

Pharmacological Treatment of Major Depressive Disorder: 2017-2018 Update Summary

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INTRODUCTION

Major depressive disorder (MDD) is one of the most common mental disorders throughout the United States and much of the developed and developing world. Evidence indicates that MDD is the leading cause of disability amongst young individuals (i.e., 18-24), and is a frequent cause of workplace impairment and absenteeism. In addition to being a highly disabling and distressing condition, MDD complicates many other psychiatric and medical conditions, adding to, and in some cases, multiplicatively, affecting overall morbidity and mortality.

Results from patient-reported outcome literature indicate that adults with MDD prioritize quality of life improvement, function, positive mental health, resiliency, and general well-being, over conventional symptomatic improvement. Notwithstanding the high prevalence and costs of MDD, many affected individuals are not accurately diagnosed and as a consequence are not receiving timely guideline-concordant treatment. Screening for MDD is highly recommended by the United States Preventative Services Taskforce, where resources to provide treatment are available. As the population of the United States and other developed nations ages, the association between MDD and age-related disorders (e.g., Alzheimer's disease, cardiovascular disease) is of increasing concern. The biomedical literature provides evidence suggesting that MDD is associated with premature aging processes in subpopulations of affected individuals. In accordance with this hypothesis, guideline-concordant treatment for MDD may forestall and prevent some age-related conditions. Finally, the adverse effect of MDD on the workforce is stark reminder that screening for, and attention given to, best practices in mood disorders extends beyond the ecosystem of the medical clinic and involves disparate settings including, but not limited to, education settings, the workplace, and the general community.

PRINCIPLES OF TREATMENT

Similar to the 2015 Florida Best Practice Guidelines, the **2017-2018 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults** emphasize the importance of full functional recovery in MDD as the overarching therapeutic guideline. The possibility of achieving this foregoing objective is increased when individuals achieve symptomatic and syndromal remission, and attention is given to psychiatric and medical comorbidity, negative attitude towards treatment, as well as psychoeducation around the illness and its treatment (Zimmerman et al., 2017).

During the past ten years, extant evidence indicates that individuals with MDD and higher levels of pre-treatment function have higher response rates to conventional antidepressant treatment. The bidirectional association between symptoms and function in MDD raises a myriad of conceptual questions and hypotheses, as well as clinical implications. An axiomatic clinical implication derived

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from the foregoing observation is that augmenting patient function contemporaneously with symptom targeting in MDD provides a greater probability to therapeutic success and acceptability.

The integration of multimodality treatment with emphasis on positive mental health, resiliency, and human function invite the need for evidence-based psychosocial treatments combined with pharmacotherapy. The efficacy of antidepressants in improving symptoms in persons with MDD is well established, particularly for individuals with moderate-severe pre-treatment illness severity. It is recognized that drug-placebo differences in mild MDD are less replicated and/or compelling, suggesting psychosocial treatments as prioritized in many cases of MDD of mild severity.

The expert panel recognizes that there have been significant advances in computational psychiatry, machine learning, as well as data-driven approaches to predict (using big data) which antidepressant is appropriate. It is additionally recognized by the expert panel, that pharmacogenetics/pharmacogenomics testing has widespread availability, and in many jurisdictions, reimbursement, as well as clinician and patient acceptance. Notwithstanding, it is the opinion of the expert panel that compelling evidence supporting pharmacogenetics/pharmacogenomics testing as a robust method to guide treatment selection remains to be fully established (Rosenblat, Lee, and McIntyre, 2017).

MAJOR DEPRESSIVE DISORDER WITHOUT MIXED FEATURES

The expert panel did not make any substantive changes to the guidelines for MDD without mixed features. The expert panel recognizes that vortioxetine has received extensive study targeting cognition in MDD. Notwithstanding, vortioxetine, as well as many other first-line antidepressants, are considered as a first-line treatment option for most other symptoms in MDD.

MAJOR DEPRESSIVE DISORDER WITH MIXED FEATURES

The expert panel recognizes that approximately 25% of adults with MDD have mixed features (McIntyre et al., 2015). It is also recognized by the expert panel that mixed features is associated with healthcare service utilization, polypharmacy, and significant functional impairment (McIntyre et al., 2017). The expert panel recognizes that the United States Food and Drug Administration (FDA) has not approved any specific agent for MDD with mixed features. The preponderance of evidence, however, is that MDD with mixed features are less consistently responsive to conventional antidepressants, and may in some circumstances be more safely and effectively treated with mood stabilizing agents.

MAJOR DEPRESSIVE DISORDER WITH PSYCHOSIS

Major depressive disorder with psychotic features affects approximately 20% of adults with MDD, with higher percentages reported in younger and older populations. The best available evidence supports combining antidepressants with antipsychotics, or electroconvulsive therapy as the treatment of choice for MDD with psychosis. It is strongly recommended that MDD with psychosis not be treated with manualized-based psychotherapy as a stand alone modality of treatment.

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MAINTENANCE TREATMENT IN MAJOR DEPRESSIVE DISORDER

Evidence indicates that most individuals with MDD are at risk of recurrence, with each episode further increasing risk probability. The current recommendation for maintenance treatment is a minimum of 6-12 months upon completion of the acute phase pharmacotherapy. Individuals at higher risk for recurrence (e.g., residual symptoms, multiple episode frequency, comorbidity, ongoing psychosocial stressors) can remain on treatment for longer periods of time, individualized on a case-by-case basis. Most pharmacotherapeutic interventions have demonstrated acute and maintenance efficacy, while psychosocial treatments have distinct levels of evidence for each modality across phases of therapy. For example, cognitive-behavioral therapy has rigorous evidence supporting acute and recurrence prevention in MDD, while other psychosocial modalities have more rigorous evidence in relapse prevention than in acute phase treatment (e.g., mindfulness-based psychotherapy). It is also recommended by the expert panel that advocacy [e.g., Depression and Bipolar Support Alliance (DBSA)] can play a critical role in education support service access and illness/treatment literacy and should be considered an integral component of care for any person affected by MDD.

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