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Measurement-Based Care in the Treatment of Clinical Depression

Abstract: Major depressive disorder is one of the leading causes of disability in the world. Effective treatment guidelines have been developed and disseminated; however, unlike other fields of medicine, psychiatry has been slow to adapt and utilize these empirically validated treatment strategies. Measurement-based care (MBC) provides a simple way to use the established clinical treatment guidelines to provide optimal personalized evidence-based medical care. MBC is simple and easy to implement. At the core of MBC is the longitudinal measurement of symptom severity, adherence to treatment, medication tolerability, and patient safety. For a variety of reasons, published antidepressant treatment guidelines have not been adopted by most prescribing physicians. MBC offers a solution to many of the concerns that have led to the lack of integration of evidence-based clinical practice guidelines into standard care. MBC offers physicians the opportunity to provide optimal personalized evidence-based medical care to patients requiring antidepressant treatment.

Clinical context

Given the high prevalence (1) and burden of major depressive disorder (MDD) (2), it is critical to apply appropriate tools that result in the greatest probability of success. Development of the ideal standard of care involves both the discovery and testing of treatments themselves and creation and validation of methods of delivery of care. Often scientific research excels at the first two processes and lags in the second pair. Certain considerations such as length of treatment, dose level and frequency of administration, and the accurate standardized determinations of outcome are often left uncertain. Even if known, physicians must be educated and willing to prescribe treatment appropriately. Unfortunately, outcomes in routine clinical practice remain suboptimal.

In mental health care, this situation is especially acute. In particular, treatment of MDD has modest rates of success despite the broad range of therapies with proven efficacy, including medication, therapy, behavioral, and somatic treatments. Sustained remission is the goal of treatment for MDD in order to produce the most meaningful improvement in the syndrome (3, 4). Furthermore, patients who do not achieve remission have a generally worse prognosis, more frequently experiencing relapse and often experiencing poorer quality of life and work productivity (5–7). Unfortunately, only about 35% of patients will remit upon initial treatment in a given episode (8), and even with multiple subsequent trials cumulative remission rates in medication trials are far from optimal (9). Resistance to treatment is a significant problem in clinical care for MDD.

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Consensus definitions of treatment resistance have been slow to evolve but most proposals share certain features. Generally, treatment resistance applies to an episode of depression rather than to a patient and requires failure of multiple adequate trials of medication. Various systems for defining and assessing treatment-resistant depression have been developed, but few studies have attempted to validate their ability to predict treatment outcome (10).

Established effective guidelines for MDD have been developed and disseminated, but there has been a profound lag in their adoption into clinical practice. Patients typically receive treatment that is not in accord with evidence-based recommendations or guidelines, with prescribing patterns being a function of the experience and preference of the individual treating physician. As a result, patients do not receive the benefit of the substantial work that has been done to develop the current treatment guidelines. Unfortunately, in the absence of techniques such as measurement-based care (MBC), incorporated into clinical care, patients often receive suboptimal treatment, with physicians failing to utilize medications effectively (11, 12). Without techniques such as MBC, dosages and duration of treatment are often inadequate, and strategies for medication titration, switch, and augmentation can become somewhat idiosyncratic (13, 14). This problem can be largely traced back to a simple absence of standardized measurement in clinical practice. MBC is a technique that was developed to aid treating physicians in their efforts to integrate the gold-standard clinical practice guidelines that are available into clinical practice (15–24).

Treatment strategies and evidence

MBC provides clinicians the tools and techniques to deliver optimal, individualized treatment for patients suffering with depression. Conceptually MBC is an idea in long standing, having been adopted and utilized in many areas of medicine ranging from endocrinology to nephrology to oncology and beyond. In these settings MBC in its simplest form is a manualized or algorithmic application of published, accepted, clinical practice guidelines. This technique offers clinicians a straightforward, valid, standardized path to follow for prescribing treatments. The absence of which, particularly in psychiatry, has led to poorer patient outcomes.

MBC in psychiatry has been subjected to a great deal of research. Programs such as TMAP, IMPACT, followed by STAR*D, REVAMP, and COMED to name a few, have extensively utilized and studied the efficacy and effectiveness of MBC in both specialty and general practice settings (25–30). The results are consistent, in that the use of MBC to treat unipolar depression appears to have "leveled the playing field," with primary and specialty care physicians both being able to provide optimal personalized care, with no distinctions in clinical outcomes between providers. MBC strategies and algorithms are also available to psychiatrists for use in bipolar disorder and schizophrenia; however the complex nature of the population and disease states has resulted in some lag in published outcomes. There are initial indications that the use of MBC offers great promise for both these diseases, with extensive research underway.

MBC for MDD

The application of MBC for MDD is straightforward and remarkably simple to apply. There are several steps: 1) identify the population in need of treatment; 2) determine the appropriate treatment; 3) administer initial treatment and adjust treatment based upon patient response; and 4) sustain long-term monitoring and maintenance.

Step one: screening

A number of screening tools are available to help identify patients who may benefit from treatment with an antidepressant. Screening for MDD could be as simple as two questions on a clinical intake or visit form (see PHQ-2) (31) or as complicated as a diagnostic interview (typically reserved for research settings due to time constraints). Ideally in standard clinical care settings, screening would be very brief, followed by a face-to-face clinical interaction with the patient to confirm the presence and level of severity of depression and the corresponding functional impairment to determine if medical intervention is warranted.

Step two: treatment selection

Following the evaluation of the range of treatment options available, once the decision has been made to pursue antidepressant medication treatment, an appropriate medication needs to be selected. While personalized medicine-based methods of selecting the correct starting medication(s) are being developed, the current strategy is based upon the patient's treatment history and current clinical presentations. Anticipated effectiveness, tolerability, safety, and affordability are the primary driving forces behind treatment selection. Given the above factors, for treatment-naïve patients the first-line treatment is typically a generically available SSRI.

When working with patients that have had one or more trials of an antidepressant agent, obtaining an accurate treatment history is essential. For a variety of reasons patients commonly inaccurately report having had one or more failed trials. The reason for this is quite simple: patients typically do not receive an adequate trial (<30% reduction in symptoms given an adequate dosage of medication for an adequate period of time) and assume that the medication was not effective, the only exception being for instances of intolerance (intolerance constitutes an immediate failed trial). The requirements for an adequate trial for the most common antidepressant agents in use are published elsewhere (22). The typical strategy proceeds as follows: first, one or two trials with an SSRI; followed by a trial with an SNRI or bupropion. Always being mindful of how the specific side effect profile will affect the patient, for example, patients with comorbid diabetes may not be the best candidates for mirtazapine, given the associated weight gain. On the other hand, patients who are having difficulty maintaining weight may specifically benefit from mirtazapine over other treatment choices. In another example, patients with a history of eating disorders or a seizure disorder should not be given bupropion, but those with more vegetative symptoms of depression or SSRI-induced sexual dysfunction may show increased benefit.

In instances of partial response (>30% reduction in symptoms but failure to return to premorbid functioning), the addition of a second compatible agent is often the choice. In instances of SSRI partial response, the addition of bupropion is often the preferred choice. The treatment options described thus far are appropriate for both primary and specialty care physicians. When incorporating TCAs, MAOIs, or combinations of SNRIs and bupropion, psychiatric settings could offer a desirable context for treatment given potential safety concerns.

STEP THREE: MONITORING OUTCOMES AND ADJUSTING MEDICATION

This is the heart of appropriately delivered MBC. In order to minimize the clinical burden, MBC can be accomplished by the patient providing ratings on self-rated instruments in the waiting room prior to seeing a clinician followed by a review by a clinician as utilized in standard lab results. The key word in this step is measurement, specifically, standardized measurements. In order to deliver MBC, it is necessary to measure: 1) depressive symptom severity, 2) tolerability, 3) adherence to antidepressant treatment, and 4) safety. These measurements are then incorporated in the clinician decision making process and should not be viewed as a substitute for clinical judgment.

There are a number of standardized measurement tools available to assess depressive severity, such as the Beck Depression Inventory (BDI) (32), the 21-item BDI-II (33), the 20-item Zung Depression Rating Scale (34), the Carroll Rating Scale (CRS) (35), the 9-item Patient Health Questionnaire-9 (PHQ-9) (36), the 20-item Center for Epidemiologic Studies Depression Scale (CES-D) (37), the 30-item Inventory of Depressive Symptomatology—Patient Self-Report (IDS_{30}-SR) (38, 39), and the 16-item Quick Inventory of Depressive Symptomatology—Patient Self-Report ($QIDS_{16}$-SR) (40, 41). One of these measures should be used to establish pretreatment severity, and the same measure used to track change in depressive severity over time.

Tolerability is typically evaluated using a measure such as the self-report Frequency, Intensity, and Burden of Side Effects Rating (FIBSER) (42). A more comprehensive measure, such as the Systematic Assessment for Treatment Emergent Events-Specific Inquiry (SAFTEE-SI) (43) (a 55-item self-report with items rated none, mild, moderate, or severe) is also available. Adherence may be evaluated with a standardized assessment such as the 2-item Patient Adherence Questionnaire (PAQ) (determines how many days the patient was noncompliant and the reason for deviating from the prescribed dose).

The final and most important aspect of MBC is the monitoring of patient safety. Several assessments to monitor antidepressant safety per FDA guidelines (44) have been developed. The Concise Health Risk Tracking (CHRT) (45) used 14 items (patient self report and/or clinician rated interview format) to classify suicidal ideation and behavior per the Columbia Classification Algorithm of Suicide Assessment (C-CASA) criteria (46). The 14-item (patient self-report and/or clinician-rated interview format) Concise Associated Symptoms Tracking (CAST) scale (47) evaluates symptoms associated with the antidepressant "activation syndrome" described by the FDA (44). More elaborate clinician rated interviews such as the Columbia Suicide-Severity Rating Scale (C-SSRS) are also available.

With accurate assessments of depressive symptom severity, antidepressant tolerability, adherence to treatment, and safety in hand (and in the patient chart), clinicians are prepared to deliver MBC. The application of MBC to provide the patient with an adequate antidepressant trial (adequate dosage for adequate duration) is quite simple. This is accomplished by first evaluating safety and tolerability; if determined to be nonproblematic, the next step is to increase the medication (within FDA guidelines)

roughly every 2 weeks until the patient has been titrated to a minimum therapeutic antidepressant dose (22) or the patient achieves remission. Patients failing to remit may continue to have the dose increased at the clinician's discretion. Some clinicians may choose a more conservative approach and hold the patient at a minimally therapeutic dosage for up to 6 weeks to evaluate response before increasing the daily dose, while others may continue to increase the dose more aggressively. For example, during the STAR*D (8) study, dosages were titrated as follows: patients scoring a 9 or above on the QIDS had the ADM dosage increased; for patients scoring in the 6 to 8 range, dosage increase was at the clinician's discretion; and those achieving remission (QIDS <6) experienced no medication change. In clinical trials such as REVAMP (29), in instances of intolerance or if patients failed to respond to an adequate antidepressant trial (<30% reduction in depressive symptoms), medications were switched to the next antidepressant in the series described above. Additionally, in instances of partial response (patients experienced >30% reduction in symptoms but failed to return to achieve remission), a second antidepressant agent was added. The second agent was taken from a different class of antidepressants (e.g., sertraline augmented with bupropion). While augmentation strategies typically employ the use of a second antidepressant agent, the use of other agents, such as thyroid supplements, atypical antipsychotics, mood stabilizers, and psychostimulants are also accepted clinical practice. Detailed descriptions of these options are available in the current APA Guidelines for MDD.

STEP FOUR: LONG-TERM MONITORING AND MAINTENANCE

Once a patient has been stabilized at maximal antidepressant treatment response, monitoring and assessment visits become less frequent. It should be noted that remission and return to premorbid functioning are the goal of treatment. The prognosis for those stabilized, having not reached remission, is significantly worse as manifested by more frequent relapse and recurrence, and by definition, overall lower levels of social and occupational functioning. During this phase of treatment two questions often occur: 1) what to do if the antidepressant stops working effectively; and 2) after sustained remission, when should the antidepressant be discontinued. An understating of the environmental factors may be helpful in making treatment decisions. In the first instance, if patients are exposed to significant psychosocial stressors that are fleeting in nature, it may be appropriate to make no change or temporarily use an augmenting agent. If the stressors are more profoundly enduring, closer monitoring and a return to the augmentation and/or switch strategy described above may be in order. In the second case, if the environmental factors appear to be stable, discontinuation may occur 6 months to as much as 2 years after remission has been achieved, depending upon the patient's history of depression (i.e., number of previous episodes, length of current episode, and overall length of illness). Patients should be monitored more closely for relapse and recurrence and safety, as well as all instances when dosages are titrated.

QUESTIONS AND CONTROVERSY

INTEGRATION OF MBC INTO STANDARD CARE

While the American Psychiatric Association guidelines calling for the integration of MBC into routine practice are based upon empirical evidence in favor of the use of MBC, practitioners have more often than not failed to adopt these APA recommendations and do not utilize MBC in day-to-day practice (23). The failure to adopt MBC as part of clinical care often results in idiosyncratic prescribing patterns, and lack of continuity and prescribing strategies among physicians. Accurate communication between physicians and patients, and between providers, is hindered as nonstandard outcomes are used to describe treatment response. The result of which is that patients often do not receive adequate care, and research and clinical findings are minimized or have little ability to impact on care.

BARRIERS TO THE ADOPTION OF CLINICAL TREATMENT GUIDELINES

Cabana et al. (48) identified a continuum of behavior change starting with acquiring knowledge, leading to a change in attitudes, and ultimately a change in behavior. The authors further delineated barriers to the adoption of clinical practice guidelines found along the continuum. The initial concern being that there is simply too much information to assimilate, that the guidelines would not be universally accepted as the standard of care, or that they would be too nonspecific to be applied to individual patients. Other concerns were the guidelines would be difficult to apply and would provide outcomes inferior to those obtained with current practices. Physicians were also concerned that guidelines would not allow enough flexibility to accommodate individual patient wants and needs. Finally, physicians were concerned that they simply did not have the

physical (i.e., equipment) or fiscal resources to accommodate what may be somewhat inconstant guidelines that could, because they are not universally adopted, make them vulnerable to lack of compensation by payers and ultimately legal repercussions if problems arose as a result of treatment.

TIME MANAGEMENT

There is often the misperception that MBC requires a significant increase in the amount of time it takes for physicians to deliver care. However, in contrast, the systematic assessment of symptom severity, tolerability, adherence, and safety increase physician burden no more than the reviewing of results of any standard lab test. The assessment is done by the patient in the waiting room prior to seeing the clinician, and is reviewed by the clinician briefly before or while seeing the patient, all of which may take from a few seconds if all is well, to a few minutes if follow-up with the patient is required.

RECOMMENDATIONS FROM THE AUTHORS

Currently the majority of providers treat psychiatric illness quite differently than other diseases. Failure to use standardized measurements to assess treatment outcome is in contrast to other areas of medicine, such as cardiology, rheumatology, endocrinology, nephrology, and even in other practices found in psychiatry (e.g., standard labs). While this is no longer the case, historically psychiatric outcomes have been seen as more difficult to measure and inaccurate to the point of rendering them of dubious value. However, psychiatry has evolved alongside other areas of medicine, and now accurate MBC treatment guidelines are available for the treatment of depression and other disorders. The MBC guidelines for depression have been extremely well researched and proven to be effective when applied in both general and specialty care settings.

There is accumulating evidence that following MBC practices improves outcomes for patients. Implementation of MBC is feasible and cost neutral and is compatible with patient satisfaction. Furthermore, it has become clear that our health care system has become more focused on outcomes, with Medicare and major insurers implementing systems in which compensation is tied to performance. Even if these payors do not directly require use of at least some aspects of MBC, physicians working in such systems will benefit from the improved quality of care delivered, in addition to the obvious benefits to patients.

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NOTES