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How can you improve antidepressant adherence?

Talk to your patients about side effects and how long treatment will take

Practice recommendations

- Educating your patients on how to take their antidepressant medication helps adherence.
- Primary care physicians may be able to improve patient adherence to antidepressant medications by telling patients how long they will have to take them, letting them know about possible side effects, and addressing their questions and concerns.

educational messages from their primary care physician on antidepressant usage was associated with medication adherence during the first 3 months of treatment. To monitor adherence, we used electronic monitoring caps rather than self-report. Based upon prior work examining predictors of adherence,⁴ we hypothesized that patients who received specific messages about how to take their medicine would demonstrate greater adherence during the first 3 months of treatment.

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Nonadherence to antidepressants among patients with depressive disorders has been reported to be as high as 68%.¹ While research on the efficacy and effectiveness of depression treatments is voluminous, research on factors associated with antidepressant adherence is much more limited.^{2,3}

Several studies have pointed to the importance of patient education regarding antidepressants in improving adherence.^{4,5} Previous studies have found that rates of antidepressant adherence⁴ and medication discontinuation¹ were significantly associated with the how much information the physician gave the patient about the drug's use. However, a review of interventions to improve adherence concluded that patient education required further study.⁶

In this study, we prospectively examined whether patient reports of specific

■ Implications

Findings support hypothesis

We found a significant dropoff in adherence to prescribed antidepressants during the first 3 months of treatment. We also found support for our hypothesis that patients who received specific messages from their physicians would be more adherent to their drug regimen. We were able to identify several key messages that were associated with at least 80% adherence over a 3-month period. The most important messages were: How long the patient should expect to take the medicine and what to do if there are questions. Other important messages included being told to keep taking the medication even if feeling better, being advised as to how long side effects would last, and being given advice on managing minor side effects.

Methods

Participants

We enrolled 191 primary care patients in a year-long observational study. All participants were referred to the parent study by their primary care physicians.

Patients were eligible for referral if they were age 18 years or older; had been prescribed an antidepressant for the treatment of depression in the preceding 2 weeks or had been switched to a new antidepressant within the preceding 2 weeks; had no lifetime history of bipolar disorder; had no substance abuse or dependence in the preceding 6 months; or had no current psychotic symptoms or history of psychotic disorder. The study protocol was approved by the University of Pittsburgh Institutional Review Board and the Veteran's Affairs Institutional Review Board. All participants provided written informed consent.

Participants were recruited from 2 urban family practice health centers: a single-specialty group practice and 2 primary care clinics in the Veterans Health Administration (VHA). This report focuses on data obtained through interviews and questionnaires at the baseline evaluation (n=191) and adherence data from the first 3 months of the study (n=178).

Measures

Information on race, gender, education, employment, marital status, and income was obtained from each participant. A semistructured interview was administered to assess the presence of current mood, anxiety, substance use, and somatoform disorders.⁷

Severity of depressive symptoms was evaluated with the 21-item Beck Depression Inventory. Psychosocial and physical functioning was assessed with the 36-item, self-administered Medical Outcomes Study Short Form General Health Survey (MOS SF-36). The MOS scales were weighted and aggregated into the scores for the Physical Component Scale (MOS PCS) and the Mental Component Scale (MOS MCS).⁸

TABLE 1

Baseline demographic, clinical characteristics, and diagnoses of enrolled sample (N=191)

DEMOGRAPHICS	
Mean (SD) age	45.1 (15.9)
% Female	70.7
% White	93.7
% Employed full/part-time	52.9
% Married or living with partner	53.9
% Greater than high school education	55.5
CLINICAL CHARACTERISTICS	
Mean (SD) BDI	19.5 (10.3)
Mean (SD) MOS PCS	44.6 (11.5)
Mean (SD) MOS MCS	30.7 (10.7)
Mean (SD) number of current medical conditions	2.0 (1.6)
MOOD DIAGNOSIS	
No diagnosis	13.6%
Major depression only	36.6%
Major depression + dysthymia	30.4%
Partial remission of major depression	6.3%
Partial remission of major depression + dysthymia	7.9%
Dysthymia only	1.6%
Minor depression only	3.7%
COMORBIDITY (MOOD + ANXIETY)	
-Major depression or dysthymia + panic or generalized anxiety disorder	27.7%
-Any mood disorder + any anxiety disorder	50.3%

BDI, Beck Depression Inventory; MOS MCS, Medical Outcomes Study Short Form Mental Component Score; MOS PCS, Medical Outcomes Study Short Form Physical Component Score.

Medical conditions were assessed with a modified version of a checklist developed by Wells et al for use in the Medical Outcomes Study.⁹ The modified list assessed the presence of hypertension, diabetes, coronary artery disease, angina, arthritis, back problems, pulmonary problems, gastrointestinal disorders, cancer in the preceding 3 years, major neurological problems, cardiac pacemaker, kidney disease, legal blindness, eye disease, thyroid disease, lupus, and HIV/AIDS.

Electronic caps track adherence

At baseline, patients were given their medications in bottles with electronic monitoring caps. The Medication Event Monitoring System (MEMS) cap made

TABLE 2

Antidepressants taken at baseline (N=191)	
ANTIDEPRESSANT	N (%)
Citalopram (Celexa)	60 (31.4%)
Fluoxetine (Prozac)	36 (18.8%)
Paroxetine (Paxil)	28 (14.7%)
Sertraline (Zoloft)	24 (12.6%)
Bupropion (Wellbutrin)	15 (7.9%)
Escitalopram (Lexapro)	13 (6.8%)
Venlafaxine (Effexor)	10 (5.2%)
Nefazodone	2 (1.0%)
Trazodone (Desyrel)	2 (1.0%)
Phenelzine (Nardil)	1 (0.5%)

by Advanced Analytical Research on Drug Exposure (AARDEX), is a standard-looking childproof cap fitted with a microprocessor that records the date and time the cap is removed from the bottle and the amount of time until it remains off. Using this data, we calculated 2 adherence scores: the percentage of prescribed doses taken and the percentage of days with correct intake and timing over a 3-month period.

12 Questions used to assess patient education recall

We used the 12-item Patient Education Questionnaire developed by Lin and colleagues⁴ to assess what patients remembered their physicians telling them about their antidepressants. We asked patients to respond to the following questions:

- Were you given a simple explanation of how the medicine works? (yes/no)
- Were you told how long it would take before the medicine would start to have a noticeable effect? (yes/no— if yes, how long were you told it would take?)
- Were you told how long to expect to continue taking the medication? (yes/no)
- Which of the following instructions were you given about taking the medicine?

- Keep taking it even if you start to feel better (yes/no)
- Don't stop taking it without checking with the office (yes/no)
- Take it on a daily basis without interruption (yes/no)
- Did your doctor discuss side effects that are common when taking the medicine? (yes/no)
- Were you given advice on how to manage minor side effects? (yes/no)
- Were you advised on what to do if you experienced major side effects? (yes/no)
- Were you advised about when or how long you might have side effects? (yes/no)
- Were you asked about prior use of a similar medication? (yes/no).

Results

The enrolled sample was predominantly female, white, and had a mean age of 45 years. More than half had some college education, were married (or living with a partner), and were employed full- or part-time (TABLE 1).

Clinical characteristics

On average, patients reported 2 medical conditions (moderate symptoms of depression, and moderate impairment in psychosocial functioning). All participants referred to the study had been prescribed an antidepressant for the treatment of depression by their primary care physician.

At the initial interview, 67% of patients met *Diagnostic and Statistic Manual*, 4th ed¹⁰ (DSM-IV) criteria for major depression. Approximately 37% met criteria for major depression alone, while 30% met criteria for major depression and dysthymia. Four percent met the criteria for minor depression, 6% were in partial remission of major depression, and 14% of participants did not meet criteria for a DSM-IV mood disorder. Comorbid anxiety disorders were common in this sample; 28% of participants with major depression or

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Nearly one-third of the patients were taking citalopram, followed by 19% on fluoxetine

TABLE 3

3-month adherence among patients receiving specific patient education at baseline (N=178)

EDUCATION ITEM	PATIENTS RECEIVING DISCUSSION % (N)	ADHERENCE (YES ≥80%)					
		DOSES TAKEN OVER 3 MONTHS (%)			DAYS WITH CORRECT INTAKE AND TIMING OVER 3 MONTHS (%)		
		NO	YES	P	NO	YES	P
Take on a daily basis	79.2 (152)	75.0	83.1	.23	77.8	80.5	.72
Told how long medication would take to work	75.5 (145)	69.0	81.5	.08	70.4	85.4	.06
Told what to do if there were questions	75.5 (145)	66.7	86.2	.006	70.4	87.8	.03
Asked about prior use of similar medicine	71.4 (137)	71.4	73.8	.74	72.2	73.2	.91
Don't stop taking without checking with office	63.0 (121)	56.0	69.2	.10	57.4	73.2	.08
Given simple explanation of how medicine works	59.4 (114)	54.8	63.1	.31	55.6	65.9	.26
Keep taking even if feeling better	58.9 (113)	48.8	64.6	.05	51.9	65.9	.12
Discussed common side effects	46.9 (90)	41.7	47.7	.46	40.7	53.7	.16
Advised on what to do if there are major side effects	30.2 (58)	28.6	29.2	.93	25.0	39.0	.09
Told how long to expect to take this medicine	29.2 (56)	16.7	38.5	.003	20.4	41.5	.009
Advised of how long side effects will last	28.6 (55)	23.8	32.3	.25	22.2	41.5	.02
Given advice on managing minor side effects	27.1 (52)	23.8	30.8	.34	21.3	41.5	.01

dysthymia had comorbid generalized anxiety disorder or panic disorder.

More than 80% of the antidepressants the patients were taking were selective serotonin reuptake inhibitors (SSRIs). Citalopram (31%), fluoxetine (19%), paroxetine (15%) and sertraline (13%) were the most common (TABLE 2).

Adherence declines over 3 months

Overall, adherence to antidepressants significantly decreased over time. While adherence as measured by the percentage of prescribed doses taken was good (82%) at month 1, it showed a significant linear decrease to 69% at 3 months ($P < .0001$).

When the more stringent measure of adherence was examined—ie, percentage of days with correct intake and timing—adherence was even poorer, decreasing nonlinearly over time. Adherence at month 1 was only 55%; and decreased to 43% at 3 months (linear: $P < .001$; quadratic: $P = .036$). Our findings indicate that by the end of the first 3 months of treatment, between about one-third and one-

half of the patients were nonadherent to their regimen.

■ Univariate predictors of adherence

Adherent patients are older

Medication adherence of at least 80% was used as a cutpoint: $\geq 80\%$ was considered adherent, $< 80\%$ nonadherent. Univariate analyses (t -tests and chi-square tests) indicated that the following patient characteristics were significantly associated with taking the correct number of prescribed antidepressant doses at least 80% of the time within the first 3 months of treatment.

- **age**—adherent patients were significantly older than nonadherent ($P = .01$)
- **race**—whites were more adherent than nonwhites (67% vs 0%; $P = .001$)
- **gender**—men were more adherent than women (81% vs 56%; $P = .03$)
- **depression severity**—adherent patients had milder depressive symptoms than nonadherent patients ($P = .04$).

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Univariate analyses revealed that men were more adherent than women

When percentage of days with correct intake and timing was examined, depressive severity was the only variable that differentiated adherent from nonadherent patients. Individuals who had at least 80% adherence over the first 3 months initially presented with milder depressive symptoms at the baseline evaluation ($P=.02$). Other demographic and clinical characteristics did not differentiate adherent from nonadherent patients.

Regimen duration discussions linked to better adherence

Several key messages about antidepressant medication differentiated adherent from nonadherent patients (TABLE 3). For percentage of prescribed doses taken during a 90-day period, the key messages differentiating adherent from nonadherent patients were “*told what to do if there were questions*,” “*keep taking the medication even if feeling better*,” and “*told how long to expect to take medicine*.”

For the more stringent measure of adherence (percentage of days with correct intake and timing), 4 key messages differentiated adherent from nonadherent patients: “*told what to do if there were questions*,” “*told how long to expect to take medicine*,” “*advised of how long side effects will last*,” and “*given advice on managing minor side effects*.”

Multivariate predictors of adherence

3 Key issues emerge

Multivariate hierarchical logistic regression was used to examine the association between the binary outcome of adherence to antidepressants over a 3-month period (adherent vs nonadherent), significant patient characteristics, and patient recall of physician messages about antidepressant use. Two key physician messages—“*told how long to expect to take the medicine*” and “*told what to do if there were questions*”—distinguished between patients who took at least 80% of the prescribed medication doses and those who did not.

The odds of being adherent to the regimen more than tripled among those who said they had received these 2 messages when compared to those who said they had not (OR=3.8; 95% CI, 1.6–8.9; OR=3.8; 95% CI, 1.4–10.4) (TABLE 4, available online at www.jfponline.com).

One message was associated with adherence based on the percentage of days with correct intake and timing. The odds of being adherent more than doubled among patients who reported that they were “*told how long to expect to take the medicine*” compared with those who said they had not been told (OR=2.6; 95% CI, 1.1–5.9) (TABLE 5, online at www.jfponline.com). Models testing for interactions of multiple messages were nonsignificant.

Discussion

Physician messages tied to adherence

Consistent with prior reports,⁴ we found a significant decrease in adherence to prescribed antidepressants during the first 3 months of treatment. However, physicians’ educational messages about how to take the antidepressant were significantly associated with adherence in both univariate and multivariate analyses.

While more than three-quarters of study participants indicated that they were told to take the medication daily, how long it would take to work, and what to do if there were questions, the least frequently reported messages involved managing side effects, with less than a third of patients indicating that their physician had discussed this with them. The latter finding is important because univariate analyses indicated that discussion of side effects was significantly associated with future adherence during the first 3 months of treatment.

In multivariate analyses, we were able to further identify those key messages that were associated with at least 80% adherence over a 3-month period. A unique aspect of our study is the use of electronic monitoring to measure adherence, which provides detailed information on the exact

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Less than a third of patients indicated that their physicians discussed managing side effects with them

time patients took their medication and allowed us to identify predictors associated with more conservative (percentage of days with correct intake and timing) and less conservative (percentage of prescribed doses taken) measures of adherence. Our findings suggest that primary care physicians may be able to improve adherence by providing simple and specific information about using antidepressants. The most important of these being “*how long to expect to take the medicine*” and “*what to do if there are questions*.”

Limitations of this study

Our findings are limited to primary care patients from 3 types of primary care settings—private offices, university-based clinics, and VA clinics. These findings may not generalize to other types of family practice or primary care settings such as large managed care organizations, publicly funded primary care settings, and so on.

Also, it's important to note that we did not assess what physicians actually told patients; we only inquired about those messages that patients recalled. However, the information actually recalled seems more likely to influence their behavior.

In addition, because we did not perform direct observation of the physician-patient interaction, we were unable to control for other possible confounders. For example, physicians who communicate more effectively may have a positive effect on adherence through some other aspect of communication than the specific messages measured.¹¹

Finally, we did not assess patient-related factors such as health literacy. Patients with low functional health literacy may have lower recall of information provided during the visit and may have lower levels of adherence.

Keeping our sights on patient education

Future studies are needed to assess patient's literacy and record physicians' actual communications and patients' self-reports of such information in order to determine

the impact of such factors. Nevertheless, our findings provide useful information about educational messages that physicians—as well as nurses—can provide to improve antidepressant adherence. ■

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Disclosure

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Physicians may be able to improve adherence by providing simple and specific information on antidepressants