Perceived Stigma and Patient-Rated Severity of Illness as Predictors of Antidepressant Drug Adherence

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Objective: **Major depression is undertreated despite the availability of effective treatments. Psychological barriers to treatment, such as perceived stigma and minimization of the need for care, may be important obstacles to adherence to the pharmacologic treatment of major depression. The authors examined the impact of barriers that were present at the initiation of antidepressant drug therapy on medication adherence in a mixed-age sample of outpatients with major depression.** ***Methods:*** **A two-stage sampling design was used to identify adults with a diagnosis of major depressive disorder, as determined by the Structured Clinical Interview for Diagnosis, who sought mental health treatment at outpatient clinics. Additional instruments were administered to 134 newly admitted adults who had been taking a prescribed antidepressant medication for at least a week to assess perceived stigma, self-rated severity of illness, and views about treatment. The patients were reinterviewed three months later and were classified as adherent or nonadherent on the basis of self-reported estimates of the number and frequency of missed doses.** ***Results:*** **Medication adherence was associated with lower perceived stigma, higher self-rated severity of illness, age over 60 years, and absence of personality pathology. No other characteristics of treatment or illness were significantly related to medication adherence.** ***Conclusions:*** **Perceived stigma associated with mental illness and individuals' views about the illness play an important role in adherence to treatment for depression. Clinicians' attention to psychological barriers early in treatment may improve medication adherence and ultimately affect the course of illness. (*Psychiatric Services* 52: 1615–1620, 2001)**

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Despite the availability of effective pharmacologic and psychosocial treatments, major depression is often undertreated because of underrecognition, underprescription, and poor follow-through with care (1–4). An important obstacle to effective pharmacotherapy for depression is the high rate of nonadherence to prescribed medication regimens. Although estimates of nonadherence vary widely depending on the population, the method of reporting noncompliance, and the medication being monitored (5), nonadherence rates ranging from 29 percent to 46 percent have been reported in samples of psychiatric patients.

Greater attention to adherence over the past two decades has resulted in both recognition of the significant clinical and economic costs of nonadherence and a shift to a biopsychosocial model in which the patient-physician relationship is conceptualized as a partnership (4). In this model, the nature of the partnership in particular and of the patient's psychological and social contexts in general may influence the course of care. A better understanding of the psychological and social barriers to adherence, such as perceived stigma, may enable us to identify important targets for clinical intervention to improve adherence and ultimately reduce undertreatment.

Early investigations of the impact of patient characteristics on adher-

ence showed that patients' perspectives were an important factor in predicting health-related behaviors. The health belief model linked individuals' beliefs about illness and treatment with health actions such as the use of preventive health measures, sick-role behaviors—that is, actions to restore health or prevent further decline—and service use. A review of studies based on the health belief model found perceived severity of illness to be an important factor in predicting sick-role behaviors (6).

A limitation of the health belief model is its relative lack of attention to the social context of the health actions. Perceived social barriers may be particularly important in predicting treatment behaviors, such as taking an antidepressant medication, to remedy an illness whose victims may experience social stigma. Individuals who have mental illness report being shunned and avoided (7), and the Surgeon General has emphasized the need to diminish stigma as a barrier (8).

Extending the scope of patients' perspectives beyond health beliefs to investigate other aspects of the patient's psychological and social contexts, Weiden (9) found that perceived stigma and denial of illness were associated with noncompliance in a sample of individuals with schizophrenia. Previously, we found that depressed older adults who felt highly stigmatized by their illness were more likely to discontinue mental health treatment (10). In this study, we investigated patients' perceived stigma and beliefs about both their illness and treatment as predictors of adherence to antidepressant drug therapy. We expected that individuals who had lower perceived stigma and higher self-rated severity of illness would be more adherent than individuals who minimized the severity of their illness and reported higher stigma.

Methods

Sample

We used a two-stage sampling procedure to identify persons with major depressive disorder who were seeking treatment from six outpatient clinics in Westchester County, New York, from October 1995 to December 1997. One academic outpatient department with a geriatric service was included. Newly admitted patients were approached, and written informed consent was obtained for a brief depression screening (2). For individuals who screened positive for depression and consented to further interviews, the Structured Clinical Interview for Diagnosis (SCID) (11) was administered to confirm the diagnosis of major depressive disorder. Exclusion criteria included cognitive impairment, defined as a score below 24 on the Mini Mental State Examination (MMSE) (12); alcohol or substance abuse in the previous month; and presence of another axis I disorder. Institutional review board approval was obtained for the study.

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Measures

Symptoms, functioning, previous use of services, and potential psychological barriers to care were assessed at admission. Depression severity was rated with use of the Structured Interview Guide for the 17-item Hamilton Depression Rating Scale (Ham-D) (13, 14), and illness characteristics were determined during the SCID interview. The Global Assessment of Functioning (GAF) (15) was used to assess overall functioning. To record concurrent medical illness, we used the Chronic Disease Score (16), which assigns points to classes of medications prescribed for significant medical illnesses. Although personality disorders were not assessed, the 47-item version of the Inventory of Interpersonal Problems was used to screen for personality pathology (17). Service use before the index admission and during the follow-up period was recorded with use of the Cornell Services Index (CSI) (18), a patient-report measure. Age was used as a dichotomous variable; older subjects were defined as those over the age of 60.

Psychological barriers to treatment. Psychological barriers to treatment that were assessed in the study were minimization of the need for treatment and high perceived stigma. Need for treatment was assessed with use of the Patient Experience of Outpatient Treatment questionnaire (PEOT) (19), the 17-item outpatient version of the Patient Experience of Hospitalization questionnaire (20). The PEOT asks patients to endorse statements about the severity of their illness and the impact and importance of treatment. Three subscales demonstrated adequate reliability in the study sample: self-rated severity of illness (Cronbach's alpha=.67), degree of worry about the impact of the illness (Cronbach's alpha=.74), and endorsement of a need for treatment (Cronbach's alpha=.76).

Perceived stigma associated with mental illness and mental health treatment was measured with a modified version of Link's scale of perceived stigma (21). The 20-item scale used in this study includes 12 items that assess beliefs about the devaluation and discrimination directed toward persons who have mental illness and eight items that measure withdrawal as a coping orientation designed to avoid rejection. Each statement is rated on a 4-point scale ranging from 1, strongly agree, to 4, strongly disagree. By asking the respondent to report on the perspective of "most people," the scale enables stigmatizing beliefs that are not socially acceptable to be endorsed. The scale demonstrated good reliability in our sample (Cronbach's alpha=.94).

Medication adherence. Adherence was assessed through a brief interview designed to identify the pat-

tern of medication use. The patients were asked in a nonjudgmental manner the frequency and pattern of missed doses and whether they had stopped taking their medication completely. On the basis of their responses, adherence was rated on a Likert scale ranging from 0, indicating that the patient was not taking the medication, to 6, indicating full compliance with only an occasional missed dose.

Patients' self-reports of adherence have been shown to have high concordance with pill counts (5,22). However, self-reports may be unreliable as a result of deception, misunderstanding of the regimen, and poor recall. To address this issue, a validity study was conducted to determine the concordance between chart records of steady-state plasma drug concentrations and patients' reports of compliance in a subsample of 14 patients (10 percent) whose charts had data on plasma drug concentrations. It was assumed that nortriptyline was prescribed at dosages necessary to achieve the standard therapeutic plasma concentrations of 50 to 150 ng/mL and that concentrations below that range indicated noncompliance. Eleven of the 14 patients (80 percent) were within the target range, suggesting that self-reports of patients in the sample were in most cases a good approximation of patients' medication-taking behavior.

Table 1

Bivariate comparison of sociodemographic, clinical, and treatment characteristics of outpatients with major depressive disorder who were adherent and nonadherent to medication regimens

Characteristic	Total sample (N=134)		Adherent (N=96)		Nonadherent (N=38)	
	N or mean±SD	%	N or mean±SD	%	N or mean±SD	%
Sociodemographic characteristics						
Gender						
Female	82	61	62	76	20	24
Male	52	39	34	65	18	3
Age[1]						
Under 60 years	83	62	54	65	29	35
60 years or older	51	38	42	82	9	18
Type of service site						
Academic	81	60	63	78	18	22
Nonacademic	53	40	33	62	20	38
Racial group						
Minority	29	22	20	69	9	31
Nonminority	105	78	76	72	29	28
Marital status						
Married	48	36	38	40	10	26
Not married	86	64	58	60	28	74
Living situation						
Alone	43	32	31	72	12	28
With another person	91	68	65	61	26	29
Clinical characteristics						
Functioning[2]	47.8±8.3		48.1±7.3		47.1±10.5	
Distress[3]	37.3±11.3		36.7±11.3		38.9±11.2	
Severity[4]	19.9±4.7		19.6±4.4		20.7±5.4	
Previous psychiatric hospitalization	43	32	31	33	11	30
Treatment characteristics						
Side effects[5]	89	68	66	70	23	64
Number of mental health visits during follow-up	9.5±6.6		9.8±5.6		8.6±5.8	

[1] χ^2=3.84, df=1, p=.05 for difference between adherent and nonadherent groups.
[2] Measured with the Global Assessment of Functioning on a scale from 1 to 100, with higher scores indicating better functioning
[3] Measured with the Center for Epidemiological Studies Depression Scale on a scale from 0 to 130, with higher scores indicating greater distress
[4] Measured with the Hamilton Depression Rating Scale on a scale from 0 to 68, with higher scores indicating more severe depression
[5] N=130 for the total sample, N=94 for the adherent group, and N=36 for the nonadherent group

Statistical methods

To identify the sociodemographic, clinical, and treatment characteristics that are associated with adherence, bivariate analyses were conducted with Student's t tests or chi square comparisons with continuity correction. Logistic regression analysis was used to create a model of the factors present at admission to the outpatient clinics that predicted medication adherence during the three-month follow-up period. Sociodemographic, clinical, and treatment variables that were significant at a p level of .1 or less in bivariate analyses were entered into the model first. The stigma variable and subscales related to the need for treatment were then entered as a group. The subscales of the PEOT—self-rated severity of illness, worry about the impact of the illness, and belief that the treatment would be helpful—were entered in the same analysis. Analyses were conducted with SPSS for Windows (23).

Results

Most patients (1,118 of 1,242, or 90 percent) agreed to be screened; of these, 792 (71 percent) screened positive for depressive symptoms. A total of 514 of them (65 percent) consented to a diagnostic assessment. Diagnostic interviews were conducted by two research assistants and a clinical psychologist, trained in the administration of the SCID-IV and the GAF, after satisfactory interrater reliability had been achieved (intraclass correlation=.81). No significant differences in depressive symptoms were observed between patients who participated in the study and those who did not. Of the 514 patients who consented to a SCID interview, 380 (74 percent) had depression. Among these, 273 (53 percent) met criteria for unipolar major depression, and 107 (21 percent) met criteria for bipolar or schizoaffective disorder. Twenty-six patients were excluded because of cognitive impairment (MMSE score below 24) or recent substance abuse,

Table 2

Logistic regression analysis of medication adherence among 134 outpatients with major depressive disorder

Variable	Adjusted odds ratio	95% CI	Wald χ^2	p
Perceived stigma	.92	.85–1.00	4.00	.05
Patient-rated severity of illness	1.22	.99–1.48	4.69	.05
Interpersonal problems	.32	.13–.81	6.41	.02
Age 60 years or older	2.91	1.03–8.24	4.05	.04

leaving 247 patients who met the inclusion criteria and were eligible for follow-up.

Two-hundred patients completed the three-month follow-up interviews (81 percent). Of the 157 patients for whom pharmacotherapy had been recommended, 134 took the recommended medication for at least a week; these patients constituted the study sample. This sample included patients who remained adherent and received an adequate trial of antidepressant medication as well as those who did not receive adequate antidepressant treatment.

Half of the sample took a selective serotonin reuptake inhibitor (70 patients, or 52 percent), 30 (23 percent) took a tricyclic, and the remaining 34 (25 percent) took another type of antidepressant medication. Most of the 134 patients reported relatively good compliance with the recommended medication regimen; only 38 (28 percent) reported systematic nonadherence, defined as missing more than 15 percent of scheduled doses. Given the skewed distribution, we categorized patients who reported full compliance as adherent and all others—that is, those whose scores ranged from 1 to 5—as nonadherent.

Sociodemographic and illness characteristics

As shown in Table 1, older adults as a group were more adherent to the antidepressant drug therapy than were younger adults. No significant differences in adherence associated with gender, living arrangements, or minority status were observed.

None of the clinical characteristics predicted medication adherence; specifically, the duration of the index episode, previous hospitalization, and the severity of the depression as assessed by the Ham-D were unrelated to adherence. Adherence was unrelated to level of functioning as assessed by the GAF or depressive symptoms as assessed by the Center for Epidemiological Studies Depression Scale (CES-D). Comparison of contacts with mental health professionals during the follow-up period showed no association between visits recorded on the CSI and adherence.

On the basis of available follow-up data, a quarter of the sample (34 of 127 patients, or 27 percent) reported use of antidepressant medications in the three months before admission, but previous use was unrelated to adherence during the follow-up period. Many of the patients in the sample (89 of 130, or 68 percent) reported side effects that they associated with the antidepressant medication. Almost half of these (43 patients, or 48 percent) reported that the side effects were "quite" to "extremely" bothersome. Surprisingly, neither the overall report of side effects nor the report of very bothersome side effects was associated with adherence. Comparison of patients' scores on the Inventory of Interpersonal Problems found that patients who screened negative for interpersonal problems were more adherent than those who screened positive.

Multivariate analysis to predict adherence

Of the variables related to barriers that were included in the analysis, lower perceived stigma and higher self-rated severity of illness were associated with better adherence to the recommended medication regimen, even after age and the presence of interpersonal problems had been controlled for. Patients with lower levels of perceived stigma were more likely to adhere to the recommended medication regimen, as shown in Table 2. Of the patients whose perceived stigma scores were in the lower third of the sample, seven (19 percent) reported noncompliance, compared with 21 (39 percent) of the 54 patients with scores in the top third of the sample.

After the effects of age, personality pathology, and stigma were controlled for, patients who reported greater severity of illness were more adherent to the recommended medication regimen (Table 2). No significant differences were observed between adherent and nonadherent patients in functioning or in the severity of depression. Perception of the severity of illness was the only self-reported need-for-treatment variable associated with adherence.

To explore whether the age effect could be attributed to differences in the type of service site, a chi square analysis was conducted to compare younger patients who were seen at the academic outpatient department with young adults who were seen at the nonacademic clinics; no significant differences were observed. There was some indication that the older adults at the nonacademic site were less adherent (five patients, or 60 percent adherence) than those seen at the academic site (46 patients, or 85 percent adherence), but the number of elderly adults who were seen at nonacademic facilities was too small for meaningful statistical comparisons.

Discussion

The principal finding of this study was that adherence to antidepressant drug therapy was predicted by perceptions of the severity of illness and the level of perceived stigma reported before the beginning of pharmacotherapy. In addition, older adults—that is, those 60 and older—were more adherent to the antidepressant regimen, and patients with personality problems were less adherent. Neither the report of side effects nor the report of distress associated with side effects predicted adherence.

Our findings are consistent with the growing body of literature that

shows that patients' views are important in explaining treatment behaviors. Previous studies have shown that obvious patient-related factors, such as sociodemographic and clinical characteristics, were not associated with adherence, whereas more subtle factors, such as patients' attitudes and perceptions of their illness and its treatment, predicted adherence (5).

In fact, in this study patients' perceptions of the severity of illness was a more powerful predictor of adherence than was the actual severity of symptoms. The association between the perceived severity of illness and adherence may reflect the importance of accepting the illness in motivating an individual to adhere to treatment. However, perceptions of illness and treatment cannot be removed from the social context. The association we found between higher perceived stigma and noncompliance, after the effects of perceived illness had been accounted for, shows that even when an individual needs treatment, the fear that others may be critical and rejecting remains powerful. When individuals in treatment stop taking medication, it may be to counter the notion that they are now part of the devalued group of "mentally ill" individuals.

Although perceived stigma has been shown to be a barrier to seeking help (24,25), this study is the first, to our knowledge, to document the adverse effects of perceived stigma on medication adherence among adults receiving outpatient treatment for major depression. Additional work is necessary to further elucidate the mechanisms by which a social phenomenon, such as stigma, is translated into individual treatment behaviors. Such clarification could help us target our interventions toward improving the delivery of care.

Although it was not a focus of the study, we made a nonintuitive finding that side effects were unrelated to medication adherence and that side effects did not reduce the power of patients' perceptions as predictors of adherence. However, our naturalistic study design did not allow us to systematically monitor or control treatment and assess the presence or severity of side effects. It is possible that the physicians in the study were responsive to early reports of side effects and that they adjusted the medication dosages accordingly, thereby obscuring an association between side effects and adherence. Future studies should examine the effects of patients' and clinicians' views about medication and adherence in a controlled treatment trial.

Our data suggest that older adults are more compliant than younger adults. This age effect needs further comment. In our work in the Westchester County community we have found that most older adults seek mental health services from specialty clinics, and few are seen by nonacademic clinics (2). Only a small number of older adults sought care at nonacademic sites. The pharmacotherapy focus of the geriatric service and the support available may have contributed to the higher adherence. However, the adherence rate among older adults was consistent with the low nonadherence rate (18 percent) reported in a large community study of older adults (26).

When individuals in treatment stop taking medication, it may be to counter the notion that they are part of the devalued group of "mentally ill" individuals.

One of the potential limitations of this study is its reliance on patients' self-reports as estimates of adherence. The use of self-reports may result in underestimates of the rate of nonadherence to antidepressant medication. Although self-reports have been found to be correlated significantly with other objective measures of adherence (23,27), future studies of community treatment of depression should include an additional verification of patients' self-reported adherence. The estimate of nonadherence generated by this sample may be low, but the findings identify factors that may be important among individuals who acknowledge nonadherence.

Because of the naturalistic design of this study, we have no information about the treatment planning process or the information provided to patients about the importance of adherence. The physician-patient relationship and other treatment factors, such as clinicians' attitudes, patient-physician communication, and patient satisfaction, may be important mediating factors in overcoming barriers and supporting adherence. Our previous finding that three-month recovery from depression was predicted by the adequacy of pharmacotherapy (28) underscores the importance of adherence to clinical outcomes.

Conclusions

Our findings demonstrate the influence of patients' attitudes toward both their illness and their treatment on adherence. Demonstrating the need for treatment in an individual's life is often a part of effective treatment planning; we have found that it is an essential ingredient of adherence. In addition, even when an individual acknowledges the need for care, he or she may expect to be stigmatized for seeking mental health treatment for depression. Despite public awareness campaigns about mental illness and pharmacotherapy, the population still reports surprising levels of stigma (29). If stigma is still perceived from various social cues, and the impact of becoming part of a stigmatized group is not addressed, the conflict between the need for treatment and perceived stigma may become a barrier to both initiation of and adherence to acute and maintenance antidepressant drug therapy. The effect observed for adherence is even more compelling given that the individuals studied had already sought mental health services.

The impact of perceived stigma may be even more powerful in non–mental health settings that provide treatment for depression, such as primary care. Although the eradication of stigma at the public health level is being tackled through public educational interventions (30), the clinician still has the task of addressing perceived stigma with the individual who is receiving treatment. Providers can explore the anticipated adverse social consequences of seeking care and help patients decide when to disclose their illness, and to whom. This help may be an important step toward improving adherence. Additional work is necessary for understanding the individualized impact of perceived stigma and to develop effective intervention techniques when treatment is initiated. ♦

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