On May 14, 2010, Andrew A. Nierenberg, MD, from the Department of Psychiatry at Harvard Medical School and Massachusetts General Hospital, assembled a group of experts to discuss recent research and lay media reports about the efficacy of antidepressants for treating mild-to-moderate depression and the safety risks, including suicidality, associated with antidepressants. Their discussion appears here.

This special *Commentary* is another in a series of independent projects undertaken by the CME Institute of Physicians Postgraduate Press, Inc., as a service to its members and the broader academic and clinical community.

The roundtable teleconference was chaired by **Andrew A. Nierenberg, MD,** Department of Psychiatry, Harvard Medical School and Massachusetts General Hospital, Boston. The faculty were **Andrew C. Leon, PhD,** Departments of Psychiatry and Public Health, Weill Cornell Medical College, New York, New York; **Lawrence H. Price, MD,** Department of Psychiatry and Human Behavior, Brown University and Butler Hospital, Providence, Rhode Island; **Richard C. Shelton, MD,** Department of Psychiatry, Vanderbilt University Medical Center, Nashville, Tennessee; and **Madhukar H. Trivedi, MD,** Mood Disorders Research Program and Clinic, University of Texas Southwestern Medical Center, Dallas.

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The Current Crisis of Confidence in Antidepressants

The US Food and Drug Administration (FDA) has required that the prescribing information for all antidepressants carry a black box warning about suicidal thinking and behavior in children, adolescents, and young adults. Additionally, recent research has examined the efficacy of antidepressants, particularly for patients with mild-to-moderate depression, and the lay press has publicized various interpretations of these findings. These 2 circumstances have affected the public perception of the safety and utility of antidepressants and raised challenging questions for clinicians who treat patients with antidepressants.

WHAT DO THE STUDIES MEAN?

Dr Nierenberg: The lay press has interpreted data from recent meta-analyses[1–3] on the efficacy of antidepressants in a way that emphasizes the risks of these medications and minimizes the benefits. We have the unique challenge of trying to interpret the data from these complex studies so that, as clinicians, researchers, and educators, we can help the public understand the true import of these findings. Otherwise, people who should be seeking treatment might not do so, due to their fear of the perceived risks of these medications and the perception that they are not, in fact, that helpful. Part of interpreting the data from these meta-analyses is considering the strengths and limitations of randomized clinical trials and examining how informative they are for clinical practice.

Dr Shelton: A lot of media attention has focused on a recent meta-analysis[1] conducted by my colleagues and me that examined the efficacy of antidepressants for treating patients with depression. The purpose of the study was to look at controlled clinical trials to determine if a relationship existed between baseline severity of illness and the amount of drug-placebo difference demonstrated in the trials. Our study was conducted in response to earlier meta-analyses from Kirsch et al[2] and Khan et al.[3] The former suggested that, when data from all trials, including failed or unpublished trials, were aggregated, the drug-placebo difference was minimal for severe depression and no drug-placebo difference existed for patients with moderate depression. The latter indicated that baseline severity had no effect on drug-placebo differences.

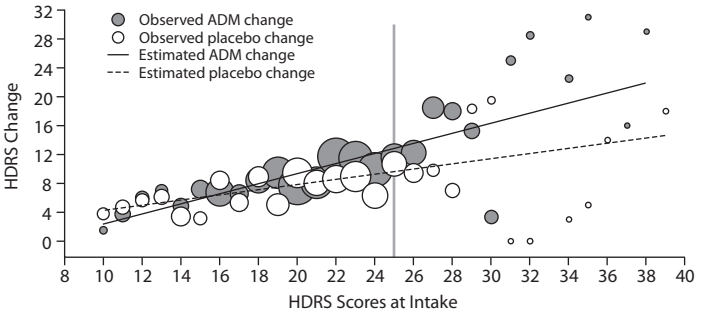
Because many industry-related clinical trials include exclusion criteria such as minimum Hamilton Depression Rating Scale[4] (HDRS) scores, the populations under study are not representative of the patients that clinicians see in their practices. Additionally, industry-related clinical trials generally put in place safeguards that reduce placebo response, including placebo wash-out periods. Therefore, our meta-analysis[1] specifically did not focus on industry-related clinical trials and instead considered data from placebo-controlled trials that included patients with a broad range of depression severity.

We found a relationship between the baseline severity of illness and the degree of difference between the response to drug versus placebo.[1] People with lower HDRS scores at baseline had no significant difference between drug and placebo effect, but, as the baseline severity of depression increased to 25 or greater (ie, more severe depression), the drug-placebo efficacy difference became clinically significant (Figure 1). This finding was predicated

FOR CLINICAL USE

- Carefully weigh the risks and benefits of antidepressants when treating patients with depression.
- Closely monitor patients, particularly younger patients, for suicidality when initiating antidepressant treatment.
- Consider evidence-based psychotherapy as the initial treatment for patients with mild-to-moderate depression.

Figure 1. Observed and Estimated Change in HDRS Scores Following Treatment With Antidepressants and Placebo[a,b]



[a]Reprinted with permission from Fournier et al.[1]
[b]Circles represent observed (raw) mean change in depressive symptoms from intake to the end of treatment at each initial HDRS score for both the ADM and placebo conditions. The size (area) of the circles is proportional to the number of data points that contributed to each mean. Regression lines represent estimates of change in depression symptoms from intake to end of treatment for ADM and placebo conditions as a function of baseline symptom severity. These regression lines were estimated from a model of the baseline severity × treatment interaction, controlling for the effects of the study from which the data originated. The threshold for clinical significance was met for intake HDRS scores of 25 or greater.
Abbreviations: ADM = antidepressant medication, HDRS = Hamilton Depression Rating Scale.

on the fact that the amount of change in HDRS scores in the patients taking placebo was about the same across the severity spectrum—patients with initial scores of 20 improved by about 8 points, and patients with initial scores of 30 also improved about 8 points. But, the amount of response to medication was greater among patients with higher baseline HDRS scores than in those who had lower baseline scores, creating a greater difference between drug and placebo efficacy.

The relationship between baseline severity of illness and the degree of drug-placebo difference was the fundamental finding of the study.[1] However, the intent of the study was also to communicate about the nature of clinical trials themselves. For example, how do you plan for studies? What factors should be taken into consideration when analyzing the results? Something we plan to test as we go forward is what happens to people over time, not just in the acute trial. For example, the relapse prevention effect of antidepressants needs to be analyzed across the severity spectrum. For instance, if a medication does not work better than placebo in mildly ill patients during the acute phase of illness, then relapse rates over time should also be equivalent between drug and placebo, although I doubt that is the case.

Dr Price: When I read the meta-analysis,[1] I thought that it reinforced what most of us in the field think about how antidepressants work and how they should be used. However, the media interpretation was completely different, and that was just stunning to me.

Dr Shelton: How would you describe the discrepancy?

Dr Price: The study showed pretty conclusively that antidepressants are effective in people who are seriously depressed and that placebo is not particularly effective for that population. This is the finding that those of us in the field would expect; and yet, because of the finding of less efficacy in milder depression, the media saw the study as more evidence that antidepressants do not really work.

Dr Shelton: Yes, although the interpretations varied considerably between different media outlets. Some seemed to understand the message, while others seemed to either misunderstand the message or have a preprogrammed, conditioned response.

Dr Nierenberg: Yes, it fits a consistent narrative that we have seen in the media for quite a while.

Dr Price: We need to recognize that this narrative is not just related to antidepressants. The issue goes to how we, as a field, have defined depression and how the public now views depression. In fact, a recent article[5] in a highly respected lay publication cited every naysayer and skeptic regarding depression in the last 100 years without giving any credence to the vast amount of scientific literature on the disorder. Although the author ended a bit equivocally, noting that depression might be similar to other syndromes that are difficult to understand, the take-home point from the article was damaging to what we in the field have been trying to do in psychiatry since the last half of the 20th century.

Dr Shelton: The popular press has a couple of different themes in this regard. First, an attitude exists that psychiatric disorders, particularly depression, should not be taken that seriously, which shows a prejudice against psychiatric patients. The second message is that people with psychiatric disorders should be treated with psychotherapy, not with medications.

My colleagues and I plan to do the same kind of meta-analysis for psychotherapy as we did for medication. However, a fundamental observation can be made about psychotherapy now—and that is that, although certain psychotherapies[6–8] have been shown to be beneficial in depression, most people do not receive the types with proven efficacy.

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Dr Trivedi: Two points from your meta-analysis should be emphasized. First and foremost, meta-analyses are, by definition, helpful in beginning to get a sense of the overall picture by looking at specific aspects of a question—for example, by looking at a factor such as severity or by analyzing a particular subgroup population—but more definitive answers require prospective studies.

The second issue, which is even more important in my view, is that, while your approach was immaculate, a meta-analysis cannot ask a very nuanced question. By definition, you had to eliminate a large amount of evidence and data in the peer-reviewed published literature. Therefore, we need to recognize that this study answers a very focused, specific question. We need to educate the public that this study should not be used to produce interpretations about evidence that was not evaluated. One has to be careful about overgeneralizing, because—as we have seen in the past—overly extensive generalizations from these focused meta-analyses can produce changes in clinical practice that are not appropriate.

Dr Leon: To follow up on Dr Trivedi's point, the meta-analysis from Dr Shelton and his colleagues included 6 studies and excluded nearly 300 studies. One aspect of the results that struck me was that the confidence intervals overlapped for the treatment effect at all levels of baseline HDRS scores. It was clear in the article—although it was not explicitly stated—that the magnitude of the treatment effect did not differ.

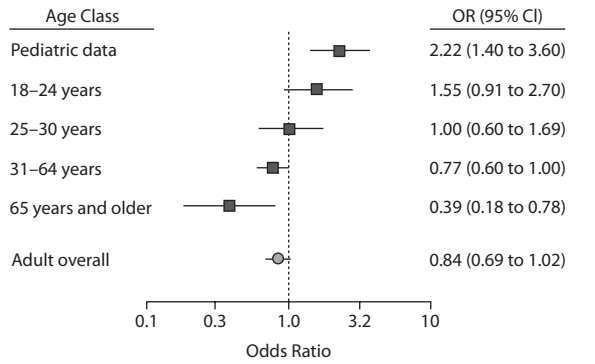
Dr Shelton: I agree with Dr Trivedi that a key issue regarding meta-analyses is that in many ways they are not informative for clinical practice. Rather than informing clinicians what to do regarding a specific question, they perhaps illuminate what needs to be done when going forward with subsequent studies. Our intent was really to inform the field of psychiatry, not necessarily to advise clinicians how they should treat patients, because many considerations need to be taken into account when treating patients.

To address Dr Leon's point regarding the results, the fact is that this was intended as a narrowly focused meta-analysis. I would refer to Khan and colleagues' meta-analysis[3] of industry-related trials that found approximately equivalent drug-placebo differences across the severity spectrum. It is possible that, in the Khan study, the placebo response may be underestimated due to the exclusion of certain patients after the placebo washout period.

Dr Nierenberg: The findings of the meta-analyses relate to Dr Price's point that the concept of major depression is defined too broadly, and may include a spectrum of people who are not that ill and for whom antidepressant treatment may not be appropriate.

Dr Trivedi: Yes, but also, in looking at 6 studies while excluding nearly 300, we have to be very careful that our interpretations are in line with the authors' and do not go beyond that. If you will remember, about 10 years ago, we had the opposite problem with another set of meta-analyses, which had the field excited that dual mechanism antidepressants were superior to selective serotonin reuptake inhibitors. However, when the pool of studies was extended to include the larger meta-analyses, or when the question was studied prospectively as in STAR*D,[9] the findings refuted that initial idea. Dr Shelton's and others' meta-analyses should be seen by those in the field as a challenge to confirm or refute the findings via prospective studies.

Figure 2. Odds Ratios (ORs) by Age Group for Suicidal Ideation and Behavior[a,b]



[a]Reprinted with permission from Leon.[10]
[b]Values > 1.0 represent an elevated risk of suicidality for those randomly assigned to an antidepressant relative to those randomly assigned to placebo. Values < 1.0 represent a protective effect for those randomly assigned to an antidepressant. Values of 1.0 indicate that there is neither an elevation in risk nor a protective effect for those randomly assigned to an antidepressant.

ANTIDEPRESSANTS AND SUICIDALITY

Dr Nierenberg: In addition to the discussion regarding the efficacy of antidepressants for depression, a considerable amount of media attention has focused on whether antidepressants increase suicidality. Evidence suggests that suicidal ideation is more likely in younger patients taking antidepressants (Figure 2).[10]

Dr Leon was asked to testify before a congressional hearing[11] in which there was great emotion over whether or not antidepressants should be used in the military due to potential suicides. From my read of it, there was a lack of understanding of the data. Dr Leon, will you comment on that?

Dr Leon: The House Committee on Veterans' Affairs held hearings in February 2010 on the issue of the relationship between antidepressants and veteran suicide. Essentially, in my testimony, I tried to counter earlier misrepresentation of data concerning antidepressants and suicidality, particularly of data from the FDA meta-analyses of antidepressants and suicide in both pediatric trials[12] and adult trials.[13] Because depression itself increases the risk for suicide, I argued for continuing to use medications to treat veterans and active military personnel who have depression, with close monitoring for suicidality.

The issue of suicidality and antidepressants, including the black box warning, has been misrepresented not only in the lay media but also in peer-reviewed psychiatric journals.

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Dr Trivedi: With reference to the antidepressant black box warning, we suffer from the same issue raised by Dr Nierenberg and Dr Price when they mentioned that the definition of depression has, at times, become unclear. Often, when people, including those at the FDA, talk about suicide, they do not clarify that they are talking about suicidality. In other words, they are talking about suicide, suicidal ideation, suicide intent, and a whole range of behaviors. The word "suicidality" was invented to encompass all of these concepts. Whether the antidepressant warning has increased or decreased "suicidality" represents a complicated scenario, with very little convincing data on how to relate suicidal thoughts and behaviors to antidepressant treatment, and even peer-reviewed publications are not always helpful.

Dr Leon: That is correct. In the pediatric trials,[12] which included more than 4,400 children, no suicide deaths occurred. About 70% to 80% of the suicidality in the trials was suicidal ideation. Another aspect of the black box warning that is misunderstood is that the warning language states that patients of all ages who are started on antidepressant therapy should be monitored for clinical worsening, even though the data supporting the warning are based on adolescents and young adults.

CHALLENGES IN THE FIELD

Dr Nierenberg: The field of psychiatry faces 2 problems: (1) data can be misinterpreted to show that antidepressants do not work, and (2) data suggest that antidepressants increase the risk of suicidality in younger patients. How do we address these challenges?

Dr Price: Our third problem is a widespread suspicion that a vast psychiatry–pharmaceutical industry conspiracy exists to profit from hurting the public. In fact, some of our most persistent and vociferous critics have explicitly made that point.

Dr Nierenberg: This widespread conviction means that any data that support efficacy of antidepressants or that suggest antidepressants do not increase suicidality are viewed with suspicion. How do we respond to that?

Dr Leon: The people who advocate the conspiracy theory are ignoring the safeguards built into clinical trials, such as blinding and the use of control groups. Those 2 aspects of randomized, controlled clinical trials prevent the manipulation of data.

Dr Nierenberg: All of us have participated in clinical trials and, I believe, in industry-funded and government-funded trials. It is difficult for us to understand the popular perception that industry trials are biased, because—at least in my experience—these trials are done meticulously and with tremendous oversight and careful monitoring. Many people simply do not understand that. So, taking these 3 problems together, no wonder a crisis of confidence exists about whether data can be trusted, whether we can be trusted, and whether our field can be trusted. Add these questions to the stigma that depression still carries, although the stigma is less than it was 25 years ago, and my concern is that people are less likely to seek the treatment that they need.

Dr Shelton: One of our challenges is that the problems that have led to this crisis of confidence are not clearly related to a single issue. For instance, if the problem was just suspicion of an industry, we could counter that with a public information campaign. However, some voices in the discussion actively promote misinformation because of the potential for personal gain. There are people with clear biases who stand to benefit if people with serious mental illnesses, particularly depression, stop going to psychiatrists or stop taking antidepressant treatment. Sometimes those potential benefits are personal, sometimes organizational or corporate, but, in the end, the misinformation needs to be acknowledged and then managed.

Dr Nierenberg: Epidemiologic studies[14,15] have shown that only about a quarter of people with serious mental illness receive adequate treatment and that there can be a delay from the onset of serious symptoms to first treatment. This problem is coupled with another problem, which is the spate of books that have been published that misrepresent psychiatric treatment. For example, one recent book warns about an emerging "epidemic" of psychiatric problems and blames the epidemic on the fact that psychiatrists are diagnosing and treating these problems.

Therefore, I think we have a role to fill in educating the public about the field of psychiatry and psychiatric treatments, as Dr Leon did masterfully at the congressional hearing. However, Dr Leon, did you feel as if the message was getting through?

Dr Leon: No, not during the hearing. It was an example of how hard it is to change preexisting beliefs, although the chair did say that the committee was not thinking of denying medication to either veterans or active military personnel.

Dr Trivedi: Obviously, we cannot hope to change society and the media, but 2 points have come out of this discussion that we need to consider. First, when looking at what treatments work or do not work for depression, we need to be considering the more severely ill patients that practitioners see in real practice—as opposed to focusing on pristine, randomized, controlled trials whose main aim is to get a signal of efficacy. A goal for all of us should be to emphasize the importance of this kind of research.

Secondly, we have not had any profound advances in the treatment of depression in the last 10 to 15 years. We have focused on the same mechanisms of action, the same monoaminergic systems, that have brought us numerous antidepressants but not really much success in developing new treatment approaches that go beyond what we know.

So, ensuring that we study the patient populations that reflect the typical presentation of the disease and that we look for novel treatment approaches are 2 things we need to do in the future. These approaches provide opportunities for us to come through this crisis of confidence.

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Dr Price: Again, part of the problem is this issue of "What is depression?" For those of us who can remember, it was a formative experience to treat profoundly depressed, melancholic patients with tricyclic antidepressants and see them get dramatically better. But now, 35 years later, we have primary care practitioners who have to assess patients in a 15-minute session, and one of the things these physicians must deal with is the response to the question, "How has your mood been?" When the patient says he or she has been feeling down, some doctors prescribe an antidepressant and tell the patient to come back in 6 months. This is a significant reason for why the public is confused about what depression really is.

In terms of the research agenda, I thoroughly agree that we need to be looking at novel mechanisms of action, and we are beginning to do that in terms of nicotinic cholinergic receptors and *N*-methyl D-aspartate receptors. But, in addition, we cannot lose sight of the importance of getting a handle on the pathophysiology of these disparate conditions that have been lumped together under the single term *depression*.

Dr Shelton: I know from talking to my colleagues in the Department of Medicine that this problem extends beyond the management of psychiatric patients. Primary care practitioners are being asked to act as gatekeepers for a vast number of medical conditions, some of which they feel quite confident about evaluating and treating and some of which they feel less confident about treating. Many psychiatric disorders are included on that list, and physicians are being asked to manage these conditions in shorter and shorter time frames. These shorter time frames for evaluating patients and for treatment planning and management are creating a real crisis for the field of medicine.

When psychiatrists think of depression, we probably have in mind the more severely ill people that we typically see in clinical practice. But medical doctors see a range of symptom severity that they must judge, from simple unhappiness through significant depression. Primary care practitioners are, in fact, treating depression less since the introduction of the black box warning, which has created a self-correcting effect, but the pendulum may be swinging too far in the other direction.[16]

Dr Leon: Regarding the need to develop newer treatments—which is certainly essential for the field—even new treatments might not resolve the problem with public confidence if the public still has an antiscience and antipsychiatry attitude.

Dr Nierenberg: For example, a recent study[17] tested repetitive transcranial magnetic stimulation (rTMS) for treatment-resistant depression and reported that the remission rate was 14% with rTMS versus 5% with sham treatment. The authors carefully said that, although it was not a large effect, the treatment did produce a clinically meaningful difference. However, a prominent newspaper reported that few patients were helped.

Dr Trivedi: I recognize that we may confront that problem even after finding newer treatments. But I do argue that some of the lack of confidence from the public comes from the fact that we have not introduced any new treatments for some time now.

PSYCHOTHERAPY FOR MILD-TO-MODERATE DEPRESSION

Dr Nierenberg: Let me ask for your comments on a question that is related to how both our primary care colleagues and the public should think about this subject. Is it your collective sense that patients with less-than-severe depression should receive one of the evidence-based psychotherapies rather than immediately being treated with an antidepressant?

Dr Price: That is how I was trained and I agree with it; in fact, if a member of my family had mild depression, that is exactly the course of treatment that I would recommend he or she pursue. I do not think psychotherapy is a panacea, but evidence supports the efficacy of certain forms of manualized psychotherapies for mild-to-moderate depression.[6–8] Although I identify myself as a psychopharmacologist, I think it is better to start with psychotherapy rather than drugs for those conditions. But the reality of health care is that psychotherapy is relatively more expensive than medication.

Dr Trivedi: I agree in principle, but I would emphasize that the kind of psychotherapy used and how well the therapist is trained have a bearing on whether or not psychotherapy will be effective. Also, I would feel more confident if Dr Shelton's meta-analysis or other meta-analyses had shown psychotherapy effective in controlled conditions for those patients for whom the medication effect size was not superior to that of placebo.

Dr Shelton: I agree. The kinds of meta-analyses that we are talking about have simply not been done with evidence-based psychotherapies. To my knowledge, at this point a meta-analysis has not been done to demonstrate whether or not mildly depressed patients respond better to cognitive-behavioral therapy or another evidence-based psychotherapy than they do to placebo treatment.

From an econometric analysis standpoint, our data show that the cost of treating patients with medication versus treating patients with psychotherapy reaches a break-even point about a year or so after initiation of treatment. That is, if we continue antidepressant medication indefinitely, the medication costs catch up to the cost of psychotherapy.

I would also stress that when we recommend that people should be treated with psychotherapy for mild-to-moderate depression, we should emphasize that they need to receive evidence-based psychotherapy delivered in a rigorous manner.

Dr Price: However, a recent meta-analysis[18] that examined the efficacy of psychotherapies for depression suggested that a substantial overestimation of effect size exists for psychotherapy due to the same kind of publication bias that we psychopharmacologists have been vilified for.[19] This

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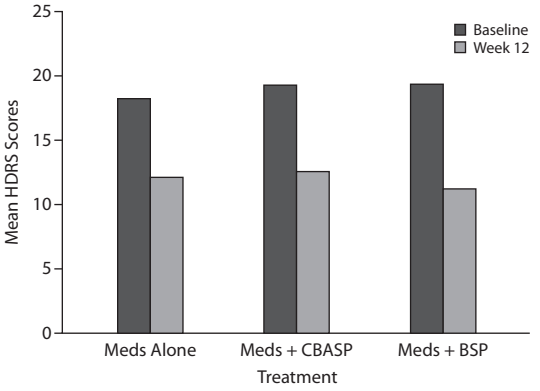
Figure 3. Outcome of Medications Versus Medications Plus Psychotherapy for Chronic Depression[a]



[a]Data from Kocsis et al.[20]
Abbreviations: BSP = brief supportive psychotherapy, CBASP = cognitive behavioral analysis system of psychotherapy, HDRS = Hamilton Depression Rating Scale, Meds = medications.

meta-analysis, though, did not stratify studies or results by severity of depression.

And, similarly, the REVAMP trial,[20] which Dr Leon and Dr Trivedi participated in, undermined the suggestion that psychotherapy is the only treatment necessary for those with mild-to-moderate depression.

Dr Trivedi: Yes, in the REVAMP trial[20] we compared psychotherapy and medication with medication alone. The study was comprised of chronically depressed patients and patients with recurrent depression, including those with mild depression. After an initial 12-week, open-label treatment phase during which patients received medication based on a treatment algorithm and measurement-based care, patients who did not remit were randomly assigned to 1 of 3 arms. Patients in all 3 arms received a next-step medication option, while 1 arm also received the cognitive behavioral analysis system of psychotherapy (CBASP) and 1 arm received adjunctive brief supportive psychotherapy.

The hypothesis was that, for patients who failed to achieve full remission on an antidepressant alone, adding CBASP would produce a better effect than either optimizing the medication alone or adding supportive psychotherapy. What we found was that none of the 3 arms produced significantly different outcomes (Figure 3).[20] This finding suggested that measurement-based pharmacotherapy produces a robust effect that is difficult to improve by adding adjunctive psychotherapy.

CONCLUSION

Dr Nierenberg: Several points have come out of our discussion. One is that the data are complex, making it easy to misinterpret meta-analyses regarding the efficacy of antidepressants. Second, the issue of suicidality is quite complicated. Dr Leon came to the conclusion, with the FDA panel, that the hypothesis that an association may exist between antidepressants and suicidality could not be rejected, which is different than saying that there is an association. However, although people should be monitored for suicidality, it is not enough of a risk that antidepressants should be abandoned.

Dr Leon: Yes, that is correct.

Dr Nierenberg: Also, we have discussed that the field of psychiatry may have made the concept of depression too broad, and that those patients who are more mildly depressed may, in fact, benefit from receiving evidence-based psychotherapy first instead of antidepressant medications. If these patients do not respond to psychotherapy, then perhaps they would be candidates for antidepressant treatment. For more severely depressed patients, antidepressant treatment may be beneficial from the beginning.

We also have the problem of a relative lack of innovative treatments appearing over the last 15 years, which are needed to move the field forward. This problem needs to be understood in the context of the presence of some societal skepticism about the pharmaceutical industry and its relationship with those in academia, which at times is mistakenly perceived to affect the integrity of the data and the methods used to support the efficacy of current treatments.

Dr Trivedi: We have also discussed that the diagnosis and treatment of depression should be taken very seriously, such that patients should not be simply given a drug and told to come back in 6 months. This recommendation is related not only to the black box warning, which says to monitor for suicidal ideation, but also to the fact that patients should really be followed very closely after initiating antidepressant treatment, as would patients with any other chronic medical disease.

Dr Leon: The black box warning further states that depression in and of itself is associated with an increased risk of suicide, so it warns not only about the treatment but also about the illness.

Dr Trivedi: Right, the warning is a reminder to monitor patients closely when prescribing antidepressants.

Dr Nierenberg: The paradox is that depression is a serious disorder that is difficult to treat, but it is also difficult to find definitive proof that a treatment works. However, the data strongly suggest that, the more severe the depression, the less likely a person is to respond to placebo, while response to medication is greater. Evidence also supports a role for psychotherapy. I believe there is room for a thoughtful, dispassionate debate about the facts.

Dr Trivedi: Depression is indeed a very difficult disease to treat. It is a long-term, chronic medical disease, and, like other chronic diseases, no one treatment is going to cure all patients.

Dr Price: I agree, and I think that it is distressing that, after many years of working to destigmatize psychiatric illness and the people who suffer from the conditions that we treat, more work needs to be done. We need to continue to maintain a focus on this problem and respond forcefully to

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our detractors. We also need to concentrate on the research, because therein lies our best hope and the best hope for our patients.

Dr Shelton: Several years ago, I was interviewed by many of the media outlets because of a study[21] my colleagues and I published on antidepressants and the discontinuation syndrome. The feel of those interviews was very similar to what we have experienced recently with the drug-placebo debate. However, over the years, I have been interviewed about the same topic and have found the discussion to be less strident and more sensible. Continuing to deliver an accurate message over and over again seems to have helped in that regard. Now, when I am interviewed about the subject, the media seem to be more inclined to ask how one manages the syndrome and not focus negatively on the medications themselves.

Dr Nierenberg: We have a perception that the media may be misconstruing and misinterpreting the data that we are producing. However, our goal is to help people who are suffering, and, if we communicate effectively with the media, we will be more successful in that goal. The more clearly we deliver our message, the more people we will be able to help.

Disclosure of off-label usage: The chair has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

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