

## The Role of Primary Care in the Treatment of Depression

*An interview with Robert M.A. Hirschfeld, MD, Titus H. Harris Distinguished Professor and Chair, Department of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, Texas*



**Robert M.A. Hirschfeld, MD**

Dr. Robert Hirschfeld has diagnosed and treated depression in its myriad presentations. As a psychiatrist, he has provided care for thousands of patients with this common disorder; as a researcher with the National Institute of Mental Health and World Health Organization in the 1970s and 1980s, he has witnessed rapid changes in community approaches to the disease; and more recently, as Chair of Psychiatry at the University of Texas, he has participated as a clinical investigator or consultant in many depression-related research, education, or health system management efforts.

With these varied perspectives and as a result of his ongoing work

as an editor or adviser to various journals, professional associations, state health committees, and non-profit organizations, he is uniquely qualified to comment on the current state of depression management.

Dr. Hirschfeld notes that the treatment of depression has improved dramatically over the past decade. He points out that approximately half of all antidepressant medications are now prescribed by primary care physicians and that patients are much more educated about the disease, both of which are positive changes partly attributable to the rise of managed care. He also cites the availability of more effective and safer pharmaceuticals as a key to improved care.

Dr. Hirschfeld commends most US healthcare systems for their policies of open formulary access to multiple pharmacotherapy choices, which is necessary to accommodate the patient-to-patient variability in response. But he also cautions that simple formulary access does not ensure treatment success. In particular, he advises health system administrators to provide flexibility in the frequency of patient follow-up visits. For some patients, he says, more frequent contact by the clinician is necessary to ensure compliance and to check for side effects. Long-term success, he says, requires a customization of management, and in some cases that customization requires a period of more intense contact.

**Depression: Causes,  
Risk Factors, Diagnosis**

*AJMC: What causes depression?*

*Dr. Hirschfeld:* Depression is a syndromal diagnosis. Like high blood pressure, arthritis, and congestive heart failure, it has a number of causes that include a genetic predisposition, a familial environment that fosters depression, early-life traumatizing experiences, and adverse current interpersonal events such as marital separation or loss.

*AJMC: What about brain chemistry?*

*Dr. Hirschfeld:* Certainly the activity of neurotransmitters in the brain is involved in causing depression. This activity is influenced by genetics and the environment. But we should not lose sight of the multifactorial nature of depression. Like most of the major chronic diseases, except perhaps infectious diseases, we have only a moderate understanding of the causes of depression.

*AJMC: Who is at highest risk for depression?*

*Dr. Hirschfeld:* Anyone may become clinically depressed, but it is more common in women and young adults. There are triggers that can cause an attack of depression in susceptible people. Adverse life events, especially relationship problems, often bring on an episode of depression. Other triggers are alcohol, stressful situations, or chronic diseases. Pharmaceuticals, such as antihypertensive medications, anticancer drugs, and steroids, can also lower the threshold for depression.

*AJMC: Is depression more common in the elderly?*

*Dr. Hirschfeld:* No. Suicide rates increase dramatically in the elderly, but rates of depression do not.

*AJMC: How do you diagnose depression?*

*Dr. Hirschfeld:* By interview. There is no other way. You must sit down with the patient and ask about specific symptoms, which are very straightforward and include things such as feeling of sadness or blue mood. The other main symptoms are difficulty concentrating, loss of energy, change in appetite, difficulty sleeping, loss of sex drive, feelings of guilt, and thoughts about death and suicide.

*AJMC: Some of these symptoms are pretty common. How do you prevent overdiagnosis?*

*Dr. Hirschfeld:* We look for persistence. We rarely diagnose depression unless the symptoms have remained for at least a month. The symptoms must also cause some impairment. People with depression often experience other symptoms such as gastrointestinal (GI) complaints, constipation, "nervous stomach," aches and pains, and headache. Those conditions are common, but they are not diagnostic criteria. So we make it easy: if your symptoms match the criteria, you have depression. The basic syndrome of depression has been well described since the time of Hippocrates in the fourth century BC. Clinicians may not fully agree on the diagnostic criteria, but the basic syndrome has been well described for more than 2000 years.

*AJMC: What are the challenges in diagnosing and treating depression in patients with other conditions?*

*Dr. Hirschfeld:* We need to be aware of potential drug interactions. At the same time, in making the diagnosis we need to consider medications or other illnesses as a potential underlying cause of the depression. We know, for example, that certain types of stroke, heart disease, and endocrinologic disorders can result in depression.

**AJMC:** *Do those chronic diseases cause some sort of physiologic change, or do they cause a life event-induced depression?*

**Dr. Hirschfeld:** We don't know, but we do know that in patients with heart disease, a negative influence, like depression, can adversely affect outcome. That is, someone who is depressed after a heart attack is much more likely to die than someone who is not depressed. We still don't know what happens if you treat that depression, but studies are under way.

**AJMC:** *What are the major classes of depression?*

**Dr. Hirschfeld:** Depression can be bipolar or unipolar. Bipolars have mood swings—highs and lows—but those who are unipolar simply get depressed. Beyond that classification, there is single-episode depression as opposed to recurrent depression. Chronic depression is another class and it is defined as persisting for 2 years or longer. And then there is the subtype dysthymia, a chronic mild depression with an insidious onset.

**AJMC:** *Where does anxiety fit in?*

**Dr. Hirschfeld:** Anxiety is a separate diagnosis, but the comorbidity between depression and anxiety disorders is huge. Seventy percent of all people with depression have anxiety. There is also a fair amount of overlap in the symptoms, including difficulty sleeping, fearfulness, social withdrawal, and appetite disturbances.

### Treatment Strategies

**AJMC:** *What is the overall goal in the treatment of depression?*

**Dr. Hirschfeld:** To return the patient to his or her normal state of mind, normal relationships, and normal

ability to function in the family, at work, and in the community.

**AJMC:** *How long does this typically take?*

**Dr. Hirschfeld:** I expect improvement to occur gradually during the first 1 to 2 months of treatment. But in patients with more severe and chronic depression, recovery may require from 3 to 6 months of treatment. For example,

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I'm involved in a study of patients with major chronic depression averaging 8 years in duration. Patients are being treated either with sertraline or imipramine. After 3 months, about one third of patients were partial responders—they were feeling better but were still not well. When those people were kept on the same level of medication for an additional 4 months, a substantial number of them recovered completely. Recovery from depression can take a long time. If a patient walked into my office with a first episode and said that he or she had felt sick for 2 months or so, I would expect that patient to be feeling a little bit better after 2 weeks of treatment and a lot better in a month. Total recovery might occur after 6 weeks.

**AJMC:** *How do you measure treatment success in depressed patients?*

**Dr. Hirschfeld:** Face-to-face meetings are necessary to measure changes in function. But I also like to spend a lot of time with the spouse, the sons or

daughters, or the parents of the patient, or whomever the patient is living with. In fact, early reports about the patient's functioning from family members are often much more accurate than those from the depressed patient.

*AJMC: Why is that often the case?*

*Dr. Hirschfeld:* The earliest treatment responses are usually those of a decreased level of irritability or an improvement in sleep or appetite. The people the patient lives with can say "You got out of bed without trouble" or "You didn't get up at 4 AM." But deep inside, the patient feels just as depressed as he or she did 6 weeks earlier before treatment. That inner mood seems to be the last thing to get better. So if I have the patient's spouse telling me about functional improvements, I can tell the patient that I truly believe he or she is not feeling better, but I can also say that, based on my experience, the functional improvements are a positive sign and they will likely start feeling better in time.

*AJMC: What are the major treatment choices?*

*Dr. Hirschfeld:* Medication and psychotherapy. Therapies such as electroconvulsive therapy and light therapy are less common.

*AJMC: How long does treatment last?*

*Dr. Hirschfeld:* We have different phases of therapy. If patients come in depressed, my first job is to get them undepressed. That's the acute treatment phase. Then, after they feel better, they still are at risk of reverting to a depressive episode, so I want to continue therapy beyond the initial therapeutic improvement. Just like treating strep throat with the older regimens, patients might feel better after 3 days of antibiotics but they still

need to take that full 10-day course. So, I want to treat the patient for depression for 4 or 5 additional months. Then, in most cases, especially if this was the patient's first episode of depression, therapy can stop. But if patients have experienced 6 episodes of depression already or if other risk factors are present, the likelihood of another episode is high, so I might continue treatment to prevent it. That's called maintenance therapy.

*AJMC: What are the major antidepressant drugs used today?*

*Dr. Hirschfeld:* The most widely used antidepressants today are the selective serotonin reuptake inhibitors (SSRIs). Next in line are the tricyclic antidepressants, which have been available for many years. The monoamine oxidase inhibitors, another older group, are quite effective, but the side effects they produce prevent them from being a first-line choice. And then there are special medications for specific syndromes or diagnoses, such as mood stabilizers for bipolar disorders. Also, a host of new generation drugs, such as noradrenergic reuptake inhibitors and dual action medications, are just coming on the market.

*AJMC: Is any type of drug therapy more effective than another?*

*Dr. Hirschfeld:* Basically, all the antidepressants are about equally efficacious. There is modest evidence that some of the so-called dual action drugs have some increased efficacy, but they may also cause more side effects.

*AJMC: How do clinicians choose, for example, one SSRI as opposed to another?*

*Dr. Hirschfeld:* Some patients respond to one antidepressant better

than another. They may respond to fluoxetine but not sertraline, or vice versa. That is a major factor in drug choice: Does it work for this patient? The side-effect profile is the other main factor in choosing a medication. Certain products are associated with more GI side effects, others are associated with producing more anxiety, and some can cause sexual side effects. Clinicians also consider titration, half-life, and dosing requirements. Many of those drugs are taken just once a day, but some require more frequent dosing. And finally, cost and formulary availability are always issues.

*AJMC: Are there special issues related to the treatment of patients with comorbid illnesses?*

*Dr. Hirschfeld:* The newer drugs are generally quite safe, but some of the older ones may need to be used with caution in certain patient types. For example, tricyclics may be problematic in patients with heart disease because they are associated with some arrhythmias. Also, an antidepressant's effect on metabolism in the liver can be a factor in choosing therapy for patients with other diseases or conditions. Certain antidepressants have a higher potential for causing liver-related drug-drug interactions, so the antidepressant choice may hinge on the other drugs that the patient is taking. Conversely, whether a concomitant disease has any effect on liver or kidney function is also important.

### Treating Depression in the Era of Managed Care

*AJMC: What are the main barriers to the treatment of depression today?*

*Dr. Hirschfeld:* One is a lack of clinician knowledge. Many clinicians are still not comfortable with their understanding of depression. Giving inade-

quate instructions to patients is a part of this. A clinician can't simply give patients a bunch of antidepressant pills and tell them "Here, take these." He or she needs to explain about the side effects. Clinicians need to prepare patients for nothing much to happen for several weeks, and then they must encourage patients to schedule an appointment for a week to 10 days later. There's a lot to learn and a lot to do.

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*AJMC: Who treats depression today?*

*Dr. Hirschfeld:* Currently, about half of all antidepressant prescriptions are written by primary care physicians, about one quarter by psychiatrists, and the remainder by specialists. Education about the treatment of depression is necessary for all of these clinicians, but especially among the primary care physicians and family practitioners.

*AJMC: Are patients becoming better informed about depression?*

*Dr. Hirschfeld:* Yes, they are slowly becoming better educated and more proactive in seeking help. Managed care organizations and employer groups can take some credit for that. It is critical, though, that patient education efforts in depression be expanded.

*AJMC: What are the pharmacoeconomic considerations in selecting an antidepressant?*



*Dr. Hirschfeld:* Certainly the acquisition cost of the drug is important. This will determine, in some cases, availability in the formulary or whether the drug is listed in the recommended treatment protocol as a first choice versus second choice. But perhaps even more important as a cost issue is drug tolerability. If the patient doesn't stay on the medication and then gets worse, it has been very well documented that overall utilization costs will increase substantially. If patients are depressed or anxious, they bring many more complaints to their general physician. They are also at an elevated risk for suicide or hospitalization. If the patient is treated successfully, utilization decreases. So if clinicians are prescribing a generic medication that is less expensive on a per-pill basis but has an unattractive side-effect profile, the patient is more likely to stop taking that medicine. He or she will become depressed again, and the ultimate cost to the health system increases.

*AJMC: Are most health system formularies too restrictive?*

*Dr. Hirschfeld:* There was a time when managed care companies were very reluctant to open their formularies to the new drugs, but I think those issues have diminished. The key limitation now is health system approval for follow-up visits to check for efficacy and side effects and to ensure compliance. If clinicians and patients are granted the time necessary to monitor therapy, there is a greater chance of long-term success and lower long-term costs.

*AJMC: What are some other cost considerations related to depression?*

*Dr. Hirschfeld:* In addition to the extra direct cost to the health system from undertreating depression, there may also be huge costs to society or to employers. One study by Paul

Greenberg and associates at Massachusetts Institute of Technology has estimated the global burden of depression to be approximately \$45 billion.<sup>1</sup> In terms of disability-adjusted life years lost, the World Health Organization ranked depression number 1 in the Americas in 1998, and number 5 worldwide.<sup>2</sup>

*AJMC: What does all that mean for the payers?*

*Dr. Hirschfeld:* Beside the direct health costs that might be passed along to the payer, the indirect costs associated with this personal burden of disease must be considered. In the workplace, for example, it's been reported that employers may pay about \$3000 per depressed employee annually in lost productivity or absenteeism.<sup>3</sup> One study showed that depressed workers had between 1.5 and 3.2 more short-term work-disability days over a month than did other workers.<sup>4</sup> And of course there is the cost in terms of quality of life for the individual with untreated depression.

*AJMC: Has managed care had an effect on how depressed patients are treated?*

*Dr. Hirschfeld:* Yes. In educating specialist providers and member patients, the managed care system has already moved us ahead. Now these efforts must be expanded, especially in primary care provider education and in outreach to patients and to the families of patients. In opening access to their formularies, managed care groups have also already advanced the cause of successful therapy. As new therapies become available, they need to maintain this open access policy.

*AJMC: Are you aware of many treatment algorithms for depression?*

*Dr. Hirschfeld:* Yes, various protocols have been generated. I was involved

recently, for example, in the American Psychiatric Association's Treatment Guideline for Bipolar Disorder. In the Texas Medication Algorithm Project, I am involved in the development of consensus medication algorithms for the treatment of major depressive disorders.<sup>5</sup>

*AJMC: What changes can managed care organizations make to improve the treatment of depression?*

*Dr. Hirschfeld:* One of the most important changes that now must happen is a relaxation of current restrictions on the number of patient visits allowed to treat mental illness or depression. Some patients, who are certainly a minority, simply require more frequent monitoring of their therapy. Four visits per patient per episode may not be enough. The extra time spent with these difficult patients will improve the overall treatment success rates. Another change that will improve the success rate is expanded access to credentialed psychotherapists. Again, that won't be

required for all patients, but the option needs to remain available. If physicians are educated and if we can generate adaptable algorithms for treatment, then the most costly options in the treatment of depression will be used judiciously.

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... REFERENCES ...

1. Greenberg PE, Stiglin LE, Finkelstein SN, Berndt ER. The economic burden of depression in 1990. *J Clin Psychiatry* 1993;54:405-418.
2. *World Health Report*, 1999 World Health Organization (WHO), Geneva. <http://www.who.int/whr/1999/en/report.htm>
3. Williams RA, Strasser PB. Depression in the workplace: Impact on employees. *Am Assoc Occup Health Nurses J* 1999;47:526-537.
4. Kessler RC, Barber C, Birnbaum HG, et al. Depression in the workplace: Effects on short-term disability. *Health Aff* 1999;18:163-171.
5. Crismon ML, Trivedi M, Pigott TA, et al. The Texas Medication Algorithm Project: Report of the Texas Consensus Conference Panel on Medication Treatment of Major Depressive Disorder. *J Clin Psychiatry* 1999;60:142-156.