DIAGNOSING AND TREATING DEPRESSION:

What you think you know might not be true

Clinicians may have misconceptions about the treatment and management of depression in routine clinical practice. Here, **Mark Zimmerman**, MD, Director of Outpatient Psychiatry and the Partial Hospital Program at Rhode Island Hospital in Providence, helps shed some light on these beliefs and what is found in medical literature. Dr. Zimmerman is also Professor of Psychiatry and Human Behavior at The Warren Alpert Medical School of Brown University, Providence, Rhode Island. He has performed psychiatry research for more than 2 decades, much of it in the area of assessment and diagnosis.

Q: What are some of the beliefs clinicians may have regarding the treatment and management of depression?

A: One of the significant issues I don't think clinicians fully appreciate is how limited the literature on the efficacy of antidepressants is regarding the generalizability of that literature to their clinical practice. The studies that are done by pharmaceutical companies use rather restrictive inclusion and exclusion criteria, such that most of the patients who are seen in routine clinical practice would not have qualified for a typical industry-funded antidepressant efficacy study. This is the situation we're in right now; clinicians have the belief, understandably, that medications are effective for the patients to whom they are prescribing, but, in fact, we really don't know if that is the case.

Clinicians and patients also have the belief that it takes a while for antidepressants to work. If a person takes a medication and they get better quickly, then they attribute it to the placebo response and it may well be. However, when you look at the studies and the time course of treatment response, you'll actually find that medication separates most highly from placebo during the first couple of weeks of treatment rather than at the end of a trial. Patients will often ask me, "When should I expect to see an effect? I have heard it takes a month for it to work." I will tell them that many individuals begin to feel better in the first week or 2 of starting the medication—not completely better but begin to feel better. It's a process of improvement rather than just flipping a light switch.

Q: What does the literature say about these beliefs?

A: Unfortunately, there is great difficulty in showing that a medication is effective. That is, only half of the studies comparing medication to placebo find that medication is significantly better. There are 2 criteria that have the biggest impact in selecting individuals for a clinical trial. The first is the minimum severity threshold, so that

individuals whose symptoms are not severe enough or don't score high enough on a scale are excluded. The second significant contributor is the presence of a comorbid condition, which is found in the majority of patients with Major Depressive Disorder, but those people are often excluded from the trials.

Q: How much do clinicians really know about the efficacy of antidepressant medication in treating patients routinely seen in clinical practice?

A: For most of the patients we see in clinical practice, we really don't know if medications are effective. It doesn't mean individuals don't get better. The fact of the matter is I don't know if they are getting better because of the pill itself or they are responding to those nonspecific effects of treatment, such as feeling safe to talk about personal issues, receiving support, being reassured by an authoritative source like a mental health professional, or having expectations of improvement raised.

Moreover, I think some clinicians and researchers have misinterpreted some of the implications of the STAR*D study. The study was designed to be more generalizable than the typical efficacy trial, so the inclusion criteria were loosened. However, it was an effectiveness study that didn't include a placebo-controlled group. Therefore, you're left not knowing whether or not the patients who were included in this study who responded to medication would in fact respond any better to the medication than to placebo and to the nonspecific effects of treatment. Some have interpreted those results as indicating this is how well antidepressants work. When we talk about how well antidepressants work or whether antidepressants work, we aren't talking about whether or not people get better. We are talking about whether or not people are more likely to get better compared to placebo.

Q: Can you explain why relapse does not necessarily mean the prescribed medication has stopped working?

A: When I see someone in my clinical practice and I put them on a medication and they get better, I don't know if they got better because of the medication or they responded to the nonspecific effects of treatment. Therefore when you follow them and they relapse, does

that mean the medicine stopped working or does it mean they never really responded to the medication and they lost the placebo response? We don't have a definitive answer. However, a group of researchers at Columbia developed formulas to estimate the likelihood by which the loss of efficacy is attributable to a loss of placebo response or a loss of true drug effect. Colleagues and I took their approach and applied it to studies that were conducted with the appropriate design. We found that most of the relapse could be attributed to loss of initial placebo response. So it isn't that the medicine stopped working, it probably never worked in the first place.

Q: Regarding bipolar disorders, is overdiagnosis more common than underdiagnosis?

A: There has been a significant emphasis over the past decade to improve the recognition of bipolar disorder. Certainly, you would rather not miss a diagnosis of bipolar disorder, because there are potential negative implications. An individual [with bipolar disorder] should be treated differently. Also, by not recognizing bipolar disorder it could be associated with increased cost of care. There is the increased likelihood of prescribing an antidepressant alone; thereby, the individual is at risk for switching from a depressive to a manic episode.

Clinicians, perhaps, have become so sensitized to not diagnosing bipolar disorder that they may diagnose it when the person doesn't have bipolar disorder. I can't tell you the number of charts I have reviewed of

individuals who have been diagnosed with bipolar disorder yet, when you're looking for documentation of the manic or hypomanic episode, it's lacking. I think the educational effort, the failure to follow the diagnostic criteria, and the availability of a pill to prescribe for bipolar disorder are all responsible for the tendency to overdiagnose the condition, and the primary diagnostic culprit responsible for overdiagnosis of bipolar disorder is borderline personality disorder. There are certainly some phenomenological similarities between the 2 disorders but they are also very distinct. It's detrimental to the patient to be diagnosed with bipolar disorder when they have borderline personality disorder because it leads them down the wrong treatment path.

Q: National guidelines emphasize the importance of using standardized scales to measure depression; however, data has shown that few clinicians routinely do so. In your opinion, why are clinicians reluctant to use self-report scales?

A: There are multiple reasons. Clinicians aren't trained on how to use the scales. Some clinicians don't perceive them as being helpful, they don't know which instrument to choose, and they lack knowledge about the scales, so they feel lost. Also, some clinicians believe they are burdensome and are concerned that patients will also perceive them as burdensome. However, studies have shown that patients, in fact, don't perceive them as burdensome and they don't disrupt the flow of a practice once you have incorporated it.

Q: Does it matter which depression scale is used in clinical practice?

A: All scales of have evidence of reliability and validity. Some take longer to fill out, and in a busy clinical practice that makes a difference. Some scales you have to pay for; however, there is no reason to pay for a scale because there are a number of freely available well-researched scales. Also, some scales sacrifice clarity for the sake of brevity. The Beck Depression Inventory (BDI) or the Quick Inventory of Depressive Symptoms (QIDS) scales are constructed so that each symptom is assessed by a group of items. For example, to assess depressed mood, a patient reads 4 statements and then chooses the statement that best describes how they feel. As a result, a 21-item [BDI] has 84 statements to read, which is considerably longer than measures such as the Patient Health Questionnaire (PHQ-9) or the Clinically Useful Depression Outcome Scale (CUDOS). Those have under 20 items— each one is a single statement that is rated on a scale of frequency—and take less time to complete. When you look at the American Psychiatric Association treatment guideline for mild and moderate depression, it recommends pharmacotherapy or psychotherapy. For severe depression, pharmacotherapy is the treatment of choice. The PHQ-9 tends to overclassify severity, compared with the gold standard measure of severity from the Hamilton Depression Rating Scale. Therefore, self-report scales differ in terms of the percentage they would consider severely depressed or not. To the degree that a clinician will use the APA guideline and use these scales to help them select a treatment modality, it is important to remember that different scales will lead to different results.

Q: What are you hoping attendees take away from your session at Psych Congress?

A: In treating depression, you should measure outcome. Also, bipolar disorder overdiagnosis is as important as underdiagnosis. Finally, clinicians should let patients know when they start an antidepressant that the medication often begins to work in the first week or two. They shouldn't tell them it takes a month for the medication to work. – Eileen Koutnik-Fotopoulos **MHM**