%) and specificity (74%) for $\geq 80\%$ adherence to tricyclic antidepressants based on the use of a medication event monitoring system (George et al., 2000).

Antidepressant treatment barriers were assessed with a nine-item scale (e.g. ‘There is no one to help me keep track of when to take pills’). Response options included definitely false, probably false, probably true, and definitely true (coded 0 to 3) (Voils et al., 2005). We took the average of the nine items so the score ranged from 0–3, with higher scores representing more medication barriers. Adherence and treatment barriers were only moderately associated, $r = 0.30$, $p = 0.001$. Consistent with previous research (Voils et al., 2005), neither the adherence measure nor the barriers measure specified a time period over which participants were supposed to report their behavior; therefore, the questionnaires assessed global, rather than specific, adherence and barriers.

**ANALYSES**

Bivariable associations of 12-month MADRS scores with medication adherence, demographic, clinical, and psychosocial factors were examined using Pearson correlations for continuous variables and Kendall Tau Correlations for categorical data. Then, using linear regression models, we examined the multivariable relationship between MADRS scores and these factors. To obtain the most parsimonious model, backward selection was used in which variables in bivariable models that were significant at $p < 0.20$ were removed one at a time based on the size of the $p$-value. As a variable was removed, the model was refit with the remaining variables before removing another variable. The final model is presented.
RESULTS

Demographics

The sample demographic variables and were as follows: age (mean = 69, SD = 6.7), gender (60% female), race (86% white), years of education (30% college credit), and marital status (62% married). Nearly 28% reported being nonadherent to their medication. Clinical variables included percent that experienced a previous depression episode (75%) and a history of electro-convulsive therapy (ECT) (7%). Mean MADRS scores were 14.1 (SD = 10.2) at baseline and 8.0 (SD = 7.5) at 12-months.

Bivariate results

Greater 12-month depression scores were positively correlated with poor medication adherence and more treatment barriers (Table 1). Also, greater 12-month depression was associated with poorer subjective social support, less non-family social interactions, more limitations to BADLs and IADLs, poor self-rated health, not having diabetes, and greater baseline depression.

Multivariable results

After controlling for other variables, baseline medication non-adherence remained a significant predictor of 12-month depression (Table 2). Also, poorer subjective social support, greater deficit in BADLs, not having diabetes, and greater baseline depression remained significant predictors of 12-month depression scores.

DISCUSSION

The purpose of this study was to evaluate, in a large sample of depressed older adults, the effects of antidepressant medication adherence on 12-month depression scores after considering specific psychosocial and clinical factors. The results indicated that both antidepressant medication nonadherence and perceived barriers to taking medication were significantly directly related to 12-month depression scores. In addition, psychosocial factors including inadequate subjective social support and BADL limitations remained predictive of 12-month depression scores.

The finding that poor antidepressant adherence is related to greater depression severity is important because the economic burden of depression is high, estimated to be $81.5 billion annually (Greenberg et al., 2003). Possible explanations not examined in the current study for the effect of nonadherence on depression severity include patient attitudes towards psychotropic medications, knowledge about expected benefits and risks of treatment with antidepressants (Whooley and Simon, 2000), and the fact that

Table 1. Correlations of demographic and clinical factors with 12-month depression scores (n = 241)

<table>
<thead>
<tr>
<th>Factors</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>More treatment barriers</td>
<td>0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>Poor depression medication adherence</td>
<td>0.16</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.01</td>
<td>0.95</td>
</tr>
<tr>
<td>Age</td>
<td>-0.03</td>
<td>0.63</td>
</tr>
<tr>
<td>Minority race</td>
<td>0.01</td>
<td>0.87</td>
</tr>
<tr>
<td>Employed</td>
<td>0.04</td>
<td>0.72</td>
</tr>
<tr>
<td>≤12 years education</td>
<td>0.04</td>
<td>0.55</td>
</tr>
<tr>
<td>Married</td>
<td>0.06</td>
<td>0.58</td>
</tr>
<tr>
<td>Enough money for emergencies</td>
<td>0.02</td>
<td>0.77</td>
</tr>
<tr>
<td>Enough money to meet needs</td>
<td>0.10</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Psychosocial factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative stressors</td>
<td>0.06</td>
<td>0.34</td>
</tr>
<tr>
<td>Positive stressors</td>
<td>0.04</td>
<td>0.51</td>
</tr>
<tr>
<td>Total stress</td>
<td>-0.08</td>
<td>0.24</td>
</tr>
<tr>
<td>Social network</td>
<td>-0.09</td>
<td>0.15</td>
</tr>
<tr>
<td>Instrumental social support</td>
<td>-0.07</td>
<td>0.27</td>
</tr>
<tr>
<td>Subjective social support</td>
<td>-0.25</td>
<td>0.0001</td>
</tr>
<tr>
<td>Non-family social interaction</td>
<td>-0.15</td>
<td>0.02</td>
</tr>
<tr>
<td>IADL limitation</td>
<td>0.23</td>
<td>0.0004</td>
</tr>
<tr>
<td>BADL limitation</td>
<td>0.22</td>
<td>0.002</td>
</tr>
<tr>
<td>Poor/fair self-rated health</td>
<td>0.15</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Clinical factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline depression</td>
<td>0.26</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ever had ECT</td>
<td>-0.15</td>
<td>0.13</td>
</tr>
<tr>
<td>Ever hospitalized in a psychiatric hospital</td>
<td>-0.10</td>
<td>0.32</td>
</tr>
<tr>
<td>≥60 years of age at first depression episode</td>
<td>0.02</td>
<td>0.77</td>
</tr>
<tr>
<td>≥4 prior episodes of depression</td>
<td>0.07</td>
<td>0.35</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-0.19</td>
<td>0.004</td>
</tr>
<tr>
<td>Heart disease</td>
<td>-0.08</td>
<td>0.25</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.02</td>
<td>0.79</td>
</tr>
</tbody>
</table>

Pearson correlations for continuous variables and Kendall Tau correlations for categorical variables.
BADL = basic activities of daily living; ECT = electroconvulsive treatment; IADL = instrumental activities of daily living.

Table 2. Multivariable model of factors predictive of greater 12-month depression scores

<table>
<thead>
<tr>
<th>Factors</th>
<th>Standardized beta</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication nonadherence</td>
<td>0.12</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-0.16</td>
<td>0.009</td>
</tr>
<tr>
<td>Subjective social support</td>
<td>-0.13</td>
<td>0.05</td>
</tr>
<tr>
<td>BADL limitation</td>
<td>0.21</td>
<td>0.0007</td>
</tr>
<tr>
<td>Baseline depression</td>
<td>0.16</td>
<td>0.01</td>
</tr>
</tbody>
</table>

\( F (5, 217) = 9.1, p = 0.0001, R\)-square = 0.17.

BADL = basic activities of daily living.
depression includes problems with memory and concentration (Bucci et al., 2003).

This study is not without limitations. Self-report measures tend to overestimate medication adherence. However, despite the potential bias against reporting poor adherence, nonadherence nonetheless predicted 12-month depression scores. In addition, we did not assess side effects of medication, which have been related to poor medication adherence (Frank, 1997). Adherence typically decreases with time (Demyttenaere, 1997), and while we were not able to control for the length of time of antidepressant medication use, number of prior depressive episodes was not related to depression scores. Finally, the finding that not having diabetes was associated with greater depression scores must be interpreted with caution given the small number of diabetics (14%) in the study.

Our findings make an important contribution to the literature because few studies have examined the relationship between antidepressant adherence along with other key psychosocial and clinical factors related to depression severity in elderly adults (Maidment et al., 2002). The current study was conducted in a naturalistic clinical setting, which increases the generalizability of our findings to other samples of elderly adults seeking depression treatment.

Increasing concerns about cost containment in health care delivery have carried patient adherence issues to the forefront because it is believed that certain cost control mechanisms are unlikely to succeed unless rates of nonadherence are substantially reduced (Ulmer, 1987). The treatment of depression accounts for a substantial portion of medical care expenditures (Tarlov et al., 1989), and self-care is a central element in the overall management of depression. This and the fact that depression is the second only to hypertension as the most common chronic condition seen in general medical practice (Whooley and Simon, 2000) calls for ways to incorporate psychosocial factors in the treatment of depression as well as ways to enhance treatment adherence.

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REFERENCES


