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Predictors of Attrition During One Year of Depression Treatment: A Roadmap to Personalized Intervention

Diane Warden, Ph.D., M.B.A.^{1,*}, A. John Rush, M.D.^{1,2,3}, Thomas J. Carmody, Ph.D.¹, T. Michael Kashner, Ph.D., J.D.^{1,2}, Melanie M. Biggs, Ph.D.⁴, M. Lynn Crismon, Pharm.D.⁵, and Madhukar H. Trivedi, M.D.¹

¹ Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA

² Department of Clinical Sciences, The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA

³ Presently, Duke-National University of Singapore, Singapore

⁴ Department of Internal Medicine, The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA

⁵ University of Texas College of Pharmacy, Austin, Texas, USA

* Corresponding author: Diane Warden, Ph.D., M.B.A., Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX 75390-9086. Tel.: 214-648-4614; fax: 214-648-4612.

Diane.Warden@UTSouthwestern.edu.

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Abstract

Objective—Attrition from treatment in the short and long term for major depressive disorder (MDD) is clearly an adverse outcome. To assist in tailoring the delivery of interventions to specific patients to reduce attrition, this study reports the incidence, timing, and predictors of attrition from outpatient treatment in public mental health clinics.

Methods—Outpatients with psychotic and nonpsychotic MDD receiving measurement-based care in the Texas Medication Algorithm Project (N = 179) were evaluated to determine timing and rates of attrition as well as baseline sociodemographic, clinical, and attitudinal predictors of attrition.

Results—Overall, 23% (42/179) of the patients left treatment by 6 months, and 47% (84/179) left by 12 months. Specific beliefs about the impact of medication, such as its perceived harmfulness, predicted attrition at both 6 and 12 months. Younger age ($p = 0.0004$) and fewer side effects at baseline ($p = 0.0376$) were associated with attrition at 6 months. Younger age ($p = 0.0013$), better perceived physical functioning ($p = 0.0007$), and more negative attitudes about psychiatric medications at baseline ($p = 0.0075$) were associated with attrition at 12 months.

Conclusions—Efforts to elicit attitudes about medications and tailoring educational and other retention interventions for patients with negative beliefs about antidepressants both when initiating a new medication and throughout treatment may reduce attrition. Particular focus on younger patients and those requiring frequent visits may be helpful.

Keywords

adherence; compliance; major depressive disorder; antidepressant medication; beliefs; attitudes; attrition

Introduction

Attrition from treatment for depression is a substantial concern since patients who leave treatment prematurely are less likely to reach remission.^{1,2} Rates of attrition in the first 12 weeks can be up to 65% in naturalistic settings^{3–5} and up to 36% in clinical trials.⁶

Despite the negative impact of attrition on outcomes, attrition during depression treatment has received little study. Attrition is not a random event, since some patients are more likely to discontinue treatment than others. A few predictors of attrition in treatment for depression have been identified in clinical trials including minority status,⁷ younger age,^{7,8} and sociodemographic disadvantage (e.g., fewer years of education, lower income, or unemployment).⁹ We recently found that minority status, younger age, fewer years of education, public insurance, more concurrent Axis I psychiatric conditions, higher perceived mental health functioning, and first major depressive episode were predictors of attrition.¹⁰

Patients' attitudes and beliefs about illness and medications can also have an impact on decisions about treatment adherence,^{11,12} and, unlike most sociodemographic characteristics, negative attitudes may be modifiable in clinical treatment. A positive attitude about drugs predicts adherence to antidepressants,¹³ while skepticism about antidepressants,¹⁴ and perceived stigma associated with depression,¹⁵ predict treatment discontinuation.

Attrition in public outpatient mental health clinics is especially important since patients often have substantial impairment in daily functioning¹⁶ and few alternatives for treatment. Few studies have evaluated pretreatment predictors of short- or longer-term attrition from treatment for depression in these settings. In a 75-subject, naturalistic community mental health center study, 49% of patients dropped out by 6 months, with African American race and lack of insurance predicting attrition.¹⁷

Tailoring care based on individual characteristics is the intent of personalized treatment. Population-based evidence used in making individual decisions can result in suboptimal care.¹⁸ If specific attitudes and beliefs can be identified as markers for attrition risk, interventions to reduce attrition can be personalized for patients expressing these attitudes, especially patients who are from populations at higher risk for attrition. Limited resources may therefore be focused on those most at risk.

This report focuses on attrition from treatment provided over 12 months to 179 outpatients with major depressive disorder (MDD) treated with measurement-based care^{19,20} in public mental health clinics participating in the Texas Medication Algorithm Project (TMAP).^{21,22} The following questions were addressed:

1. How common is attrition and when does it occur?
2. Do remission or response rates differ between attrition and nonattrition groups?
3. Do baseline sociodemographic or clinical characteristics distinguish attrition and nonattrition groups at 6 and 12 months?
4. Do baseline attitudes about medications predict attrition?
5. What decision rules best predict attrition at 6 and 12 months?

Methods

The rationale and design of TMAP and description of the clinic treatment assignments are described elsewhere.^{21,22} Briefly, TMAP, a comparative effectiveness trial, evaluated an algorithm-based disease management program compared with treatment as usual. Participants were adult outpatients with nonpsychotic and psychotic MDD,^{19,23} bipolar disorder,²⁴ or schizophrenia²⁵ seen in 19 public mental health clinics in Texas. Four clinics provided algorithm-based care for MDD. Participants were enrolled over the course of 13 months and treated for 2 years between March, 1998, and April 2000.

The study was approved and monitored by the Institutional Review Boards at the University of Texas Southwestern Medical Center at Dallas and the University of Texas at Austin. Written informed consent was obtained from all participants prior to study entry.

Participants

Participants were at least 18 years old with a diagnosis of psychotic or nonpsychotic MDD determined by their clinician. They had to be sufficiently symptomatic to require initiation of an antidepressant or intolerant or insufficiently responsive to current medication to require a medication switch or augmentation.

The generalizability of findings in this study was maximized by use of broad inclusion and few exclusion criteria. In addition, concurrent general medical conditions and most comorbid psychiatric disorders, including substance abuse, were allowed. However, schizophrenia, schizoaffective disorder, bipolar disorder, anorexia nervosa, and bulimia nervosa were exclusions for participation. Patients receiving services for mental retardation or from the assertive community treatment (ACT) program and patients who required inpatient detoxification at study entry were also excluded.

Clinic visit data are not available for TMAP participants with MDD who were receiving treatment as usual. Of 181 evaluable participants with MDD who were receiving algorithm-based care, 2 had no postbaseline data in the first year, so that data on 179 patients were available for analysis.

Treatment

Separate five- and seven-step, manual-based, treatment algorithms with multiple treatment options at each step were provided for psychotic and nonpsychotic MDD, respectively. The algorithms specified frequency of visits, medication options, and dosing for each medication. Consistent with a measurement-based care approach,^{20,26,27} at critical decision points, the algorithms recommended treatment strategies such as continuing, discontinuing, adjusting the dose of, or augmenting the medication based on symptoms measured at each visit using the 30-item Inventory of Depressive Symptomatology-Clinician-rated (IDS-C₃₀)^{28–30} and side effects measured by a 5-point, clinician-rated Likert scale ranging from none to very severe. Recommended frequency of visits began with every 1–2 weeks, with decreasing frequencies as symptoms improved.

Patient adherence was to be optimized with patient/family education (based on a Patient Education Plan Guidebook),^{31,32} support from a clinical coordinator, and structured follow-up systems for missed appointments. Clinical coordinators assisted physicians with implementing the algorithm and collected demographic and clinical information at baseline.

Assessments

Research coordinators who were unblinded to treatment assignment but who were not involved in treatment, obtained sociodemographic information at study entry and then collected the following measurements every 3 months for up to 2 years: the IDS-C₃₀ (primary outcome measure), and the Inventory of Depressive Symptomatology-Self Rated (IDS-SR₃₀)^{28–30} and the 24-item Brief Psychiatric Rating Scale (BPRS-24).^{33–35} The BPRS-18 was derived from the BPRS-24.³⁴

Response ($\geq 50\%$ improvement from baseline on the IDS-C₃₀) and remission (score on the IDS-C₃₀ ≤ 12 , which is consistent with a threshold of ≤ 7 on the 17-item Hamilton Rating Scale for Depression³⁶) were defined using the last research assessment before drop out or at the completion of 1 year of treatment. The presence of psychosis was determined clinically based on DSM-IV criteria. Side effects were measured using a modified Systematic Assessment for Treatment Emergent Events (SAFTEE) scale^{37,38} and functioning and quality of life were assessed using the 7-item Lehman Work and Productive Activity subscale,³⁹ derived from the Quality of Life Interview (QOLI),^{40–42} and the 12-item Short-Form Health Survey (SF-12).⁴³ Insomnia was measured by summing the early, middle, and late insomnia items of the IDS-C₃₀.

Drug and alcohol use were assessed with the Drug Abuse Screening Test (DAST)⁴⁴ (a score > 5 suggests drug abuse) and the Michigan Alcohol Screening Test (MAST)⁴⁵ (a score ≥ 5 suggests alcohol abuse).

Patients' attitudes and beliefs about medications, illness, and health were measured using the 30-item true-false Drug Attitude Inventory (DAI).⁴⁶ In this scale, a positive response is false on 15 items and true on 15 items. For example, a "true" response to "taking medications will do me no harm" and a "false" response to "medications make me feel tired and sluggish" would both be considered positive responses. A positive response is scored as plus one, and a negative response as minus one, and scores are summed. This scale has high internal consistency and accurately identified adherence to medication in 89% of 150 outpatients with schizophrenia in the validation sample.⁴⁶

Definition of Attrition

Patients who went without a medication visit for ≥ 100 days were defined a priori as dropouts, if the onset of the 100-day period began within the first year of treatment. Data were drawn

from an administrative database developed to assess utilization of services in TMAP.⁴⁷ Medication visits were defined by a visit code of “psychiatric diagnosis” or “medication-related service” and a provider type that reflected one of the types of providers licensed to prescribe medication in Texas (MD, DO, physician assistant, or nurse practitioner).

Data Analyses

Logistic regression was used to assess the association between visit frequency and attrition and between baseline characteristics and attrition. Because of the large number of predictors relative to the sample size, we did not attempt to create a multivariate model of attrition but examined each predictor in a univariate model.

We used classification trees^{48,49} to select combinations of predictors to best predict attrition at each time point. This method first selects a predictor variable and cutoff value that splits the sample into two groups that are as homogeneous as possible (i.e., one group composed mostly of dropouts and another group mostly of completers). Each group is then further split, if possible, by selection of another predictor variable and cutoff value to create homogeneous groups. This process continues until groups become too homogeneous to allow further splitting or too small (less than 10). The set of rules thus produced to classify patients is presented in a tree diagram (see Figure 1) in which the ellipses indicate nodes which need further splits and boxes indicate “branches” which represent the final classification of a participant as a dropout or completer.

The weight parameter was chosen with the assumption that misclassification of a dropout was a serious error, while misclassification of a completer was not as serious an error.

Receiver operating characteristic (ROC) analysis⁵⁰ was used to select optimal thresholds for DAI total scores 1) to correctly identify at least 75% of dropouts (sensitivity) and 2) to maximize the correct identification of completers (specificity) consistent with objective #1. The performance of the optimal threshold is described by:

- Percent correct—percent of patients whose attrition status was correctly predicted
- Sensitivity—percent of patients who were predicted to drop out among patients who did drop out
- Specificity—percent of patients who were predicted not to drop out among patients who did not drop out
- Positive predictive value (PPV)—percent of patients who did drop out among those who were predicted to drop out
- Negative predictive value (NPV)—percent of patients who did not drop out among those who were predicted not to drop out.

Results

Table 1 summarizes the baseline characteristics of the sample. Overall, this patient sample was a disadvantaged group burdened with severe depression, recurrent depression (almost 90%), psychotic symptoms (18%), minimal employment, and less than a high school education.

Rates and Predictors of Attrition

Overall, 23% (42/179) of the sample had dropped out by 6 months and 47% (84/179) had dropped out by 12 months. Of the 84 dropouts, 12 dropouts (14.3%) occurred in the first quarter, 30 (35.7%) in the second quarter, 22 (26.2%) in the third quarter, and 20 (23.8%) in the fourth quarter. The mean time in medication treatment for dropouts was 6.2 ± 3.1 months. The mean

number of visits per month during the first 12 months of treatment was 1.74 (SD = 1.2) (range 0–7.6 visits) for dropouts and 1.33 (SD = 0.4) (range 0.5–2.5 visits) for completers. A higher number of visits per month was associated with greater likelihood of attrition. For each additional visit/month, the likelihood of attrition increased by 88% (OR = 1.88, $p = 0.0120$). Severity of depression did not differ in dropouts and completers at baseline (data not shown).

No significant differences in response and remission rates were found between dropouts and completers at either 6 or 12 months (Table 2).

The likelihood of leaving treatment in the first 6 months of treatment was predicted only by younger age ($p = 0.0004$) and fewer side effects at baseline ($p = 0.0376$) (Table 3). For each 5-year increase in age, the likelihood of attrition was reduced by 26% (Table 3).

Predictors of attrition within the first 12 months of treatment included younger age ($p = 0.0013$), higher perceived physical functioning ($p = 0.0007$), and greater negative attitudes about psychiatric medications ($p = 0.0075$).

Figures 1 and 2 show classification trees with decision rules to determine attrition at 6 and 12 months, respectively. The rules to predict attrition at 6 months result in a percent correct of 0.87, sensitivity of 0.64, specificity of 0.94, PPV of 0.77, and NPV of 0.90. The rules at 12 months result in a percent correct of 0.69, sensitivity of 0.88, specificity of 0.53, PPV of 0.62, and NPV of 0.83. For example, in Figure 2, if the patient is younger than 40 years old, assume the patient will drop out. In this sample, 79 patients were < 40 years old, and 65% dropped out. If the patient is at least 40, with a DAI score ≥ 24 (more positive attitude about drugs), assume the patient will complete (completer rate 85%). If the DAI score is < 24, and the DAST score is > 1, assume the patient will complete (completer rate 81%). If the DAST score is ≤ 1 (low likelihood of drug abuse), assume the patient will drop out (dropout rate 57%). This set of rules classified 119 patients as dropouts, of whom 74 actually dropped out and 45 did not. It also classified 60 patients as completers, of whom 50 were completers while 10 were dropouts. Therefore, 74/84 (88%) of the dropouts were correctly identified, while 45/94 (48%) of the completers were incorrectly identified as dropouts.

Since all of the variables were examined as possible predictors of attrition, these classification trees are exploratory and may be useful for generating hypotheses for additional studies. The first two decision rules in each analysis, however, are based on variables that were also highly significant in the univariate logistic regressions and are thus likely to be replicated.

Drug Attitude Inventory Scores and Items as Predictors of Attrition

Based on ROC analysis, which used the DAI scores alone to predict attrition, the optimal threshold of the DAI total score to predict attrition at 6 months is ≤ 25 . This threshold provided a high sensitivity with modest specificity (percent correct = 0.37, sensitivity = 0.78, specificity = 0.24, PPV = 0.24, NPV = 0.78) and identified 78% (33/42) of dropouts; however, 76% (103/136) of completers were also incorrectly identified as dropouts. This threshold also predicted attrition at 12 months with high sensitivity (percent correct = 0.52, sensitivity = 0.80, specificity = 0.26, PPV = 0.49, NPV = 0.59). Table 4 presents the five questions that were the best (highest sensitivity) predictors of attrition at 6 and 12 months.

Discussion

In this public sector sample treated with measurement-based care,^{20,26,51} nearly half of the patients dropped out of medication treatment within the first year. Of those who dropped out, 14% left in the first 3 months and 36% in the second 3 months. Response and remission rates were very low and did not differ between those who did and did not drop out. Younger age

and fewer side effects at baseline were associated with attrition at 6 months. Younger age, better perceived physical functioning, and more negative attitudes about psychiatric medications were associated with attrition at 12 months. More clinic visits was also associated with greater attrition.

The overall attrition rate in the first 3 months (7%, 12/179) following initiation or change in antidepressant treatment was less than the 26% reported in our prior analysis of a mixed public and private sector sample in the first 12 weeks in the STAR*D trial.¹⁰ The 6-month attrition rate (23%, 42/179) was also lower than the 6 month 49% attrition rate reported in a community mental health center sample beginning algorithm-based pharmacotherapy care.¹⁷ It may be that the patient and family education program improved retention.

Since sustaining attendance at medication treatment visits is of substantial importance, it is encouraging that 93% of this public sector group remained in treatment for at least 3 months, and 77% did so for at least 6 months, allowing continuing opportunities to intervene to maximize ongoing retention. It is possible, however, that the patients who agreed to study participation were more highly motivated to remain in treatment than the general population of public sector patients.

The relationship between increased frequency of visits and attrition suggests that visit burden may play a role in patients' willingness to continue in treatment in algorithm-based care or perhaps reflects the difficulty of retaining the more seriously burdened or complicated cases. This is important since the number of visits required to ensure vigorous dosing and careful monitoring of efficacy and side effects is generally more than in standard clinical practice. Increased frequency of visits among dropouts may also have been related to the need for multiple changes in dosing or treatment strategy due to side effects or lack of efficacy, which in turn may have contributed to drop out.

It was a somewhat unexpected finding that the remission and response rates of dropouts and completers at both 6 and 12 months did not differ, although completers at 12 months had had a full year of treatment compared with a mean of approximately 6 months of treatment for dropouts. Modest expectations for remission are, however, consistent with the socioeconomic disadvantage, extensive history of depressive illness, and probable treatment-resistant illness characterizing this group.^{19,23} Given the very high relapse rate with MDD following both remission and especially response without remission,⁵² it is possible, however, that dropouts in this public sector group are at greater risk for relapse or symptom worsening when discontinuing medication.

Younger age was associated with attrition at both time points, consistent with previous reports.^{7,8,10} Older age has been similarly associated with an increase in perceived need for medications.⁵³ Experience with side effects from previous or concurrent medication, as seen by reports of side effects at baseline, predicted retention at 6 months. Side effects and lack of efficacy are the most frequently reported reasons for dropout.^{54,55} The findings presented here, however, suggest that side effects related to medications at study entry may be a signal of perseverance in this population and may be associated with already having engaged in treatment.

Those with better perceived physical functioning were less likely to remain in treatment for a year. Higher perceived mental health functioning, although not higher physical functioning, was associated with discontinuation in the STAR*D study,¹⁰ as well as in a recent naturalistic study.⁵⁶ Both findings may be related to decreased perception of need for help as a reason for treatment discontinuation.

Decision rules for identifying those at risk for dropping out of treatment by 6 months are driven primarily by younger age (under 49 years), increased monthly visit frequency, and MAST scores generally below the threshold that suggests alcohol abuse. Decision rules for those at risk for dropping out by 12 months are driven by younger age (under 40 years) and older age along with more negative perception of medications, especially among those with very low DAST scores suggesting no drug abuse.

It is of interest that greater likelihood of alcohol abuse and somewhat more risk of drug abuse are decision rules suggesting retention in the classification tree. It may be that prior experience with problems has taught participants that treatment is needed. In the STAR*D sample, prior experience with episodes of depression was similarly associated with retention.¹⁰

In this study, Hispanic ethnicity, depressive symptom severity, or years since first onset of depression were not related to attrition, although these predictors were present in the large STAR*D trial.¹⁰ These factors may be of less importance in a public sector population already burdened with comorbid conditions and issues related to lower socioeconomic status, or this sample may not have had sufficient power to identify them.

The finding that negative perception of medications is associated with attrition at 12 months and a trend toward attrition at 6 months is consistent with earlier findings concerning negative attitudes and nonadherence.¹³ This is a useful finding, since attitudes may be modifiable both at the inception of and during treatment. Specific items on the DAI predicted the likelihood of attrition with a reasonable level of sensitivity. The question that best predicted attrition at 6 and 12 months addressed the perception that medications do harm, which is consistent with an earlier report linking skepticism about antidepressants with attrition.¹⁴ The content of the five items that were most sensitive in predicting attrition at both time points focused on perceived negative effects or lack of positive effects of medications rather than broader attitudes about medication or treatment found in other DAI items. Since the DAI assessment was originally developed to evaluate adherence in patients with schizophrenia, however, its content may not be ideally targeted to the symptoms of depression or the effects of antidepressants. Other assessment tools that are shorter and easier to use, such as the Beliefs About Medicines Questionnaire,⁵⁷ merit further investigation for their usefulness in predicting attrition during treatment of MDD.

Findings in this study have policy implications for guiding a personalized approach to minimizing attrition in public sector clinics and allocating scarce resources. All patients may benefit from basic education about depression, expectations about the timing and likelihood of improvement, the likelihood and management of side effects, as well as other basic activities that may assist with retention such as appointment reminders and ease of access. However, the most important choice for clinicians in considering an intervention is not whether it works for *most* patients, but whether it works for a *particular* patient.⁵⁸ Public sector clinics may therefore consider maximizing retention by conducting an individualized review with patients of their beliefs and attitudes about antidepressant treatment both when initiating treatment and again as treatment progresses. This may be especially important with younger patients and patients who require more frequent visits. Clinicians and researchers can easily ask simple questions about beliefs and then draw on the answers to focus personal or support staff resources on responding to specific fears, negative attitudes, and irrational or uninformed perceptions about treatment that the patient may have. Enhancing attitudes about medications has previously been found to be associated with greater adherence to antidepressant medication treatment⁵⁹ and may be helpful in reducing attrition as well.

Ongoing objective self monitoring of symptoms and side effects with feedback from staff may also help all patients achieve a more realistic perception of functioning and self-management.

Such education, support, and monitoring may help substitute for the learning that can come with age and may assist with retention.

Limitations of this study include the lack of randomization of either patients or physicians, lack of blinding of the research outcome assessors to treatment assignment, and likely variability in physician fidelity to the algorithm. Results are exploratory and need to be confirmed in additional studies. The size of the study sample was relatively small, resulting in decreased power to identify differences between groups and to construct more complex models to predict attrition. The study also did not assess whether dropouts and completers received non-medication services at their clinics during the study period, which could have had an impact on retention. It is possible that dropouts received treatment for depression from primary care or other clinicians. Reasons for discontinuation of medication treatment were not collected. Some discontinuations could have involved patient-clinician consensus about treatment completion and based on limited information available, some involved medical reasons for discontinuation. Factors related to clinicians (e.g., experience, race), the patient/clinician alliance, the healthcare system (e.g., appointment wait times) or treatment (e.g., side effects, efficacy) were also not assessed.

This study showed that attitudinal variables are important predictors of treatment attrition. Efforts to elicit attitudes about medications and to use resources to tailor educational or other retention interventions to patients with negative beliefs about antidepressants may be of use in public sector clinics when initiating a new medication and throughout treatment, with particular focus on younger patients and those requiring frequent visits.

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References

1. Melfi CA, Chawla AJ, Croghan TW, et al. The effects of adherence to antidepressant treatment guidelines on relapse and recurrence of depression. *Arch Gen Psychiatry* 1998;55:1128–32. [PubMed: 9862557]
2. Warden D, Rush AJ, Wisniewski SR, et al. What predicts attrition in second step medication treatments for depression?: A STAR*D Report. *Int J Neuropsychopharmacol* 2008 Jul 9;1–15. [epub ahead of print]. 10.1017/S1461145708009073
3. Katon W, Von Korff M, Lin E, et al. Adequacy and duration of antidepressant treatment in primary care. *Med Care* 1992;30:67–76. [PubMed: 1729588]

4. Lin EHB, Von Korff M, Katon W, et al. The role of the primary care physician in patients' adherence to antidepressant therapy. *Med Care* 1995;33:67–74. [PubMed: 7823648]
5. Maddox JC, Levi M, Thompson C. The compliance with antidepressants in general practice. *J Psychopharmacol* 1994;8:48–53.
6. Machado M, Iskudjian M, Ruiz I, et al. Remission, dropouts, and adverse drug reaction rates in major depressive disorder: A meta-analysis of head-to-head trials. *Curr Med Res Opin* 2006;22:1825–37. [PubMed: 16968586]
7. Arnow BA, Blasey C, Manber R, et al. Dropouts versus completers among chronically depressed outpatients. *J Affect Disord* 2007;97:197–202. [PubMed: 16857266]
8. Demyttenaere K, Van Ganse E, Gregoire J, et al. Compliance in depressed patients treated with fluoxetine or amitriptyline. Belgian Compliance Study Group. *Int Clin Psychopharmacol* 1998;13:11–7. [PubMed: 9988362]
9. Last CG, Thase ME, Hersen M, et al. Patterns of attrition for psychosocial and pharmacologic treatments of depression. *J Clin Psychiatry* 1985;46:361–6. [PubMed: 4030699]
10. Warden D, Trivedi MH, Wisniewski SR, et al. Predictors of attrition during initial (citalopram) treatment for depression: A STAR*D report. *Am J Psychiatry* 2007;164:1189–97. [PubMed: 17671281]
11. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999;47:555–67. [PubMed: 10661603]
12. Horne R. Patients' beliefs about treatment: The hidden determinant of treatment outcome? *J Psychosom Res* 1999;47:491–5. [PubMed: 10661596]
13. Brook OH, van Hout HP, Stalman WA, et al. Nontricyclic antidepressants: Predictors of nonadherence. *J Clin Psychopharmacol* 2006;26:643–7. [PubMed: 17110823]
14. Aikens JE, Kroenke K, Swindle RW, et al. Nine-month predictors and outcomes of SSRI antidepressant continuation in primary care. *Gen Hosp Psychiatry* 2005;27:229–36. [PubMed: 15993253]
15. Sirey JA, Bruce ML, Alexopoulos GS, et al. Perceived stigma as a predictor of treatment discontinuation in young and older outpatients with depression. *Am J Psychiatry* 2001;158:479–81. [PubMed: 11229992]
16. Lesser IM, Leuchter AF, Trivedi MH, et al. Characteristics of insured and noninsured outpatients with depression in STAR*D. *Psychiatr Serv* 2005;56:995–1004. [PubMed: 16088018]
17. Bastiaens L. Response to antidepressant treatment in a community mental health center. *Community Ment Health J* 2004;40:561–7. [PubMed: 15672694]
18. Levy H, Young JH. Perspectives from the clinic: Will the average physician embrace personalized medicine? *Clin Pharmacol Ther* 2008;83:492–3. [PubMed: 18253143]
19. Trivedi MH, Rush AJ, Crismon ML, et al. Clinical results for patients with major depressive disorder in the Texas Medication Algorithm Project. *Arch Gen Psychiatry* 2004;61:669–80. [PubMed: 15237079]
20. Trivedi MH, Rush AJ, Wisniewski SR, et al. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: Implications for clinical practice. *Am J Psychiatry* 2006;163:28–40. [PubMed: 16390886]
21. Crismon ML, Trivedi M, Pigott TA, et al. The Texas Medication Algorithm Project: Report of the Texas Consensus Conference Panel on Medication Treatment of Major Depressive Disorder. *J Clin Psychiatry* 1999;60:142–56. [PubMed: 10192589]
22. Rush AJ, Crismon ML, Kashner TM, et al. Texas Medication Algorithm Project, phase 3 (TMAP-3): Rationale and study design. *J Clin Psychiatry* 2003;64:357–69. [PubMed: 12716235]
23. Rush AJ, Trivedi M, Carmody TJ, et al. One-year clinical outcomes of depressed public sector outpatients: A benchmark for subsequent studies. *Biol Psychiatry* 2004;56:46–53. [PubMed: 15219472]
24. Suppes T, Rush AJ, Dennehy EB, et al. Texas Medication Algorithm Project, phase 3 (TMAP-3): Clinical results for patients with a history of mania. *J Clin Psychiatry* 2003;64:370–82. [PubMed: 12716236]
25. Miller AL, Crismon ML, Rush AJ, et al. The Texas Medication Algorithm Project: Clinical results for schizophrenia. *Schizophr Bull* 2004;30:627–47. [PubMed: 15631256]

26. Trivedi MH, Rush AJ, Gaynes BN, et al. Maximizing the adequacy of medication treatment in controlled trials and clinical practice: STAR*D measurement-based care. *Neuropsychopharmacology* 2007;32:2479–89. [PubMed: 17406651]
27. Trivedi MH, Daly EJ. Measurement-based care for refractory depression: A clinical decision support model for clinical research and practice. *Drug Alcohol Depend* 2007;88:S61–S71. [PubMed: 17320312]
28. Rush AJ, Gullion CM, Basco MR, et al. The Inventory of Depressive Symptomatology (IDS): Psychometric properties. *Psychol Med* 1996;26:477–86. [PubMed: 8733206]
29. Rush AJ, Carmody TJ, Reimnitz PE. The Inventory of Depressive Symptomatology (IDS): Clinician (IDS-C) and self-report (IDS-SR) ratings of depressive symptoms. *Int J Methods Psychiatr Res* 2000;9:45–59.
30. Trivedi MH, Rush AJ, Ibrahim HM, et al. The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: A psychometric evaluation. *Psychol Med* 2004;34:73–82. [PubMed: 14971628]
31. Toprac MG, Rush AJ, Conner TM, et al. The Texas Medication Algorithm Project patient and family education program: A consumer-guided initiative. *J Clin Psychiatry* 2000;61:477–86. [PubMed: 10937605]
32. Toprac MG, Dennehy EB, Carmody TJ, et al. Implementation of the Texas Medication Algorithm Project patient and family education program. *J Clin Psychiatry* 2006;67:1362–72. [PubMed: 17017822]
33. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep* 1962;10:799–812.
34. Ventura J, Green MF, Shaner A, et al. Training and quality assurance with the Brief Psychiatric Rating Scale: “The drift busters”. *Int J Methods Psychiatr Res* 1993;3:221–44.
35. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale: Recent developments in ascertainment and scaling. *Psychopharmacol Bull* 1988;24:97–9.
36. Rush AJ, Giles DE, Schlessner MA, et al. The Inventory for Depressive Symptomatology (IDS): preliminary findings. *Psychiatry Res* 1986;18:65–87. [PubMed: 3737788]
37. Levine J, Schooler NR. SAFTEE: A technique for the systematic assessment of side effects in clinical trials. *Psychopharmacol Bull* 1986;22:343–81. [PubMed: 3774930]
38. Rabkin JG, Markowitz JS. Side effect assessment with SAFTEE: Pilot study of the instrument. *Psychopharmacol Bull* 1986;22:389–96. [PubMed: 3774932]
39. Lehman AF. A quality of life interview for the chronically mentally ill. *Eval Program Plann* 1988;11:51–62.
40. Frisch, MB. Manual and treatment guide for the quality of life inventory. Minneapolis: National Computer Systems; 1994.
41. Russo J, Roy-Byrne P, Reeder D, et al. Longitudinal assessment of quality of life in acute psychiatric inpatients: Reliability and validity. *J Nerv Ment Dis* 1997;185:166–75. [PubMed: 9091598]
42. Frisch MB, Clark MP, Rouse SV, et al. Predictive and treatment validity of life satisfaction and the quality of life inventory. *Assessment* 2005;12:66–78. [PubMed: 15695744]
43. Ware JE, Kosinski M, Keller SD. A 12-item Short-Form Health Survey. Construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–33. [PubMed: 8628042]
44. Skinner HA. The drug abuse screening test. *Addict Behav* 1982;7:363–71. [PubMed: 7183189]
45. Selzer ML. The Michigan alcoholism screening test: the quest for a new diagnostic instrument. *Am J Psychiatry* 1971;127:1653–8. [PubMed: 5565851]
46. Hogan TP, Awad AG, Eastwood R. A self-report scale predictive of drug compliance in schizophrenics: Reliability and discriminative validity. *Psychol Med* 1983;13:177–83. [PubMed: 6133297]
47. Kashner TM, Rush AJ, Altshuler KZ. Measuring costs of guideline-driven mental health care: The Texas Medication Algorithm Project. *J Ment Health Policy Econ* 1999;2:111–21. [PubMed: 11967419]
48. Breiman, L.; Friedman, JH.; Olshen, RA., et al. Classification and regression trees. Monterey: Wadsworth and Brooks/Cole; 1984.

49. Therneau, TM.; Atkinson, EJ. Technical Report #61. Rochester, MN: Department of Health Sciences Research, Section of Biostatistics, Mayo Clinic, Rochester; 1997. An introduction to recursive partitioning using the RPART routines.
50. Kraemer, HC. Evaluating medical tests: objective and quantitative guidelines. Newbury Park, CA: Sage Publications; 1992.
51. Rush AJ. Strategies and tactics in the management of maintenance treatment for depressed patients. *J Clin Psychiatry* 1999;60(suppl 14):21–6. [PubMed: 10408422]
52. Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: A STAR*D report. *Am J Psychiatry* 2006;163:1905–17. [PubMed: 17074942]
53. Aikens JE, Nease DE Jr, Klinkman MS. Explaining patients' beliefs about the necessity and harmfulness of antidepressants. *Ann Fam Med* 2008;6:23–9. [PubMed: 18195311]
54. Beasley CM Jr, Koke SC, Nilsson ME, et al. Adverse events and treatment discontinuations in clinical trials of fluoxetine in major depressive disorder: An updated meta-analysis. *Clin Ther* 2000;22:1319–30. [PubMed: 11117656]
55. Vis PM, van Baardewijk M, Einarson TR. Duloxetine and venlafaxine-XR in the treatment of major depressive disorder: A meta-analysis of randomized clinical trials. *Ann Pharmacother* 2005;39:1798–807. [PubMed: 16189284]
56. Olfson M, Marcus SC, Tedeschi M, et al. Continuity of antidepressant treatment for adults with depression in the United States. *Am J Psychiatry* 2006;163:101–8. [PubMed: 16390896]
57. Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire (BMQ): The development and evaluation of a new method for assessing the cognitive representation of medicine. *Psychol Health* 1998;14:1–24.
58. Mant D. Can randomised trials inform clinical decisions about individual patients? *Lancet* 1999;353:743–6. [PubMed: 10073531]
59. Lin EH, Von Korff M, Ludman EJ, et al. Enhancing adherence to prevent depression relapse in primary care. *Gen Hosp Psychiatry* 2003;25:303–10. [PubMed: 12972220]

Figure 1. Classification Tree to Predict Attrition at 6 Months

Ellipse: Node that can be further split

Rectangle: Terminal node

MAST: Michigan Alcohol Screening Test SAFTEE: Systematic Assessment for Treatment

Emergent Events SF-12 Mental: Mental subscale of the Short-Form Health Survey

Figure 2. Classification Tree to Predict Attrition at 12 Months

Ellipse: Node that can be further split

Rectangle: Terminal node

DAI: Drug Attitude Inventory

DAST: Drug Abuse Screening Test

Table 1
Baseline Characteristics of the Sample In Measurement-based Care

	%	Mean (SD)
Age		41.3 (11.6)
Female	80.4	
Race:		
Hispanic	24.0	
Black	15.6	
White/Other	60.3	
Years of Education		11.3 (2.8)
Marital Status		
Never Married	19.6	
Separated/Divorced/Widowed	49.7	
Married	30.7	
Living Alone	20.7	
Employed	18.2	
Length of Illness		12.1 (11.0)
Single major depressive episode	10.6	
Psychotic symptoms	18.4	
General Medical Condition		
0	41.9	
1	31.8	
2+	26.3	
<i>Symptom severity</i>		
30-item Inventory of Depressive Symptomatology–Clinician-rated (IDS-C ₃₀)		42.5 (13.6)
IDS-C ₃₀ insomnia items		4.8 (2.7)
18-item Brief Psychiatric Rating Scale		39.9 (8.7)
<i>Function and Quality of Life</i>		
12-item Short-Form Health Survey – Mental		27.7 (9.7)
12-item Short-Form Health Survey – Physical		38.5 (11.6)
Quality of Life Interview		2.8 (1.5)
Drug Abuse Screening Test		2.3 (3.3)
Michigan Alcohol Screening Test		4.8 (6.4)
<i>Medication Side Effect Burden</i>		
Systematic Assessment for Treatment Emergent Events		13.9 (4.7)
Drug Attitude Inventory		18.2 (8.5)

Table 2
Response and Remission Rates by Attrition Status in Measurement-based Care (N=178^a)

	Dropouts 6 Months (n=41)	Completers 6 Months (n=137)	Dropouts 12 Months (n=83)	Completers 12 Months (n=95)
% Responders	17.1%	23.4%	21.7%	22.1%
% Remitters	9.8%	8.8%	8.4%	9.5%

^aOne patient is missing all values for IDS-C30, so response/remission status is unknown.

No significant differences were found between dropouts and completers for response rates (chi-square=0.7, df=1, p=.3934) or remission rates (chi-square=0.04, df=1, p=.8448) at 6 months, or for response rates (chi-square=0.01, df=1, p=.9463) or remission rates (chi-square=0.06, df=1, p=.8088) at 12 months.

Table 3
Baseline Characteristics as Predictors of Attrition at 6 and 12 Months

Predictor	6-Month Findings			12-Month Findings		
	OR	CI	p-value ^a	OR	CI	p-value ^d
Age ^b						
Gender (male relative to female)	0.74	0.62-0.87	0.0004	0.80	0.70-0.92	0.0013
Race	1.40	0.61-3.22	0.4279	1.93	0.91-4.09	0.0870
Hispanic relative to white	0.93	0.39-2.20	0.4962	1.09	0.53-2.21	0.4899
Black relative to white	1.66	0.67-4.14		1.67	0.72-3.86	
White (reference category)	1.00			1.00		
Years of education	1.08	0.95-1.23	0.2330	1.03	0.93-1.15	0.5482
Marital status			0.2112			0.6238
Never married relative to married	2.35	0.88-6.24		1.42	0.61-3.34	
Separated/divorced/widowed relative to married	1.30	0.56-3.04		0.98	0.50-1.92	
Married (reference category)	1.00			1.00		
Living alone (relative to not living alone)	1.14	0.48-2.73	0.7667	1.85	0.87-3.91	0.1095
Employed (relative to unemployed)	1.87	0.67-5.20	0.2324	0.66	0.30-1.42	0.2879
Length of illness ^b	0.94	0.79-1.12	0.4854	1.07	0.93-1.22	0.3494
Single/recurrent major depressive episode (single relative to recurrent)	2.08	0.76-5.69	0.1522	1.29	0.50-3.35	0.5989
Psychotic symptoms (relative to nonpsychotic)	1.47	0.56-3.85	0.4302	1.70	0.78-3.71	0.1811
General medical conditions (GMCs)			0.2093			0.3384
None relative to 2 or more GMCs	1.80	0.69-4.72		1.75	0.83-3.67	
1 GMC relative to 2 or more GMCs	2.43	0.91-6.49		1.45	0.66-3.18	
2 or more GMCs (reference category)	1.00			1.00		
<i>Symptom Severity</i>						
Inventory of Depressive Symptomatology–Clinician-rated, 30-item (IDS-C ₃₀) ^b	0.96	0.85-1.09	0.5356	1.01	0.91-1.13	0.8559
IDS-C ₃₀ insomnia items	0.98	0.86-1.12	0.7355	1.00	0.90-1.12	0.9478
Brief Psychiatric Rating Scale (18-item) ^b	1.01	0.82-1.23	0.9500	1.05	0.88-1.24	0.6010
<i>Function and Quality of Life</i>						
Short-form Health Survey (SF-12) Mental ^b	1.09	0.91-1.30	0.3405	1.01	0.87-1.18	0.8859

Predictor	6-Month Findings				12-Month Findings			
	OR	CI	p-value ^a		OR	CI	p-value ^a	
Short-form Health Survey (SF-12) Physical ^b	1.10	0.95-1.28	0.2211		1.27	1.10-1.46	0.0007	
Quality of Life Interview (QOLI) subscale	0.99	0.78-1.25	0.9244		0.97	0.80-1.19	0.7920	
Drug Abuse Screening Test (DAST)	1.05	0.96-1.15	0.3041		1.00	0.92-1.09	0.9818	
Michigan Alcohol Screening Test (MAST)	0.93	0.87-1.01	0.0857		0.99	0.95-1.04	0.8117	
<i>Medication Side Effect Burden</i>								
Systematic Assessment for Treatment Emergent Events (SAFTEE)	0.93	0.86-1.00	0.0376		0.97	0.91-1.03	0.2657	
Drug Attitude Inventory (DAI-30)	0.97	0.93-1.01	0.1007		0.95	0.92-0.99	0.0075	

^aAll p-values are based on Wald Chi-square tests with 1 degree of freedom except for race, marital status, and GMCs, which have 2 degrees of freedom.

^bOdds ratio is the change in odds for a 5-year (for age) or a 5-point or 5-year increment in the predictor. All other odds ratios of continuous predictors are for a 1-point increment in the predictor.

OR = odds ratio; CI = confidence interval

Table 4
Drug Attitude Inventory Items That Best Predict Attrition at 6 and 12 Months

Item	Sensitivity	Attrition at 6 Months		
		Specificity	NPV	PPV
7. Taking medications will do me no harm. (negative response)	0.46	0.71	0.81	0.32
21. My thoughts are clearer on medication. (negative response)	0.39	0.74	0.80	0.31
6. I am more aware of what I am doing, of what is going on around me, when I am on medication. (negative response)	0.38	0.76	0.80	0.33
15. I get along better with people when I am on medication. (negative response)	0.36	0.74	0.79	0.30
18. I feel more normal on medication. (negative response)	0.33	0.80	0.80	0.34

Item	Sensitivity	Attrition at 12 Months		
		Specificity	NPV	PPV
7. Taking medications will do me no harm. (negative response)	0.42	0.74	0.59	0.59
12. Medication makes me feel tired and sluggish.	0.42	0.63	0.55	0.50
6. I am more aware of what I am doing, of what is going on around me, when I am on medication. (negative response)	0.36	0.80	0.58	0.61
21. My thoughts are clearer on medication. (negative response)	0.36	0.77	0.58	0.58
15. I get along better with people when I am on medication. (negative response)	0.35	0.78	0.57	0.58

PPV-positive predictive value

NPV-negative predictive value