Translating Science Into Service: Lessons Learned From the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study

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Objective: The purpose of this review is to summarize lessons learned from, and limitations of, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, focusing on measurement-based care.

Data Sources: PubMed and MEDLINE were searched from 1980 through 2006 using terms such as *depression*, *major depressive disorder*, *augmentation*, *switching*, *measurement-based care*, and *remission*. Other relevant articles were identified by checking reference lists of the identified studies.

Study Selection: A total of 60 studies were initially identified, which resulted in 34 studies used in this review. The salient criteria used for selection of studies centered on whether results had implications for clinical practice and provided lessons that could be learned and practically applied to real-life settings.

Data Extraction: Data were extracted from the STAR*D trial and associated studies that were pertinent to everyday problems encountered by mental health professionals in the community: determination of whether the optimum strategy for a particular patient involves "augmentation" or "switching" of a patient's medication.

Data Synthesis: Measurement-based care is essential in order to identify the two thirds of patients who do not achieve remission with the first treatment strategy. Timely changes in antidepressant therapy can improve outcomes.

Conclusions: The STAR*D trial underscores the importance of measurement-based care in identifying patients who may not have achieved remission with an initial antidepressant, enabling alternative options such as augmentation or switching to be prescribed to meet this ultimate goal of therapy.

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A prominent characteristic of depression is the diverse nature of the disorder that varies in multiple dimensions: quantity and nature of symptoms, patient age at onset, path and result, severity, associated conditions, reaction to treatment, extent of impairment, and occurrence or absence of antecedents.[1] Congruent with the diversity of the disorder is the variety of available pharmacologic agents (or combinations thereof), their mechanisms of action on different receptors, the multitude of talk therapies, the degrees of response to treatment, and the ways of defining treatment success.[1]

The World Health Organization has estimated that depression affects approximately 340 million people globally[2,3] and 35 million adults in the United States.[4] The National Comorbidity Survey estimated the lifetime prevalence of depression to be more than 17% with a disproportionate impact on women.[5,6] Worldwide, in 2020, unipolar major depression is predicted to be the second greatest contributor to the burden of disease behind ischemic heart disease.[7]

Treatment guidelines regarding antidepressant effectiveness following failure of previous treatments were murky before the advent of results from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study because previous studies were not based on strong empirical findings. Individual trials were often undersized and lacked the necessary statistical power to differentiate "good" from "better." Oftentimes, patients included in trials were not representative of clinical practice, and restrictive exclusion criteria were employed. Trials were

frequently too short in duration to determine effectiveness of treatments, and the sponsorship of almost all trials by pharmaceutical companies raised the suspicions of patient advocacy groups.[8]

The STAR*D study provided credible research-based data. Physicians were understandably enthusiastic for the accurate data and recommendations applicable to their practices resulting from this antidepressant mega-trial.[8] Scientific data identifying the most precise, effective, next-step treatment choices for treatment-resistant depression (TRD) should improve clinical results and may decrease the cost of care.[9] It will be important to summarize and apply lessons learned from STAR*D to help primary care physicians make rational decisions and develop personalized care for patients with nonpsychotic depression. This review summarizes lessons learned from and limitations of STAR*D, focusing on measurement-based care. PubMed and MEDLINE were searched from 1980 through 2006 using terms such as *depression*, *major depressive disorder (MDD)*, *augmentation*, *switching*, *measurement-based care*, and *remission*. Other relevant articles were identified by checking reference lists of the identified studies. A total of 60 studies were initially identified, which resulted in 34 studies used in this review. The salient criteria used for selection of studies centered on whether results had implications for clinical practice and provided lessons that could be learned and practically applied to real-life settings.

TEXAS MEDICATION ALGORITHM PROJECT

The Texas Medication Algorithm Project (TMAP),[10] which was a forerunner of STAR*D, developed practical algorithms or rule-based deductive systems that operated with inputs, sequences, time frames, and outputs. The purpose of this "tool" was to assimilate and revise existing research information and clinical experience into the development of user-friendly flow diagrams called medication decision trees.[10,11]

In general, as a problem-solving aid, algorithms can reduce unnecessary variation in clinical practice patterns, facilitate strategic and tactical decision making, make clinical decisions explicit, improve the overall quality of treatment, and facilitate the measurement of patient progress.[10,11] There are potential dangers associated with algorithms: inadequate evidence base for strategies, opinions not derived from consensus, heightened costs and consumption of services, surrogate for clinical judgment, and reduced overall standard of care delivered to patients.[10]

The methods for developing algorithms are variable and can involve formal and informal consensus development, and both evidence-based and explicit guideline development.[10] Barriers to using guidelines include the reluctance by physicians to accept the outcome of a flow diagram as opposed to using their own judgment, the initial and ongoing training required to successfully implement and sustain the use of algorithms, the perception that guidelines are more static than dynamic in nature, and the anxiety related to patient adherence to guideline-directed treatment.[10] Yet, there is evidence supporting the use of algorithms. Randomized controlled trials (RCTs) have demonstrated that the use of algorithms improves outcomes for depressed patients compared with usual care.[12]

The groundwork for the development and implementation of medication treatment algorithms for patients treated in public mental health systems was provided by TMAP.[11] A study comparing TMAP with usual care demonstrated the value and practicability of treatment algorithms.[12]

SEQUENCED TREATMENT ALTERNATIVES TO RELIEVE DEPRESSION (STAR*D)

The STAR*D study was a multisite, multistep, prospective, randomized, clinical trial of outpatients with nonpsychotic MDD.[9] This mega-trial was more rooted in the real world than previous clinical trials characterized by restrictive inclusion and exclusion criteria. The study provided pertinent data on real-world outcomes in everyday patients.[13] The estimated cost was $35 million over 6 years.[14] Importantly, STAR*D was not sponsored by the pharmaceutical industry, and there were hardly any dosing restrictions. The inclusion criteria were broad, and there were few exclusion criteria; results are applicable to general practice.[8]

Ultimately, the strategic vision is personalized care. According to Thomas Insel, M.D., director of the National Institute of Mental Health (NIMH), "By beginning to identify which particular treatment benefits which patient, the STAR*D trial takes us a little closer by realizing this vision for nonpsychotic depression."[14] Dr. Insel also stated that "The real goal of STAR*D is how best to help the 70% of patients for whom treatment with a representative selective serotonin reuptake inhibitor (SSRI) is not enough for remission."[14]

The stated primary goal of the STAR*D study was to assess the effectiveness of adequately delivered treatments in "real-world" outpatients who have MDD.[15] The study included 4 levels of treatment.[9] All participants began at level 1 and were treated with the SSRI citalopram. If the participants did not achieve satisfactory outcomes, they were allowed to progress to level 2, which determined the most effective next-step treatments for the participants who did not become symptom free or could not tolerate initial treatment with citalopram in level 1.[9,16,17]

In order to define an adequate (or inadequate) response to treatment, there must be some agreement regarding definitions. It is now commonly accepted that depression can and should be treated to within normal limits.[18] Re-

mission has been defined as the key goal of treatment because remitters are less likely to relapse and overall societal costs are reduced.[19] Ultimately, treatment must be satisfactory to patients, be predictably successful, and convey minimal adverse effects.[19]

A satisfactory clinical response, instead of remission, is no longer viewed as impossible to achieve. Primary outcome is measured via a clinician-rated 17-item Hamilton Rating Scale for Depression,[9,20–22] administered at entry and exit from each treatment level during telephone interviews. Secondary outcomes include self-reported depressive symptoms, physical and mental function, and side effect burden.[9] An inadequate or unsatisfactory response has numerous definitions: pseudoresistance due to inadequate treatment,[23,24] failure to respond to conventional treatment[25] as measured operationally,[25] or failure to recognize comorbid conditions.[26] Thus, difficult to treat depression consists of TRD that intrinsically does not react to effective treatments optimally delivered and suboptimal delivery of effective treatments (e.g., use of subtherapeutic doses, nonadherence, unbearable adverse effects, concurrent Axis I, II, or III conditions).[27]

Level 1

In level 1 of the study, 2876 outpatients received flexible-dose citalopram for up to 14 weeks.[15] Rates of response and remission were 47% and 28%, respectively. In general, remission rates were higher among participants who were white, female, employed, better educated, and highly paid. Lower remission rates were associated with more concurrent general medical and psychiatric disorders, worse pretreatment physical and mental function, lower satisfaction with life, and a longer current depressive episode. Overall, approximately two thirds of the participants did not achieve remission in level 1 of the STAR*D study.[15] The authors point to the open-label study design, the inclusion of citalopram as the only antidepressant under evaluation, and the absence of a placebo control as possible explanations for the relatively low rate of remission.[15] An alternative explanation may be the broad inclusion criteria that did not distinguish between patients with unipolar and bipolar depression; antidepressants may be ineffective in the bipolar patient, as they can trigger a switch from the depressive to the manic phase.[28]

Citalopram was well tolerated in this study.[15] More than two thirds of participants reported adverse events as mild or moderate in intensity, and only about 9% of participants discontinued the study due to intolerable adverse effects.[15]

Level 2

Level 2 of the study offered 7 different treatments: 4 options switched study participants from citalopram to an alternative treatment strategy (either new medication or psychotherapy), and 3 of the options augmented citalopram treatment by adding a new medication or psychotherapy to the regimen of citalopram they were already receiving.[9,16]

Due to participants' choices, 51% of those who entered level 2 of STAR*D (727/1439) agreed to treatments that included a switch to a different medication, and those patients were randomly assigned to receive the medication.[29] These participants were given 1 of 3 widely used medications, bupropion sustained release (SR), sertraline, or venlafaxine extended release (ER), for up to 14 weeks. About 1 in 4 of the 727 people who participated in the switch study became symptom free. Remission rates were 25% for venlafaxine ER, 21% for bupropion SR, and 18% for sertraline. Although an "out of class" switch produced numerically higher remission rates than a "same class" switch, these differences did not separate statistically.[29] All 3 medications were also equally safe and well tolerated; nearly two thirds of the associated adverse effects were reported as mild or moderate in nature, and an average of only 23% of participants discontinued due to intolerable adverse effects.[29]

In an attempt to explain the lack of significant differences between the medications included in STAR*D,[29] the authors admit that the absence of a placebo group precluded the conclusion that the observed results can be attributed to the specific effects of the medications chosen for comparison. In addition, the study design was perhaps statistically underpowered, and a significant 7% to 10% differentiation between treatments may have been detected if the study had included a larger number of participants.[30–32]

Nevertheless, the authors concluded that any of the 3 switch medications is a useful second step in the treatment of people with MDD who do not become symptom free after initial treatment with an antidepressant.[29] The implications for clinical practice argue in favor of switching: decreased medication-related outlays, fewer possible side effects, and improved patient adherence with monotherapy.[11] Cumulative remission rates after citalopram and the switch to another treatment were approximately 50%. These data underscore the value of repeated attempts to achieve remission and the need, if there are setbacks, to continue trying to achieve remission.[29]

Thirty-nine percent (565/1439) of the participants who entered level 2 agreed to treatments that included adding another medication to the citalopram they were already receiving and were randomly assigned to receive medication augmentation.[17] These other medications were either bupropion SR or buspirone, which were added to their treatment for up to 14 weeks. Approximately one third of the 565 patients in the augmentation study achieved remission when a second medication was added to citalopram. Response rates for bupropion SR and buspirone were approximately 32% and 27%, respectively.[17] The adverse event intensity (≈70%) and discontinuation rates

(≈17%) were similar to those in the level 2 switch group.[17]

While the percentage of people with remission and the amount of time it took them to become symptom free were about the same with both medications, there were advantages of bupropion SR over buspirone on secondary outcome measures (i.e., greater adherence to treatment, decreased rates of discontinuation, and a lower rate of treatment cessation).[17] Participants receiving bupropion had a slightly better outcome in terms of reduction of symptoms and tolerability of side effects.[17] As with the switch study,[29] these results demonstrate the value of a second step (in this case augmentation) following failure of initial treatment.

Psychotherapy (Switch/Augment) Treatment Study

The remaining 147 (of 1439) participants in level 2 were randomly assigned to switch to cognitive therapy alone or to augment citalopram with cognitive therapy.[29] These data have not yet been published.

Level 3

Level 3 of the STAR*D study offered 4 different treatments: 2 options switched study participants to an alternative treatment strategy (either mirtazapine or nortriptyline), and 2 options augmented treatment with either lithium or triiodothyronine.

In the switch study, mirtazapine and nortriptyline were compared as a third-step antidepressant monotherapy regimen.[33] A total of 114 participants were randomly assigned to mirtazapine and 121 to nortriptyline for up to 14 weeks.[33] Only a modest proportion of participants attained symptom-free status. Rates of response and remission were 13% and 12%, respectively, for mirtazapine and 17% and 20%, respectively, for nortriptyline. The 2 antidepressants did not statistically differ in response, remission, tolerability, or adverse events. The authors noted that neither underdosing nor inadequate treatment durations were likely to have influenced remission rates. Overall, they concluded that there are only modest odds of achieving remission after switching antidepressants as a third-step treatment strategy for MDD following 2 consecutive failed treatment trials.[33]

The augmentation study compared the efficacy and tolerability of lithium and triiodothyronine as a third-step treatment for MDD.[34] A total of 69 participants were randomly assigned to augmentation with lithium and 73 to augmentation with triiodothyronine for up to 14 weeks. Remission rates were approximately 16% for lithium and 25% for triiodothyronine augmentation. Although no statistical differences in efficacy were observed between groups, triiodothyronine showed slight benefits over lithium in terms of symptom reduction.[34] In addition, triiodothyronine augmentation was better tolerated than lithium augmentation, which was associated with significantly more frequent side effects. Also, nearly twice as many participants who received lithium withdrew from the study because of side effects. The authors concluded that while both augmentation treatments were associated with similar, modest rates of remission, the lower side effect burden and ease of use of triiodothyronine suggest that the drug may have slight advantages over lithium augmentation in difficult to treat depression.[34]

Level 4

Level 4 of the STAR*D study offered 2 different switch options for patients who had not adequately responded to the 3 prior medication trials.[35] A total of 58 participants were randomly assigned to tranylcypromine and 51 to venlafaxine ER plus mirtazapine. Remission rates were 7% for the tranylcypromine group and 14% for the venlafaxine ER plus mirtazapine group. Although the remission rates were modest and not statistically different, it is important to note that the medication doses used in the study did not approach the upper limit of the protocol-recommended dosing.[35] Significant differences between groups were observed in tolerability; participants in the tranylcypromine group were more likely to withdraw early from the trial and to withdraw due to side effects. Overall, the authors concluded that the lower side effect burden, lack of dietary restrictions, and ease of use of venlafaxine XR plus mirtazapine suggest that the combination may have slight advantages over tranylcypromine in patients with highly treatment-resistant MDD.[35]

Follow-Up

Participants who achieved a satisfactory benefit from treatment, preferably symptom remission, from any level of the STAR*D trial were eligible to enter a 12-month naturalistic follow-up phase.[36] At entry into the follow-up phase, participants who were in remission had a better prognosis than those who had symptom improvement without remission. However, regardless of remission status at entry into the follow-up phase, rates of relapse during follow-up were significantly higher among participants who required more treatment steps. Furthermore, mean time to relapse was shorter among patients who required more treatment steps. Overall, participants who needed more treatment steps (i.e., were more treatment resistant) during the STAR*D trial had poorer outcomes in the longer-term phase.[36] These data are consistent with findings from the acute treatment phase, in which progressively lower rates of remission were associated with each of the 4 treatment levels during the trial. Remission rates for the first, second, third, and fourth acute treatment levels were approximately 37%, 31%, 14%, and 13%, respectively. While participants who needed more acute treatment steps (i.e., were more treatment resistant) during the STAR*D trial had a greater illness burden (i.e., depression chronicity, psychiatric or general

comorbidity), little is known yet about the clinical factors, such as particular acute treatments or baseline clinical features, associated with better longer-term outcomes in the STAR*D trial.[36]

Nontreatment Findings

Several studies have examined baseline clinical characteristics of the first 1500 consecutive participants enrolled in STAR*D. Gaynes and colleagues[37] compared clinical features of depression in patients who entered the trial from primary care and specialty care settings and found that MDD is more similar than different among patients in the 2 settings. In general, patients from primary care and specialty care settings presented with equivalent degrees of depressive severity and similar symptom presentations.[37] A few core symptoms—depressed mood, anhedonia, and weight loss—were more common among specialty care patients. Prior suicide attempts were also twice as common in specialty care patients. Primary care patients reported a slightly higher quality of life, but more general medical comorbidities, a longer current depressive episode, and a slightly older age at first onset of depression.[37]

Rush et al.[38] examined concurrent psychiatric comorbidities and associated clinical and sociodemographic features. Approximately 60% of the STAR*D participants had at least 1 concurrent Axis I condition. The most common comorbid conditions were social anxiety disorder (29%), generalized anxiety disorder (21%), and posttraumatic stress disorder (19%).[38] Participants with more concurrent Axis I conditions had younger ages at first onset of MDD, longer histories of MDD, greater depressive symptom severity, more general medical morbidity, worse mental and physical function, and a greater likelihood of being seen in a primary care setting.[38]

Marcus and coworkers[39] explored gender differences in the rates and course of MDD among the STAR*D participants. Women comprised approximately 63% of the sample and reported a somewhat earlier age at onset of first major depressive episode, as well as a somewhat longer length of the current depressive episode.[39] Women were significantly more likely to have more symptoms consistent with generalized anxiety disorder, somatoform disorder, and bulimia, as well as atypical symptoms, including mood reactivity, interpersonal sensitivity, and increased appetite and weight gain. Men were more likely to have symptoms of obsessive-compulsive disorder and alcohol and drug abuse.[39]

IMPLICATIONS FOR CLINICAL PRACTICE

Prominent arguments in favor of augmentation include prevention of the abandonment of partial response with monotherapy and the resultant patient discouragement over an unsuccessful treatment trial, apprehension associated with depressive symptoms when a partially effective antidepressant is discontinued, and evidence that some augmentation tactics convert partial responders, and even nonresponders, to full remitters.[11] As with the switch study,[29] the fact that an additional 30% of patients achieved remission following initial failure highlights the need to make timely and rational changes in therapy in order to achieve remission.[17]

It is important to avoid comparing results of the switch and augmentation trials. Study design allowed for patients to opt out of particular strategies. For example, patients could decline switching altogether but accept randomization to achieve augmentation, or consider psychotherapy as either a switch or augmentation strategy.[9] Hence, the patients who ended up in the level 2 switch study were not the same as those in the level 2 augmentation trials.[17,29] Specifically, the patients in the switch group experienced a more severe depression at level 2 baseline and had achieved less of a therapeutic response during level 1 than those in the augmentation group.[17,29]

OVERALL MESSAGE

The knowledge available to guide treatment choices for people with depression is greatly enhanced by the STAR*D findings. For the first time, practitioners and individuals with MDD have extensive information on antidepressant treatments from a single, large, long-term study directly comparing the drugs with each other.[9,16]

It can now be stated with some confidence that approximately 30% of patients will achieve remission following initial treatment with an SSRI[13,14] and that switching to or augmenting with another medication results in an additional one fourth[29] to almost one third[17] of patients achieving remission. Hence, approximately 50%[16] of patients will achieve remission with 2 treatment steps. In clinical practice, this highlights 2 very important principles: (1) Measurement-based care is essential.[25,27] Unless we are monitoring our patients' progress, we will not be able to identify the two thirds of patients[15,17] who do not achieve remission with the first treatment strategy. (2) Timely changes in antidepressant therapy can improve outcomes.[17] Robust clinical evidence documents the value of changing the treatment strategy following failure of an adequate trial of an initial medication.[17,29]

It is important to note that because there were too few patients who accepted randomization to both the switch and augmentation options, STAR*D will not be able to directly compare these strategies.[29] Thus, practitioners do not yet know how to predict which patient will do better with either the switching or augmentation strategy.

The overall message of STAR*D is that if the first-step treatment does not work, a range of effective second-step treatments are available. It is important for patients to work with their providers and to persist with therapy. The

STAR*D results also indicate that for some patients, while early benefits may occur with these treatments within the first 3 to 6 weeks, achieving full benefits may take up to 12 weeks.[9] During treatment, it is important to adjust the dose as tolerated and not stop therapy prematurely. In addition, the results[9,17,29] show that 50% of people[13,29] with depression can achieve remission with the 2 treatment steps outlined in the study.[9,16]

LESSONS LEARNED AND LIMITATIONS

Because the inclusion and exclusion criteria were more relaxed as compared with RCTs, and were more reflective of real-world practice, the generalizability of the results is undeniable. Furthermore, because of the real-world foundation of the patients and the medication administration, the study possesses ecologic validity. Sponsorship by NIMH[8] enhances the credibility of the results, and the extended length of treatment was important.[8] In addition, aggressive dosing proved to be indispensable, as was the employment of "critical decision points" with measurement-based care.[15]

As mentioned previously, limitations of the study included the open treatment design, the use of a single antidepressant agent (citalopram) in level 1, the lack of a placebo control, and the inclusion of patients with previous SSRI treatment experience (likely decreased citalopram response).[15] Ultimately, study design, to a great degree, influences the kind of data the clinical trial produces.[8] The equipoise randomization scheme,[9] although extremely useful in a statistical sense, prevented comparisons across strategies.[29] The sample size in individual substudies might not have been powered to detect potentially clinically meaningful differences among treatments.

A major shortcoming of the STAR*D trial, in terms of real-world treatment decision making, was the absence of a mood stabilizer monotherapy option for subjects who failed at levels 1 and 2. Because DSM-IV diagnostic criteria were used in the study, patients with bipolar disorder were excluded from participation.[15] Many experts take issue with the current diagnostic scheme, positing that the boundaries of MDD and bipolar depressions are more ambiguous than the DSM-IV constructs.[40] Current diagnostic practices, they argue, lead to MDD being both overdiagnosed and overtreated at the expense of bipolar disorder.[40] These experts submit that there is a broad bipolar spectrum between the extremes of psychotic manic-depressive illness and strictly defined unipolar depression. The narrow concepts of bipolar and unipolar disorders would thus deprive many patients with lifelong depressive episodes the benefits of mood stabilizing agents.[40] This observation is relevant to the STAR*D results, since studies have shown that short-term nonresponse is more frequent in bipolar than unipolar depression.[41]

Those patients least responsive to treatment in the STAR*D trial may have fared better if they had been treated as if they were bipolar. Bipolar disorder may be underrecognized because the current conceptualization of these mood disorders does not take into account those patients whose "highs" are not severe. As a rule, bipolar patients lack insight into their elevated mood states, seeking help only when depressed. Only with questioning by the clinician, and additional information from a patient's friend or family member, does it become evident that mood cycling occurs. Therefore, depressed patients with an early onset of depression, multiple recurrences of depression, close family members with a history of mania or hypomania, and a family history of alcoholism may in fact represent a subtype of mood disorder that responds poorly to antidepressants, but responds well to drugs like lamotrigine or quetiapine, agents that have been shown to benefit bipolar depression. Given the decreasing likelihood of response and remission among those patients needing to go to levels 3 and 4, not to mention the increased risk of relapse and recurrence among that group, it would be useful to know if a mood stabilizer alone or in combination with an antidepressant would yield a better outcome.

FUTURE STUDIES

The results of STAR*D are instructive in that they can greatly inform future studies. For example, future studies could use population subsets in the STAR*D format. The most relevant population subsets for primary care physicians are the high utilizers of health care services, hypochondriacs, patients with somatic complaints, and those with mixed anxiety and depression.[42] The STAR*D study was designed prior to the publication of data supporting the efficacy of augmentation of antidepressants with atypical antipsychotic agents for TRD.[43] Perhaps a future study could include an atypical antipsychotic option. One also wonders how the outcome of the STAR*D study might have differed if innovative treatments for depression such as vagal nerve stimulation or transcranial magnetic stimulation were available during study design and included as alternative treatments.[44] In addition, the incorporation of valid comparisons of psychotherapy in a study would be useful as would the use of medication combinations as first-line treatment, rather than SSRIs alone, in an attempt to achieve greater remission rates.

SUMMARY

In one sense, the STAR*D results are discouraging: at least half of patients with depression did not achieve remission following 2 attempts at adequate dose/duration. In addition, there is a scarcity of statistically significant differences among individual treatments. All medications employed were roughly equivalent, negatively impacting

our understanding of the pathophysiology of depression. Last of all, these results—which show that more than 75% of patients with recurrent depression experience an average duration of 16 to 17 years—confirm the insidious and chronic nature of the disease.[13]

Effectiveness trials, such as STAR*D, help us identify new targets for treatment and patients for whom the treatments will be most effective and best tolerated. The STAR*D results provide an empirical basis for practice guidelines, thereby reducing the reliance on clinical consensus and small uncontrolled trials.[9,15] Finally, these data demonstrate that vigorous, measurement-based care is both realistic and essential in the context of real-world clinical practice.

Drug names: bupropion (Wellbutrin and others), buspirone (BuSpar and others), citalopram (Celexa and others), lamotrigine (Lamictal and others), lithium (Eskalith, Lithobid, and others), mirtazapine (Remeron and others), nortriptyline (Pamelor, Aventyl, and others), quetiapine (Seroquel), sertraline (Zoloft and others), tranylcypromine (Parnate and others), venlafaxine (Effexor and others).

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