Strategies to improve medication adherence in patients with depression

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Depression is second only to hypertension as the most common chronic condition seen in general medical practice,[1] with more than half of all depressed patients seen exclusively by primary care providers.[2] Deficiencies in depression management have become a major health policy concern,[3] and, according to the Global Burden of Disease Study, major depression is the fourth leading cause of disability worldwide.[4] Recent projections from the World Health Organization predict by 2020 depression will become the second leading cause of disability worldwide, surpassing hypertension, arthritis, diabetes, and chronic back pain.[3,4]

Adherence is defined as the extent to which a person's behavior (medication use, diet, lifestyle changes) conforms to medical or health advice.[5,6] Adherence to antidepressant therapy is essential for a positive patient outcome, and guidelines issued by the Agency for Healthcare Research and Quality and the American Psychiatric Association recommend continued antidepressant treatment for at least four to nine months after depressive symptoms resolve to prevent relapse.[7,8] However, nearly half of medical outpatients who receive an antidepressant prescription discontinue treatment during the first month.[1] The discontinuation rates within three months after the start of treatment can reach 68%, depending on the population studied and the agent used.[8] In one study, premature discontinuation of antidepressant treatment was associated with a 77% increase in the risk of relapse or recurrence, potentially increasing health care costs associated with retreatment.[9] Other studies found that less than 33% of patients diagnosed with depression receive and take their medications appropriately, and only 40% reach an adequate dosage and duration of treatment.[2]

This paper summarizes the reasons for nonadherence to antidepressant therapy, reviews tools to identify patients at risk for nonadherence, and offers suggestions to improve medication adherence.

Factors affecting adherence to antidepressant therapy. Numerous barriers contribute to the nonadherence of antidepressant pharmacotherapy, the majority of which are related to a lack of knowledge, on the part of both clinicians and patients, about the nature of the disease and its treatment. Adverse effects of antidepressants are major contributors to medication nonadherence.[7] Nonadherence may occur more frequently during particular stages of treatment. For example, more intensive contact with and support from one's provider are particularly helpful to patients who have just started treatment or require long-term maintenance therapy.[7]

Additional barriers to adherence to antidepressant therapy relate to the nature of the disease itself and include problems with memory and concentration, hopelessness, and a focus on somatic symptoms that can interfere with the patient's involvement in therapy.[7] Depression often carries a stigma and may be viewed as a moral weakness or character flaw.[1] The patient's desire for confidentiality can preclude the sharing of information with the patient's family, who could offer social support.[7]

Other reasons for nonadherence include guilt associated with the illness, physician failure to provide reassurance and hope, lack of continuity of care, complex treatment regimens, the high cost of medical care, chronic illness, comorbid symptoms such as panic attacks and severe anxiety, and displeasure with treatment response (e.g., efficacy).[10] The efficacy of the

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antidepressant can be a major factor in patient nonadherence. Patients can become nonadherent because of a lack of efficacy or perceived lack of efficacy (e.g., not giving the drug enough time to work) or because they have discontinued therapy without medical advice to see if the drug is still necessary.[10] Extreme guilt may cause depressed patients to feel that they do not deserve treatment or to develop fears that they cannot afford the cost of taking the medication.[11]

Additional reasons cited by patients for nonadherence to antidepressant therapy include unawareness of the importance of consistently taking their medication, perceived lack of a friendly relationship with their provider, too much time spent in the waiting room, the need to take the medication multiple times per day, and adverse effects.[10] Medications that cause a higher rate of adverse effects clearly necessitate more skill on the part of the clinician to maintain patient adherence.[11] Although not specific to the treatment of depression, the patient's ability to purchase medications can also influence adherence to prescribed antidepressant therapy.

Practitioners should treat depression aggressively in patients with comorbid medical conditions because depression increases a patient's sensitivity to somatic distress, leads to poor self-care, and worsens the prognosis associated with certain disorders such as cardiovascular disease.[1] In fact, the total direct medical costs for patients with depression are much greater than those realized by the general population, partly due to the increased comorbidity of those afflicted.[3]

Several ethical issues should also be addressed when working to improve adherence to antidepressant therapy. The clinical diagnosis must be correctly established, the treatment must have known efficacy for depression and be used appropriately, and patients' rights to refuse treatment must be respected.[12]

Interventions to improve adherence to antidepressant therapy. Pharmacists, nurses, and physicians from many different practice settings have implemented interventions to improve adherence to antidepressant medications. A collaborative pharmacy practice model managed by clinical pharmacy specialists, involving a combination of scheduled office visits and telephone calls, increased medication adherence in patients with mild to moderate depression.[3] Effective pharmacist monitoring of patients receiving antidepressant therapy was shown to play an important role in improving therapy adherence, especially for patients taking an antidepressant for the first time.[13] The results of a randomized, controlled prospective trial demonstrated that a monthly mail-based educational intervention to patients and prescribers can positively influence patient adherence to antidepressants.[14]

Physicians who integrate specific educational messages into primary care visits found that patients were more likely to maintain antidepressant therapy during the first month of treatment.[15] A multifaceted intervention, including patient education, visits with a depression specialist, and telephone monitoring and follow-up over a one-year period significantly improved adherence to antidepressant therapy.[16]

Not all interventions directed toward improving patient adherence to antidepressant therapy have been completely successful. Patients who received counseling about their drug treatment showed improved adherence; however, informational leaflets related to the patient's antidepressant therapy had no significant effect on medication adherence.[17] Although nurse telehealth care was shown to improve clinical outcomes of antidepressant therapy, the telehealth-based model did not improve patients' adherence to their prescribed medication.[18]

Tools to identify patients at risk for nonadherence. The reasons for patient nonadherence to prescribed medications are numerous and multifactorial, as no variable has been identified as consistently predictive.[19,20] Recognition of patients who do not adhere to drug therapy is further complicated by the lack of accurate and affordable objective measures that are suitable for widespread implementation.[12,19] Understanding the reasons for poor medication adherence allows clinicians to develop a profile of patients at risk for nonadherence and develop strategies to intervene and maximize antidepressant therapy.[21]

Several methods of evaluating patient adherence to antidepressant therapy were studied for 12 weeks in 88 patients who were prescribed tricyclic antidepressants in Great Britain.[22] Patients were asked four standard questions about their medications, using a previously published self-reported measure of medication adherence.[23] The results indicated that the questionnaire had a sensitivity of 72.2% and a specificity of 74.1% for at least 80% adherence.[22] The authors concluded that the self-reported scores were useful to screen for nonadherence to antidepressant therapy. The application of these results to current practice in the United States may be limited because selective serotonin-reuptake inhibitors (SSRIs) are generally preferred over tricyclic antidepressants. Given this possible limitation, this questionnaire may be useful for clinicians to identify nonadherence in patients prescribed other antidepressant agents.

Published information describing specific features of patients at risk for nonadherence to antidepressant therapy is limited. Age, sex, and ethnicity have not been related to early discontinuation of antidepressant therapy.[7] Failure to attend scheduled medical appointments is an early indicator of possible nonadherence.[12,21] The lack or loss of responsiveness to a usually or

previously adequate drug dosage also warrants further evaluation.[21]

Directly asking patients about their antidepressant therapy is an efficient method for clinicians to assess nonadherence, as it can identify more than 50% of patients with low adherence to therapy with a specificity of 87%.[12,21] Questioning patients about their antidepressant therapy is particularly important during the early phase of treatment. The acute onset of adverse effects with antidepressants is a major obstacle to adherence, particularly if patients have not noticed any benefits from the therapy.[7] The adverse effects from antidepressants usually appear at the start of therapy and may account for many patients abruptly discontinuing treatment within the first month.[10,15] Adverse effects were the most common reason for discontinuing or switching SSRI therapy within the first three months of treatment.[8]

One question to ask patients is "Have you missed any pills in the past week?" A response of missing one or more pills indicates a problem with adherence.[12] A more detailed patient interview using questions as a probe is also an effective method to assess adherence.[20] Clinicians should realize that patients tend to overestimate their actual adherence to therapy and that the accuracy of the self-report depends on the patient's cognitive abilities and honesty.[12,20] When following up with these patients, clinicians should ask several simple questions to assess the level of patient adherence.[23] Examples of such questions include (1) How are you taking your medications? (2) Have you ever forgotten to take your medications? (3) Are you experiencing any adverse drug reactions?, and (4) How are you feeling since you started your medication?

Patient adherence to antidepressant medication can also be assessed by asking patients to report the number of days they took the prescribed drug during the previous month.[2] These self-reported data for antidepressant adherence were shown to have excellent reliability when compared with automated pharmacy data.[2,16]

Practical tips to improve adherence to antidepressant therapy. Health care providers may be able to enhance adherence to antidepressant therapy using simple and specific educational messages at the start of therapy and at each follow-up visit. Table 1 provides potential reasons for nonadherence, strategies to improve adherence, and tips for counseling patients with depression.

Table 1.
Tips for Enhancing Medication Adherence in Patients Receiving Antidepressant Therapy[7,10,11]

Reasons for Nonadherence	Strategies to Improve Adherence	Counseling Tips
Lack of knowledge regarding the nature of depression	Discuss epidemiology of depression; refer to depression as a medical condition	21 million Americans suffer from depression every year. Depression is a medical condition, just like asthma and diabetes.
Guilt associated with diagnosis of depression	Discuss the chemical basis for depression	Having depression is not your fault, and there is no reason to feel guilty or ashamed.
Need for reassurance and support	Reinforce that depression is treatable; discuss appropriate duration of treatment	No one knows exactly what causes depression, but in people with depression, a chemical called serotonin may be out of balance. Medications are available that can correct serotonin imbalance. To effectively treat depression, four months or more of therapy may be needed.
Lack of belief in treatment's effectiveness	Discuss efficacy of medications	Antidepressants have been shown to effectively treat depression.
Belief that treatment regimen is too complex	Reinforce that simplified regimens are available	Consider a once-daily administration regimen.
Belief that treatment does not help with other symptoms associated with depression	Remind patients of the delayed therapeutic effects of antidepressants	With medication, you may start to feel better in two to four weeks, but because everyone is different, it may take longer.
Fear of medication's adverse effects	Reinforce that most patients do not have to stop therapy because of adverse effects	Some people may have no adverse effects while taking antidepressants.
Belief that adverse effects will make it difficult to tolerate therapy	Review most common adverse effects; reassure patient that, over time, adverse effects should be less of a problem	Common adverse effects include dry mouth, indigestion or mild stomach upset, diarrhea, or trouble sleeping. Sometimes, antidepressant therapy may cause patients to lose interest in sex. Over time, adverse effects should be less of a problem.

These targeted messages are designed to address the most common reasons for nonadherence to antidepressant therapy. Table 2 lists general strategies and tips for improving adherence to any medication regimen.

Predictors of adherence during the early phase of treatment (at least 30 days after filling the initial prescription) may be different than those of the later phase of treatment (at least 90 days after filling the initial prescription). Early medication adherence may be enhanced by the provision of educational information concerning medication use and discussions of behavioral strategies, such as taking the medication at the same time each day and not discontinuing the medication if symptoms improve. Inform patients of the most common adverse effects and query them about troublesome adverse effects at follow-up visits to assess potential reasons for nonadherence. Unlike early adherence, the only significant predictor of late adherence found in one study was whether the patient had previously used antidepressants.[15]

Educational messages regarding the initiation of antidepressant therapy are easily incorporated into a primary care visit.[15] Alternatively, these messages may be adapted for use in an outpatient pharmacy. Third-party payers have begun to realize the value of medication adherence, and some may be willing to reimburse for adherence-related services. Pharmacists may be able to develop a core network of physicians who can refer patients for adherence-related services.[20] The ability of the health care provider to effectively communicate with the patient about antidepressant therapy has been shown to influence adherence to therapy. Effective communication includes establishing rapport, assessing patient attitudes and beliefs, negotiating provider–patient differences in beliefs and expectations of treatment, and maintaining a hopeful attitude about the patient's eventual recovery from depression. Strategies to promote effective communication include expressing enthusiasm, establishing a therapeutic alliance, using a variety of communication strategies, providing the correct amount of information at a level appropriate for the patient, soliciting questions from the patient, and ensuring that the patient intends to take the medication as prescribed.[10]

For patients who cannot afford the prescribed medications, several patient assistance programs have been developed by pharmaceutical manufacturers to aid low-income and uninsured patients meeting eligibility criteria. A directory of member companies that participate in client assistance programs is available from the Pharmaceutical Research and Manufacturers of America or online at www.needymeds.com.

Conclusion. Nonadherence to antidepressant therapy is a major problem in the management of depression. Patients should be individually assessed so that a targeted and tailored intervention or combination of interventions can be provided to optimize adherence. Regular patient follow-up is key to long-term medication adherence.

Table 2.
General Strategies and Tips for Improving Medication Adherence

Strategies[19,24]	Tips
Educate and help patients understand the importance of medication adherence.	Enhance communication and encourage patients to discuss compliance issues and concerns.
Motivate patients to follow their prescribed treatment regimens.	Simplify the treatment regimen.
Reinforce the importance of medication adherence at all health care visits.	Anticipate barriers to medication adherence and discuss solutions.
	Involve all of the patient's health care providers.
	Provide oral and written instructions.
	Discuss the link between the medical condition and treatment benefits.
	Suggest the use of practical medication reminders (e.g., calendars, dose counters).
	Tailor the treatment to fit the patient's lifestyle.
	Assess medication adherence at each patient visit.
	Reinforce compliance achievements.
	Recognize that not every strategy works in all patients. Develop a multicomponent approach (e.g., cognitive and behavioral).

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