Depression in the Primary Care Setting

TO THE EDITOR: In the Clinical Practice article by Park and Zarate (Feb. 7 issue)[1] on depression in the primary care setting, the authors do not address the considerable financial barriers and stigma that many patients with depression encounter with regard to accessing psychotherapy. We would like to call attention to a promising model that we are using in our practice — the collaborative care model — that allows us to embed a behavioral health care manager into our usual clinical care.[2]

The Centers for Medicare and Medicaid Services recently introduced billing codes for services provided by a behavioral health care manager working collaboratively with primary care providers within their own practice.[3] In this model, patients in primary care settings are screened for depression with the use of a validated instrument such as the Patient Health Questionnaire 9 (PHQ-9). If the results are positive, the patients undergo consultation with a psychiatrist, are enrolled in a registry, receive a brief course of evidence-based psychotherapy such as cognitive behavioral therapy, and are monitored with the use of measurement-based targets. Numerous randomized, controlled trials have shown the effectiveness of this approach as compared with usual liaison psychiatry.[4] Such innovative approaches will allow more patients to access expanded mental health services within their own primary care practice, which is both cost-efficient for the patient and sustainable for the practice.

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TO THE EDITOR: As Park and Zarate discuss, nonresponse to first-line antidepressants is common. The authors comment that, "Although improvement may be noted at as early as 2 weeks, full relief of symptoms may not be seen for 8 to 12 weeks." Unfortunately, this does little to challenge the commonly held belief that antidepressants take longer than 2 weeks to take effect. In a meta-analysis of 47 randomized, controlled trials, 35% of clinical improvement was seen during the first week and a further 25% during the second week.[1] Furthermore, clinical improvement by 2 weeks is a powerful predictor of subsequent response and remission.[2] In line with a 2015 guideline,[3] we would therefore advocate reassessment 2 weeks after the initiation of antidepressant therapy to assess efficacy, side effects, and suicide risk. If there is no improvement 4 weeks after initiation, despite adherence to the regimen and an absence of coexisting substance use, it would be prudent to consider a medication change. Given that protracted depression causes suffering, functional decline, and even structural brain changes,[4] clinicians may minimize this burden by making proactive changes to ineffective therapy.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: In their review article about depression, Park and Zarate mention that a Lyme

titer should be obtained as clinically appropriate. It is somewhat unclear why Lyme disease was singled out. The vast majority of patients with untreated Lyme disease (at least 70%, but more likely closer to 90%) present with the skin lesion erythema migrans.[1] A recent systematic study involving adult patients with erythema migrans showed no evidence that such patients were significantly more likely than matched healthy controls to have a major depressive disorder on presentation.[2] The mildly elevated Beck Depression Inventory–II scores at baseline strongly and directly correlated with the total number of somatic symptoms and, as in another study,[3] were more likely to be attributable to somatic symptoms rather than to affective depressive symptoms.

Overall, no convincing evidence has supported the notion that any psychiatric illness might be the primary manifestation of untreated Lyme disease.[4] If all patients with depression were tested for Lyme disease, thousands of misdiagnoses would occur owing to false positive tests as well as background seropositivity from earlier resolved infections.

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Dr. Wormser reports receiving research grants from Immunetics, Institute for Systems Biology, RareCyte, and Quidel, owning equity in Abbott–AbbVie, being an expert witness in malpractice cases involving Lyme disease, and being an unpaid board member of the American Lyme Disease Foundation; and Dr. Hassett, receiving consulting fees from AbbVie and Precision Health Economics. No other potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Park and Zarate provide helpful guidance on antidepressant use in primary care, but they mention the antidepressant discontinuation syndrome — sometimes considered to be a withdrawal syndrome — only in Table 2 of their article. They correctly identify the agents with a short half-life, paroxetine and venlafaxine, as being more likely than other antidepressants to provoke the discontinuation syndrome.[1] However, their statement that controlled-release or extended-release formulations of these drugs "may decrease risk" of the discontinuation syndrome is not well supported. Extended-release formulations slow the rate of drug entry and reduce peak plasma levels but do not extend the elimination half-life of the drugs. Thus, sudden discontinuation of extended-release venlafaxine may provoke adverse effects in as many as 78% of patients within 3 days.[2]

Although most instances of discontinuation syndrome are of mild-to-moderate severity and last days to weeks, some cases are more severe and prolonged.[3] Besides the avoidance of agents with a short half-life, discontinuation syndrome is probably best prevented by using a very long tapering schedule of 2 to 6 months, especially in patients who have been taking antidepressants for more than a year.[4] Careful monitoring of the patient's response to dose reduction is essential.

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Ellis and colleagues highlight the role of financial barriers and stigma as obstacles to psychotherapy and describe the delivery of mental health care by means of a collaborative care model with an embedded behav-

ioral health manager. We acknowledge the difficulty in accessing psychotherapy, applaud their efforts, and strongly advocate for innovative approaches to mental health care delivery.

Moulton and Young describe a developing view in the field that response to first-line antidepressants may occur earlier than previously thought, and they advocate for a more aggressive pharmacologic approach that considers a medication switch within 4 weeks. We are sympathetic to this approach but believe that it may be better suited to patients with urgent or refractory presentations than to those with mild-to-moderate depression. In the meta-analysis of clinical trials cited by Moulton and Young,[1] 60% of the improvement was seen within the first 2 weeks, but a substantial amount (40%) was seen after this time. In addition, the final end point of the analysis was 6 weeks, so abatement of symptoms after this time was not captured. Real-world assessments of antidepressant effects — such as the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial[2] — suggest that greater improvement may be seen after 8 weeks.

Wormser and Hassett question whether Lyme disease should be considered as a cause of or contributor to depressive symptoms. We agree that erythema migrans is not significantly associated with depression; moreover, we are not suggesting that Lyme disease causes depression. Rather, we believe that the neuropsychiatric symptoms of Lyme disease (e.g., fatigue, sleep disturbance, and somatic depressive symptoms[3]) may manifest in a manner similar to depressive syndrome and thus that Lyme disease should be a diagnostic consideration. For the same reasons that Wormser and Hassett provide, we do not recommend screening for Lyme disease in all patients with depression but only when clinically appropriate.

Finally, Pies contends that "controlled-release or extended-release formulations . . . do not extend the elimination half-life of the drugs." At face value this seems logical. However, pharmacokinetic studies of venlafaxine have shown an overall lower maximum concentration and more gradual and narrower range of plasma concentration changes per equivalent dose with the extended-release formulation than with the immediate-release formulation.[4] This suggests that missed doses or abrupt discontinuation may result in fewer side effects in the short term with the extended-release formulation than with the immediate-release formulation. Although the analysis by Fava and colleagues[5] showed that 78% of the patients discontinuing extended-release venlafaxine reported adverse events, no events were judged to be severe, and there was no immediate-release comparator. Still, for either formulation, it seems prudent to be aware of discontinuation symptoms and to use a gradual taper.

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Since publication of their article, the authors report no further potential conflict of interest.

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Teamwork in Medicine

TO THE EDITOR: In her article in the February 21 issue,[1] Rosenbaum convincingly argues that effective team collaboration is crucial in today's complex health care system. One underutilized approach to improving clinicians' ability to collaborate is to start early in their professional