With a lifetime prevalence rate of 13%, depression accounts for a higher percentage of emergency department visits and readmission rates for both psychiatric and medical reasons.\(^1\) Treatment-resistant depression (TRD) is a challenging, difficult-to-treat disease, for which single interventions such as pharmacologic treatment are often inadequate. Strategies for pharmacologic treatment when a first-line antidepressant regimen fails include switching to another antidepressant (interclass or intraclass), augmentation with a mood stabilizer or atypical antipsychotic, or initiation of thyroid hormone therapy. Drugs with glutamatergic actions, such as ketamine, have proven to be promising in addressing TRD symptoms, and will likely witness widespread use in the next few years. Treatment resistance can occur in up to one-fifth of patients with depression, and psychotherapy can help patients manage symptoms and achieve remission status. Psychotherapy can help target depressive symptoms, as well as comorbid symptomatology, that exacerbate or trigger depression, such as anxiety, personality disorders/traits, and medical issues. The most studied therapeutic interventions are cognitive-behavioral therapies, but evidence exists for Acceptance and Commitment Therapy, Cognitive Behavioral Analysis System of Psychotherapy, Dialectical Behavioral Therapy (DBT), and Mindfulness-Based Cognitive Therapy in the treatment of TRD. Additionally, comorbidity of TRD with maladaptive personality traits or disorders is recognized but often not systematically addressed.\(^2\) Evidence supports the efficacy of antidepressant medications and the addition of adjunctive treatment;\(^3\)\(^,\)\(^5\) however, for many patients, treatment interventions based solely on medication compliance are not feasible due to factors such as side effects, high costs of medications, and religious, cultural, or personal beliefs regarding pharmacologic interventions.\(^6\)

Therapeutic approaches like intensive outpatient programs (IOPs) provide a cost-effective, practical, and less restrictive alternative to hospitalization for those needing more frequent follow-up care but who do not meet inpatient criteria. Additionally, patients who are transitioning from inpatient care but require additional supportive services prior to fully reintegrating back into the community also greatly benefit from IOPs. IOPs offer ongoing group and individual psychotherapy and allow opportunities for frequent medication follow up to monitor changes in the symptom report. Most research on IOPs has focused on the efficacy of DBT with mood and personality disorders.

Novel approaches like neurostimulation for the treatment of TRD include transcranial magnetic stimulation (TMS), deep brain stimulation (DBS), and electroconvulsive therapy (ECT). Although each has shown variable success in the treatment of TRD, ECT is still considered the gold standard and most efficacious. There are numerous challenges in the implementation of neurostimulation techniques, which include: (1) mandated inpatient visits and...
extended protocols for treatment; (2) potential psychiatric consultations and external referrals; (3) additional test expenses for TMS and DBS; (4) state regulation procedures; and (5) stigmas that patients have to overcome. When encountering treatment resistance in a depressed patient, it is highly recommended that clinicians consider neurostimulation options early, and not as a last resort, because longer durations of depressive symptoms correlate with poorer treatment regardless of the chosen modality.

Finally, depression alone is neither essential nor sufficient to determine medical decision-making capacity, and mental illness or depression do not equate to a lack of aptitude. Unipolar major depression is in the top 10 for global disease burden. Cost estimates for depression care rank as the second most costly disease in the United States. Costs, both in the form of direct expenditures on depression care and indirect forms such as absenteeism and decreased productivity, are projected to continue to increase. Costs from TRD, specifically, seem to account for a large portion of these expenditures. However, given the many cognitive impairments and distortions that can occur in psychiatric patients, clinicians have to establish a low threshold for the evalu-
ation of medical decision-making in patients with mental illness or depression because executive capacity in depressed patients can be compromised. The articles in this issue discuss treatment options for TRD like psychopharmacologic approaches, but also identify options like IOPs, ECT, and TMS.

REFERENCES

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