

SUPPLEMENT TO

**M A N A G E D**

# Care

## Diagnosing and Treating Depression In a Managed Care Environment: Concerns, Perceptions, and Misperceptions

Proceedings of the Economic Working Group Advisory Board  
October 2003, Philadelphia

### HIGHLIGHTS

- If so many patients currently are prescribed antidepressants, why is the disease still undertreated?

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- If so many people suffer from depression, why are physicians not diagnosing it?

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- Did patients who were noncompliant with antidepressant therapy need the medications in the first place?

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- Aren't depression disease management programs extremely expensive?

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- Don't national guidelines stipulate discontinuation of antidepressant therapy at or before 6 months?

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- Does the Health Plan Employer Data and Information Set (HEDIS) play a big role in improving the care of patients with depression?

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M A N A G E D  
**Care**

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## INTRODUCTORY MESSAGE

PATRICIA WOLFANGEL

Director of Client Services, The Zitter Group

In a June 2003 article in the *Journal of the American Medical Association*, lifetime- and 12-month prevalence data were reported for major depressive disorder, documenting once again that depression is a widespread and serious illness. Of the diagnosed cases of depression, 51 percent were classified as severe or very severe. Role impairment was significant, and depression was commonly a comorbid condition with other disorders.

These statistics, however unfortunate, are not surprising, nor do they run counter to earlier epidemiological data. The same article reported that of individuals diagnosed with depression within a 12-month period, fewer than 22 percent were adequately treated. Thus, most patients suffering from depression still do not receive adequate care. These grim statistics have, in part, been a motivating force in the establishment of the Economic Working Group (EWG) Advisory Board and have been fundamental to its progress over the past 2 years.

The EWG has struggled to understand why depression remains underdiagnosed and, when diagnosed, undertreated. Exploratory discussions with providers from managed care environments have yielded several perspectives that might help to explain the well-documented poor performance in the treatment of depression.

This supplement to MANAGED CARE highlights perceptions (and misperceptions) of a segment of the managed marketplace and examines them in light of the published literature and the expertise of the EWG. This supplement continues with an examination of the strengths and weaknesses of HEDIS, its effect on improving quality of care, and how well it measures quality.

This publication also synthesizes four faculty presentations on the underdiagnosis and undertreatment of depression. The first is a discourse on the Mini International Neuropsychiatric Interview; the second is a profile of the MacArthur Initiative on Depression in Primary Care; the third is a case study describing the Quality Partnership Program, a disease management program designed to improve the quality of depression management; and the fourth is a look at the varying ways in which patients gain access to the managed behavioral health system.

These pages conclude with an examination of the Sequenced Treatment Alternatives to Relieve Depression Study. This study was supported in part by the National Institute of Mental Health and intended to address major clinical information gaps and evaluate theoretical principles and clinical beliefs that guide pharmacotherapy of major depressive disorder.

Through frank and grounded discussion, such as the one that follows — along with an exploration of the results of the major nationwide studies, also cited in this publication — we hope that treatment of patients with depression soon will be optimal for all who suffer from this chronic and debilitating disease.

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## ABOUT THIS PUBLICATION

**T**he Economic Working Group Advisory Board comprises professionals from various disciplines, including managed behavioral health, psychiatry, pharmacy, academia, policy/accreditation, primary care, the employer segment, and payers. The EWG, with nationwide representation, met in Philadelphia in October 2003 to discuss depression with respect to diagnosis, treatment, and overall performance on measures such as the Health Plan Employer Data and Information Set, which are designed to be a proxy for quality of care.

Rather than synthesize the proceedings of the 2-day meeting, as has been done previously, the decision was made to highlight key issues deserving of exploration. Those issues are presented as perceptions and misperceptions regarding the diagnosis and treatment of patients with depression in a managed care environment.

This publication explores those perceptions and captures advisers' opinions and experiences regarding them. In addition to expert consensus, we present a great many studies from the published literature accessed through MEDLINE. For the most part, only studies published within the past 3 years are included. A few earlier seminal studies are included for cases in which no new research or data were readily available. In the hundreds of abstracts reviewed, not one study was found that documented overtreatment or overdiagnosis of depression.

Quite the contrary situation was found. Yet, from the perspective of the managed care professional who is faced with antidepressants as one of the most common and costly items in his or her pharmacy budget, there appears to be a reasonable incongruity. We explore this seeming contradiction and present the latest information on best practices in terms of diagnosis and treatment, illustrating the latter with two disease management programs that show promising preliminary results.

It is not easy to treat depression. The disease is rife with social stigma and potentially negative economic consequences. Our health care systems are not adequately structured to care for patients with depression; the issues with coding and reimbursement constitute a primary example. Much has yet to be done. Recognizing common perceptions and misperceptions surrounding depression allows us to begin, as a multidisciplinary profession, to address and dismantle those misperceptions and to practice more clinically effective and cost-effective medicine for affected patients.

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This supplement has undergone appropriate peer review by a qualified physician expert in mental health, selected by MANAGED CARE.

The content of this supplement was based on a MEDLINE literature search as well as transcripts from the EWG Advisory Board and was prepared by Susan Keller, Senior Associate, The Zitter Group.

## FACULTY DISCUSSION AND LITERATURE SEARCH

# Diagnosing and Treating Depression in A Managed Care Environment: Concerns, Perceptions, and Misperceptions

### LITERATURE REVIEW

#### Perceptions and Misperceptions Regarding Diagnosis and Treatment of Depression

**A**mong payers and providers of health care, numerous perceptions and misperceptions exist regarding depression in the areas of prevalence, diagnostic accuracy, appropriate management, length of therapy, and costs of optimal treatment. The objective of this supplement is to enumerate those perceptions and explore them in light of the published literature, as well as from the perspectives of the Economic Working Group (EWG) advisers.

From discussions with and focus groups attended by managed care providers and payers, the EWG has gathered a number of perceptions regarding the diagnosis and treatment of depression. Here they are voiced as if a managed care professional were expressing them:

- 1. If so many of my patients are prescribed antidepressants, how can the disease — as reported in the literature — be so massively undertreated?*
- 2. If so many people suffer from depression, why are my physicians not detecting, diagnosing, and documenting it?*
- 3. A large percentage of my patients who are prescribed antidepressants never complete their course of therapy. Perhaps they did not need the drugs in the first place.*
- 4. Whenever our patients begin a course of antidepressant therapy, especially if it is integrated into a disease management program, we see costs go way up.*
- 5. Guidelines stipulate discontinuation of therapy at a maximum of 6 months; some of my patients take antidepressants for years, however, and it is costing me a bundle.*

We address each of these perceptions in turn, looking at the complexity of the issues, acknowledging the everyday reality of the managed care professional, and exploring what is known and published in the literature.

#### **1** If so many of my patients are prescribed antidepressants, how can the disease — as reported in the literature — be so massively undertreated?

One does not have to look far in the literature to find studies documenting significant increases in the number of patients receiving treatment for depression, including increased prescribing of antidepressants. For example, researchers reported that the rate of outpatient treatment for depression increased from 0.73 per 100 persons in 1987 to 2.33 in 1997, more than a 300 percent increase (Olfson 2002). During the same period, the proportion of treated individuals prescribed antidepressants increased from 37.3 to 74.5 percent, a 200 percent increase.

These figures might convince any reasonable person that depression finally has been recognized as a significant public health problem and is now being adequately addressed. Olfson and colleagues characterized the study period as one of greater involvement of physicians, greater use of psychotropic medications, and expanding availability of third-party payment. These apparently positive changes also coincided with the introduction of better-tolerated antidepressants, such as selective serotonin reuptake inhibitors (SSRIs); with increased penetration of managed care; and with the development of more effective methods for the diagnosis of depression in the clinical practice environment. All these elements seem to point to significant strides toward optimal treatment of patients with depression (Olfson 2002).

In an earlier *Journal of the American Medical Association* study, authors quantified the change in the use of antidepressant drugs and the frequency of office visits for depression in the year 1985 and the period from 1993 to 1994 (Pincus 1998). The authors reported that from the earlier survey period to the later, the number of office visits during which a psychotropic medication was prescribed increased from 32.7 million to 45.6 million; the proportion of these visits, in relation to all visits, in-

creased from 5.1 to 6.5 percent. The number of prescriptions for antianxiety or hypnotic drugs — previously the largest category — decreased and is now surpassed by that of prescriptions for antidepressant drugs. Office visits for depression increased from 10.99 million in 1988 to 20.43 million in the period from 1993 to 1994.

The following, from the study's conclusion, is of particular interest: "Although visits for depression doubled for both primary care physicians and psychiatrists, the *proportion* of visits for depression during which an antidepressant was prescribed increased for psychiatrists but not for primary care physicians" [italics added] (Pincus 1998).

### Primary care versus specialty practice

Well documented in the literature, in addition to professional experience, is the fact that most patients with depression are treated in a primary care setting. Because this is the case, it might be deduced from the Pincus study that although patients with depression may be more commonly seeking help for it now than they were 15 years ago, their disease is not being adequately treated with antidepressants in the primary care setting (Pincus 1998).

Also well accepted in the literature, and in clinical practice, is the fact that women are afflicted with depression at approximately twice the rate that is found in men. With data from the Centers for Disease Control and Prevention's National Health Care Survey, trends in utilization of medications associated with ambulatory care visits by women were examined. Prescribing trends from 1995 to 2000 for 10 therapeutic drug classes were quantified. During women's ambulatory care visits in the years 1999 to 2000, antidepressants were the most frequently mentioned therapeutic class. The next most frequently mentioned classes were hormone replacement therapies, antiarthritics, and medications for acid and/or peptic disorders. Overall, the number of medications prescribed increased by about 13 percent, from 144 to 162 per 100 visits, between study commencement in 1995 and its conclusion in 2000 (Burt 2003).

Another group that is prone to depression is the elderly. One team of researchers set out to examine psychotropic drug usage in the noninstitutionalized elderly by conducting a retrospective analysis of the 1996 Medical Expenditure Survey (MEPS). MEPS is the third (and most recent) in a series of national probability surveys conducted by the Agency for Healthcare Research and Quality (AHRQ) on the financing and utilization of medical care in the United States. According to MEPS data, more than 6 million, or 19 percent, of community-dwelling elderly persons used psychotropic medications in 1996. Nearly half those people were taking antidepressants. The authors concluded that "Nearly one in five community-dwelling elderly persons [surveyed] used psychotropic medications, primarily antidepressants" (Aparasu 2003).

In view of studies such as those cited, it must be acknowledged that utilization of antidepressants is rising among the general population as well as subgroups. Nevertheless, when nationwide prevalence rates of depression, such as those recently reported in "The Epidemiology of Major Depressive Disorder: Results from the National Comorbidity Survey Replication," published in *JAMA* (Kessler 2003), are considered, the increased numbers of people now receiving care for depression still only represent *just over half* of all patients diagnosed.

### An epidemic of undertreatment

Highlights from the National Comorbidity Survey Replication follow. Using the World Health Organization's diagnostic tool, the Composite International Diagnostic Interview, the authors determined that the lifetime prevalence of major depressive disorder was 16.2 percent of the population, or 32.6 to 35.1 million adults in the United States. Twelve-month prevalence rates translated into 6.6 percent of the population, or 13.1 million to 14.2 million U.S. adults who are experiencing a major depressive disorder in a given 1-year period.

Just over half (51.6 percent) of individuals suffering from a major depressive disorder receive treatment for the disease. Although this statistic in itself is startling and a cause for alarm, of greater concern is that, as reported by Kessler et al, treatment was considered adequate in only 41.9 percent of individuals who received it. Thus, only 21.7 percent of persons afflicted within a 12-month period with major depressive disorder were adequately treated. The authors concluded: "While the recent increase in treatment is encouraging, inadequate treatment is a serious concern. Emphasis on screening and expansion of treatment needs to be accompanied by a parallel emphasis on treatment quality improvement" (Kessler 2003).

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*"An overall low false-positive rate immediately raises a red flag. It's a real indicator of underdiagnosis. People are not entering the system who should be. We're missing a lot of true positives out there."*

— BERNARD BLOOM, PhD

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In addition to the National Comorbidity Survey Replication discussed above, literally dozens of epidemiological studies have documented the epidemic proportions of depression undertreatment, generally characterized as the lack of follow-up care as well as high rates of inadequate antidepressant treatment in both primary and specialty care (Dawson 1999, Keller 2001, Keller 2002, Salzman 2001, Simon 2001a, Simon 2002, and others).

## Type of health care system makes little difference

“Despite considerable mental health access and generous pharmacy benefits,” undertreatment of depression also is seen in integrated health systems such as the Veterans Health Administration (Charbonneau 2003). Similar situations have been reported in large, staff-model health maintenance organizations (HMOs). Researchers found that among elderly HMO patients with a diagnosis of depression, with a prescription for antidepressants or who used specialty mental health services, “the rate of adequate antidepressant use remained below 30 percent” (Unutzer 2002). Other studies reported adequate use of antidepressants to be in the range of 35 to 44 percent (Ohayon 2002, Steffens 2000). Even under a universal health care system (Canadian), only half of depressed patients received treatment and only 18 percent were prescribed antidepressants (Parikh 1999).

Researchers attempting to determine sociological influences on antidepressant prescribing found that insurance status influences whether depressed patients are prescribed an antidepressant; for example, self-paying patients were far less likely to receive a prescription for an antidepressant than were those with insurance coverage. The authors concluded: “Health care providers need to take the time to help patients without insurance obtain antidepressant medication if it is needed” (Sleath 2003).

## Direct-to-consumer advertising

A group of researchers from the Harvard School of Public Health sought to determine whether direct-to-consumer advertising (DTC) was driving up utilization of prescription drugs inappropriately, thus resulting in higher and unnecessary costs of care (Rosenthal 2002). As they reported in the *New England Journal of Medicine*, in the 5 years between 1996 and 2000, there was an approximate tripling of annual spending on DTC advertising. DTC advertising, however, still accounts for only 15 percent of all money spent on drug promotion. The remainder of the promotional budget is targeted to physicians as well as advertisements in medical journals and the distribution of drug samples. Overall, promotion as a percentage of sales has remained fairly constant since the early 1990s. Although the increased use of television advertisements for pharmaceutical products that are directed to consumers is, and must continue to be, monitored by the U.S. Food and Drug Administration, the study authors reported no measurable effect in terms of patients requesting and being prescribed medications for which they did not present with clinical symptoms. Thus, although DTC advertising may be highly visible, its effect relative to driving utilization of medications, including antidepressants, remains negligible.

## 2 If so many people suffer from depression, why are my physicians not detecting, diagnosing, and documenting it?

Again, a MEDLINE literature search resulted in numerous studies documenting high rates of incorrect or missed diagnosis. For example, a well-regarded expert on the diagnosis and treatment of depression worldwide reported that “roughly half of psychiatric cases presenting in primary care go unrecognized, and one third of cases recognized are misdiagnosed. Although treatment is offered in nearly 60 percent of recognized cases, it is seldom in the context of a specific diagnosis and is only appropriate in about 5 percent of cases overall” (Lecrubier 2001).

Rates of diagnosis that were only slightly more accurate were documented by another group of investigators (Wittchen 2001, 2002). They reported that correct diagnosis of major depressive disorder occurred in 59 to 75 percent of cases presenting to primary care physicians, depending on the diagnostic tool employed; higher rates of recognition are achieved with criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV), than with the *International Classification of Diseases*, 10th edition (ICD-10).

Among the patients with correct diagnoses, primary care physicians prescribed medications in nearly 73 percent of cases classified with DSM-IV and in 61 percent of cases classified with ICD-10. Using multiple logistical regression, the study authors identified factors that contribute to diagnostic accuracy; these factors include whether patients had presented with prior depressive episodes, a higher number of depressive symptoms, older age, and greater experience of the physician (physicians in practice longer than 5 years had more accurate rates of diagnosis) (Wittchen 2001, 2002).

## Diagnosis and chronic nature of depression

Even among the small percentage of patients who are adequately treated for their depression, it is likely that they will face the crushing weight of depression again. The chronic nature of the disease is documented frequently in the literature, and practitioners who treat depressed patients are well aware that because of the cyclic nature of the disease, these patients will probably return to their offices, presenting with the same symptoms.

As Wittchen et al documented, the chronic nature of the disease contributes to its correct diagnosis. The recurrent nature of depression was quantified as: “Depression is a chronic and disabling illness that frequently requires long-term maintenance treatment. The probability of recurrence after recovery is very high, especially among patients who have experienced previous episodes of depression. Indeed, once a patient has suffered from three

episodes of depression, the likelihood that he or she will have another episode within the next 2 years exceeds 95 percent. Despite this, depression remains an underrecognized and undertreated disease” (Keller 2002).

### Repercussions of the diagnosis

Given the strong likelihood of recurrence, the high prevalence of the disease, and the well-accepted diagnostic tools available to physicians, there remains the question of why depression is either missed accidentally or, for other reasons, intentionally not coded as a primary diagnosis. Numerous explanations exist. Here is an overview of those that are most significant:

- Depression is a common comorbid condition accompanying many chronic diseases; this comorbid nature of the disease complicates diagnosis and coding.
- Health care providers lack well-established, reliable systems for adequately treating patients once depression is diagnosed.
- Nonparity of medical and behavioral health benefits is a barrier to adequately diagnosing and treating depression.
- A nonalignment of payment mechanisms, wherein providers are not always reimbursed for treatment (e.g., telephone consultations), diminishes the likelihood of optimal care.
- Social stigma for the depressed patient still exists.
- Providers may believe they are not equipped to deal with the social, familial, economic, and/or spiritual factors that may play a role in the onset and treatment of the disease.

**The clinical challenge:** The comorbid nature of depression complicates the diagnosis, especially among patients presenting with somatic symptoms or among those who have not previously been diagnosed with the disease. A study at the Department of Medicine and the Regenstrief Institute for Health Care at the Indiana University School of Medicine showed that somatic symptoms “are the predominant reason why patients with common mental disorders such as depression and anxiety initially present in primary care. At least 33 percent of somatic symptoms are medically unexplained, and these symptoms are chronic or recurrent in 20 to 25 percent of patients. Unexplained or multiple somatic symptoms are strongly associated with coexisting depressive and anxiety disorders” (Kroenke 2003).

**The system challenge:** Among our health care systems today, there is a dearth of well-established, reliable systems to treat patients adequately once depression is diagnosed. There also are several obstacles to providing comprehensive, effective health care for people with depression; primary among these are insufficient provider

time for adequate diagnosis and follow-up care, a lack of experienced behavioral health care specialists for patient referral, and difficulty in gaining access to those services. Investigators found that general practitioners viewed obstacles to providing effective treatment of depression as resulting from external causes, as opposed to internal factors such as deficits in their own knowledge, experience, or skill set. Complicating the picture is the excessive workload that many physicians must face and persistent difficulties surrounding communications between primary and secondary mental health service providers (Telford 2002).

**The benefits challenge:** Nonparity of medical and behavioral health benefits has been implicated as a barrier to diagnosing and treating depression. For example, in an analysis of mental health insurance benefits offered by 336 Fortune 500 companies, researchers found that the carve-out contracts of these firms generally covered a wide range of services and could be characterized as generous in comparison with those reported for other integrated and carve-out plans. Nevertheless, mental health care benefits did not reach parity with typical medical benefits, nor did they protect enrollees from the risk of catastrophic expenditures (Merrick 2001). Companies not in the Fortune 500 category generally offer even more limited mental health care benefits (Umland 1997).

The issue of parity between medical and mental health care benefits has been a concern for Rand researchers as well. They asked, “How expensive is unlimited mental health care coverage under managed care?” The answer: “not very.” Rand researchers found that removing the average annual limit of \$25,000 for mental health care would increase insurance payments by only about \$1 per enrollee per year overall. Children would be the main beneficiaries of expanded (unlimited) benefits. The authors cautioned against unfounded concerns about costs, which unfortunately have defeated many health system reform proposals. Policy decisions, they argued, must be based on correct assumptions and current valid data. In the absence of such reliable information, dramatic overestimates regarding the cost of unlimited managed mental health care benefits will flourish (Peele 1999, Sturm 1997).

**The reimbursement challenge:** Because follow-up with depressed patients is a key factor in the success of a treatment regimen, patient-provider interaction in and out of the office setting is important. Nonoffice visits might include reminder mailings to patients to refill prescriptions for antidepressants, e-mails (for which prior consent has been obtained from the patient), and telephone consultations. Until there is a payment mechanism that reimburses providers for out-of-office treatments such as these, follow-up care will never reach optimal levels.

**Patient stigma:** Social stigma for the patient with a diagnosis of depression still exists and flourishes. Because



of a self-imposed stigma, patients themselves may deny the severity of their symptoms and may be reluctant to discuss somatic and cognitive/behavioral symptoms with their physicians (Barkin 2000). Depressed employees hesitate to share their diagnosis with managers and supervisors, and this is understandable. In a study conducted with human resource officers in the United Kingdom, “a label of depression significantly reduced the chances of employment, compared with one of diabetes.” The primary reason given by potential employers for this bias was the expectation of poor work performance. The authors suggested that greater dissemination of information may alleviate some of the stigma associated with depression and employment (Glozier 1998).

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*“Confidentiality issues surrounding depression are a challenge to any quality improvement effort.”*

— STACEY BRENNAN, MD

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Researchers in Australia and members of the national depression initiative examined barriers to social participation experienced by people with depression. They found barriers to employment, inadequate primary health care, lack of nonpharmacological interventions, and stigmatizing attitudes of many health care providers. These negative attitudes and barriers are similar to those experienced by persons with other psychological disorders (McNair 2002). Even family members of persons with a behavioral health diagnosis have reported feeling stigmatized, and many reported concealing a family member’s hospitalization for mental illness (Phelan 1998).

Alleviation of stigma is a worthwhile goal of both medical education and public information campaigns (Goldstein 2002, Paton 2001).

**The physician’s tendency to avoid the diagnosis:** As reported previously (McNair 2002), attitudes of health care providers may hamper a diagnosis of depression. For a host of reasons — including inadequate reimbursement — some physicians do not even *want* to diagnose the disease. In a qualitative study of physicians’ attitudes regarding the management of their patients with depression, researchers found that physicians regarded depression as an everyday problem of practice, rather than as an objective diagnostic category. In other words, they viewed depression as a common and normal response to life events or change, as opposed to a true illness.

For patients living in socioeconomically deprived environments, the problems — and therefore the depression — were viewed by surveyed practitioners as insoluble. This perception “has an important implication for

the construction of educational interventions around improving the recognition and treatment of depression in primary care” (Chew-Graham 2002). Certain physicians may be reluctant to recognize and respond to depressed patients in depth. This is due to the broader structural and social factors that they have little or no control over and that they believe may contribute to the condition (Schuyler 2000).

Regardless of whether depression is recognized, accurately diagnosed, and adequately treated, patients with undiagnosed and/or undertreated depression utilize health care resources extensively. Eventually, irrespective of their course of treatment, these patients become a cost burden to managed care. In a frequently cited study, researchers looked at a sample of 767 extensive utilizers of health care (Katon 1990, 2003). More than half were identified as distressed by their primary care physician or by an elevated score on the Symptom Checklist anxiety and depression scales or the Symptom Checklist somatization scale. In the prior year, members of this group made an average of 15 medical visits and 15 telephone calls to the health care facility. The good outcome was that when these extensive utilizers — the majority of whom were depressed — were assigned to an intervention group, two thirds received a revised treatment plan (Katon 1990, 2003). (The cost and clinical outcomes of depression disease management programs are reviewed later in this supplement.)

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### **3 A large percentage of my patients who are prescribed antidepressants never complete their course of therapy. Perhaps they did not need the drugs in the first place.**

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No MEDLINE studies documenting overdiagnosis or overtreatment of depression could be located; therefore, from the literature it appears that most patients being prescribed antidepressants are being prescribed appropriately but discontinue their medications for reasons other than misdiagnosis. Unfortunately, patient compliance appears to be the exception rather than the rule.

An examination of noncompliance, or dropout, reveals a number of causative factors:

- Poor communication between patient and physician
- Tolerability of the drug
- Real or perceived lack of efficacy
- Prohibitive cost
- Ethnicity of the patient population

**Quality of communication between patient and physician:** Investigators attempted to detect “predictors of adherence to antidepressant therapy and to identify specific educational messages, side effects, and features of doctor-patient collaboration that influence adher-

ence.” They concluded that primary care physicians may be able to enhance patient compliance with antidepressant therapy by integrating simple and specific educational messages into primary care visits (Lin 1995). Varying levels of literacy as well as language barriers must be kept in mind when any educational messages are delivered to patients and/or their caregivers.

In an article published in *JAMA* (Bull 2002), investigators examined noncompliance with antidepressants as a function of the quality of communications between patients and physicians. In the context section of their study, they remarked, “Although current depression treatment guidelines recommend continuing antidepressant therapy for at least 4 to 9 months [after remission of symptoms], many patients discontinue treatment prematurely, within 3 months.”

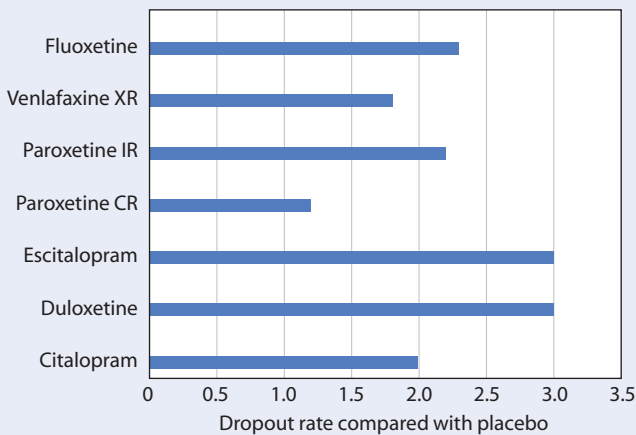
The main outcomes measure of this study was the quality of physician-patient communication about antidepressant therapy duration, potentially adverse effects, and optimal length of therapy. The study authors reported a discrepancy between physician-reported quality of communications and patient reports as to what their physicians told them to expect from therapy. For example, 72 percent of physicians reported instructing patients to take antidepressants for a 6-month period, whereas only 34 percent of patients agreed that they received this instruction, and 56 percent reported receiving no instruction whatsoever.

Patients who were counseled by their physicians about potential adverse effects were less likely to discontinue therapy than were patients who had not received this counseling. The authors stated, “Explicit instructions about expected duration of therapy and discussions about medication adverse effects throughout treatment may reduce discontinuation of SSRI use. Our findings that patients with three or more follow-up visits were more likely to continue using the initially prescribed antidepressant medication suggest that frequent patient-physician contact may increase the probability that patients will continue therapy” (Bull 2002).

It is interesting to note that in this study, three or more visits improved compliance. This is the intent behind the Health Plan Employer Data and Information Set (HEDIS) measure that number of visits with the prescribing health care professional can be viewed as a proxy for quality care. (The role of HEDIS in enhancing quality of care is discussed later.)

One further aspect of poor physician-patient communication is a “side effect” of the disease itself: many depressed patients experience extremely low levels of self-esteem and do not feel entitled to take up their physicians’ time. Quality of care in depression depends, in part, on quality physician-patient communication, but depressed

**FIGURE 1 Dropout rates due to adverse effects versus placebo in clinical depression trials**



CR=controlled-release; IR=immediate-release; XR=extended-release.  
 SOURCES: BEASLEY 2000, GLAXOSMITHKLINE 2003, NEMEROFF 2002, PRESCRIBING INFORMATION FOR EACH PRODUCT, ST. LAMBERT 2003. (SERTRALINE DATA UNAVAILABLE.)

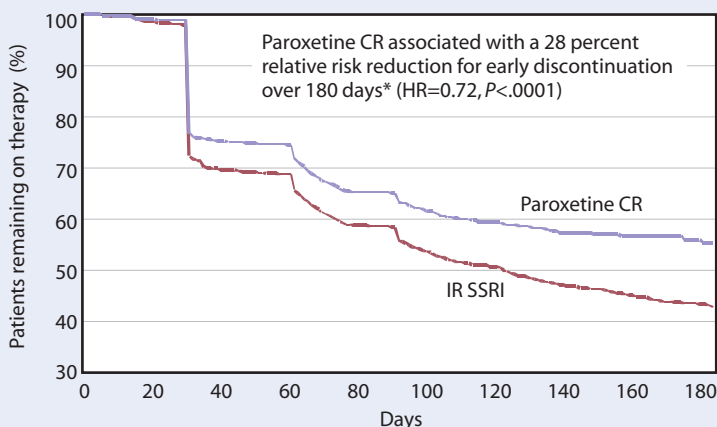
patients often experience difficulty discussing their depression. Their disease also makes seeking and keeping follow-up appointments an uncertainty. Some patients even wonder whether their disease is a legitimate reason for a visit to the physician. Therefore, physicians must be highly aware of patients’ anxieties in this regard and act to assure them that they are entitled to time with the clinician and that their problem is important (Gask 2003, Pollock 2002).

**Tolerability of medication:** Figure 1 illustrates dropout rates of commonly prescribed SSRIs and serotonin-noradrenaline reuptake inhibitors in comparison with placebo in depression clinical trials (Beasley 2000, Nemeroff 2002).

An earlier study reported that approximately 28 percent of patients newly prescribed antidepressants stopped taking the medication during the first month of therapy. When the group of patients who had been compliant until the end of the first month was interviewed at the end of the third month, 44 percent of them had stopped taking their antidepressants. Only severe side effects were associated with early noncompliance, suggesting that noncompliance is not highly associated with issues of tolerability (Lin 1995). We do know, however, that treatment-emergent nausea is one cause of early discontinuation of therapy. Antidepressant formulas with a controlled-release mechanism mitigate some of this dropout resulting from nausea.

Figure 2 illustrates the difference in findings with controlled-release (CR) versus immediate-release (IR) SSRIs, based on the National Managed Care Database (NMCD)

**FIGURE 2 National Managed Care Database phase 2: time to discontinuation results**



\*Controlling for age, gender, specialty care, depression/anxiety diagnoses, comorbidity and frailty using Cox proportional hazards modeling over a 180-day follow-up period.  
CR=controlled-release; IR SSRI=immediate-release selective serotonin reuptake inhibitor.  
SOURCE: EADDY 2003

study. This landmark national study included 38 million patients, who were enrolled in 64 managed care organizations (MCOs) around the country. This is the largest naturalistic retrospective managed care database study ever conducted in depression/anxiety, representing more than 1 million patients taking antidepressants. Time to discontinuation between IR and CR SSRIs was measured. Study authors found that paroxetine CR demonstrated a 28 percent relative risk reduction for discontinuation in comparison with IR SSRIs during the first 180 days of therapy (HR=0.72;  $P<.0001$ ). In addition, paroxetine CR is associated with a 17 percent reduction in the risk of changing medications in comparison with IR SSRI products.

The major limitation of the NMCD study is that the reason for discontinuation of therapy is unknown and may be related to factors other than tolerability. Also, differences in discontinuation found in this study do not establish superior safety or efficacy, inasmuch as these drugs have not been systematically compared in head-to-head, placebo-controlled trials.

Phase 3 of the NMCD study will focus on the economic effects of varying drug therapies during a 1-year period (Eaddy 2003).

**Perception of efficacy:** As just mentioned, robust, scientifically sound, randomized controlled trials comparing the efficacy of SSRIs in head-to-head investigations have not been completed. Yet, it is certain that a drug that enables a patient to remain on medication long enough to reach remission is a more efficacious treatment choice than is a medication that, for whatever reasons, results in

patient noncompliance with the therapeutic regimen.

In an article published in the *Journal of Clinical Psychiatry*, an author asked, “Are all antidepressants the same?” In the past, clinicians relied on tolerability profiles to answer that question, assuming that efficacy was essentially equal. Nevertheless, with newer agents now on the market that have superior tolerability profiles and with the advent of controlled-release formulations, the question of efficacy has taken on an added dimension (Moller 2000).

In general, antidepressants are reported to be equal in *efficacy*. *Effectiveness*, however, may differ significantly due to patient-specific factors. In weighing these factors, clinicians must take into account potential drug-drug interactions, the patient’s prior drug response, comorbid conditions, and the patient’s age and other pharmacotherapy-mediated events (Barkin 2000).

Although clinical trials have not yielded evidence, selecting a medication by matching its side effect profile to patient characteristics is supported by case reports and probably enhances compliance (Sutherland 2003).

It must be acknowledged that the issue of SSRI efficacy remains an area of uncertainty in the treatment of patients with major depressive disorder. Further research is needed to enable clinicians to make the most informed choice of pharmacotherapy for their patients with depression.

*“If you can show that utilizing a sustained-release dosing form would have better compliance earlier on, get patients accustomed to the drug, and then maybe move them over to an immediate-release product, I think you are going to see health plans take on this type of strategy in terms of dealing with noncompliant patients.”*

— LARRY PESKO, MS, SCD, RPH

**Cost:** With patients increasingly sharing costs, in the form of increased copayments, higher deductibles, and fewer pharmaceuticals and/or services covered, the price of a prescription is a motivating factor for many patients and their prescribers. In one study, 615 adult primary care patients with depression were surveyed with regard to the amount they were willing to pay for depression treatment. Mean baseline measurement was

\$270 ± \$187 per month, or about 9 percent of the subjects' household income. Willingness to pay was highly associated with income and severity of depressive symptoms. At 6 months, subjects' willingness to pay for therapy decreased as severity of their depressive symptoms diminished. "Measurements of willingness to pay may be a promising method for assessing the value of treatments for common mental disorders" (Unutzer 2003).

In fact, many providers are required by their health plans to initiate antidepressive therapy with the lowest priced generic option. Also, there is literature that documents cost savings when intensive drug utilization review is conducted. For example, in one study, significant cost savings were demonstrated through intensive drug utilization review of SSRIs (Dobscha 2003).

Study subjects included both inpatients and outpatients served by a Veterans Affairs Medical Center. The intervention included identification of a preferred agent, tablet splitting, education and feedback for prescribers, and an electronic record and ordering system to facilitate changes in prescriber behaviors. During the intervention (of 35 months' duration), researchers analyzed Veterans Affairs databases for changes in SSRI utilization and cost data.

After the nearly 3-year study period, they documented that both the number of patients treated with SSRIs and the amount spent on the drug class were on the rise. Mean monthly cost per patient decreased, however, from \$57.12 to \$42.19. Projected cost savings over the course of the study period was approximately \$700,000; 25 percent of the savings was attributed to tablet splitting, and 75 percent to a shift in the proportions of SSRIs prescribed, whereby lower-cost drugs accounted for a larger percentage of the whole. The authors concluded that multifaceted interventions, including provider education, changes in prescribing patterns, reductions in amount of medication prescribed, and increased use of generic medications can result in substantial cost savings for institutions (Dobscha 2003).

While the purely economic argument just presented initially could be construed as compelling, it must be emphasized that researchers were measuring only drug costs. They presented no information on total medical costs or on any clinical outcomes. From numerous published studies, in depression as well as other disease states, there is a clear and unmistakable inverse relationship between reduced drug costs and increases in overall medical costs. When the former decrease, the latter almost inevitably increase. This is a primary and fundamental problem with viewing costs in silos. Reducing cost in one area — pharmacy, for example — has ramifications in other areas, such as number of emergency department visits, office visits, and hospitalizations.

Furthermore, cost is just one aspect of the issue. Clinical outcomes were not measured, nor were length of

therapy and/or patient adherence to therapy. Studies such as this one, done in isolation and without inclusion of critical measures of remission, changes in patient functionality, levels of patient satisfaction, relapse rates, changes in comorbid conditions, and other key clinical indicators, as well as the utilization of added medical resources, present a myopic view of treatment for depression or any other disease.

It also must be remembered that in a percentage of patients, a generic drug is simply not indicated. For those patients, an SSRI of optimal tolerability should be considered as the therapy of first choice, regardless of drug acquisition cost alone.

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*"We must continually remind ourselves that we are not in the business of saving money; we are in the business of providing high-quality, cost-effective, compassionate care for patients."*

— JEFF WEILBURG, MD

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In other disease states, the practice of starting with the least expensive therapy is not always cost effective. The literature shows that starting with the best known treatment — commonly used for rheumatoid arthritis, for example — yields the best outcomes and the least loss over time.

It must be acknowledged, nonetheless, that there is a significant need for credible data documenting the effect of generic drugs versus branded SSRI products on the total cost of depression care as well as on clinical outcomes of relevance. Until these studies have been concluded, disseminated, and accepted by the majority of plans and primary care providers, there will be close and isolated scrutiny of drug costs. The true cost of depression will be misunderstood and miscalculated, and patient outcomes will be suboptimal. Without the most efficacious and tolerable medication, taken for an appropriate length of time, patients will not reach remission, functionality will not be restored, medical resources will continue to be utilized inappropriately, and the cycle will continue.

**Ethnicity of the patient population.** Studies in the published literature report on the significant differences among a range of ethnic groups with regard to their willingness to accept treatment for depression. In a nationwide telephone survey of 829 patients with major depressive disorder — 659 non-Hispanic white patients, 97 black patients, and 73 Hispanic patients — researchers found that both Hispanic and black patients were less likely to accept pharmacological treatment for their depression than were white patients. Hispanic patients, on the other hand, were more likely to accept counseling as

a means of treatment than were their white counterparts. The message to prescribing clinicians is that racial and ethnic differences among their patient panel can have an effect on compliance with the therapy that is selected. "Future research should identify other attitudinal barriers to depression care among ethnic minority patients" (Cooper 2003).

#### **4 Whenever our patients begin a course of antidepressant therapy, especially if it is integrated into a disease management program, we see costs go way up.**

Initially, this observation may appear true, especially if costs are not measured several months before commencement of the disease management program. Consider data from the NMCD study, in which total medical costs incurred by patients 6 months before initiation of SSRI therapy and 6 months after initiation were measured. It is evident from Figure 3 that medical charges were increasing before diagnosis and commencement of treatment. Yet, after initiation of SSRI therapy, overall medical costs decreased to essentially the same level at which they were 6 months before treatment (Eaddy 2003).

The cost effectiveness of numerous disease management programs for depression has been documented in the literature. Published studies also have quantified the *additional* costs associated with a disease management program for patients with depression. Both these divergent study results are probably correct. The distinction must be made between *cost effectiveness* and *cost savings*.

Expanding access to high-quality depression treatment will increase clinical and patient functional benefits but will entail additional costs to the health care system. Nevertheless, the *overall costs* to the health care system and the duration of increased health care resources utilization are issues of prime importance in determining the cost benefit of a disease management program for depression. The variable element here is time. Cost savings generally are viewed in a short time frame (1 to 3 years), whereas cost effectiveness ideally should be assessed with a multiple-year perspective.

According to one study in which the 1-year incremental costs of a depression management program for extensive utilizers of medical care were analyzed, "systematic identification and treatment of depression produce significant and sustained improvements in clinical outcomes as well as significant increases in health services costs" (Simon 2001a).

Among persistently depressed patients, but not those classified as "high utilizers," the investigators found that a stepped collaborative care program resulted in significantly improved patient outcomes with only moderate increases in costs. Improving outcomes for depressed patients participating in a disease management program required additional resources beyond those typically associated with "usual care." The return on investment, however, was comparable with that of many other widely accepted medical interventions as reported in other randomized trials (Simon 2001b, 2002).

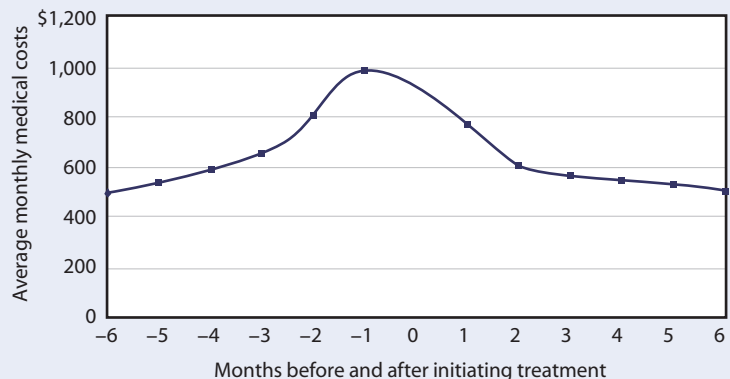
In another study, researchers found that, in comparison with a matched cohort without depressive symptoms, geriatric patients with depression utilized more outpatient health care, which was associated with higher charges, but they did not require more inpatient care. The study authors concluded that programs targeted to geriatric patients whose depression is comorbid with other chronic medical conditions might be cost effective and particularly appropriate for this population of patients (Fischer 2002).

As mentioned previously, it is necessary to make a distinction between *cost effectiveness* and *cost savings*. In view of the expanded access to high-quality depression care that most disease management programs entail, few published studies report *cost savings* associated with these programs. It must be remembered, however, that what is initially a higher expenditure of health care resources may become *cost effective* with enough time and with the accurate capture of utilization data associated with the sequelae of disease.

#### **Location, location, location...**

Lack of communication or collaboration between medical and behavioral health professionals also must be examined as a reason for mediocre outcomes from de-

**FIGURE 3 National Managed Care Database study results**  
**Medical costs over time**



SOURCE: EADDY 2003

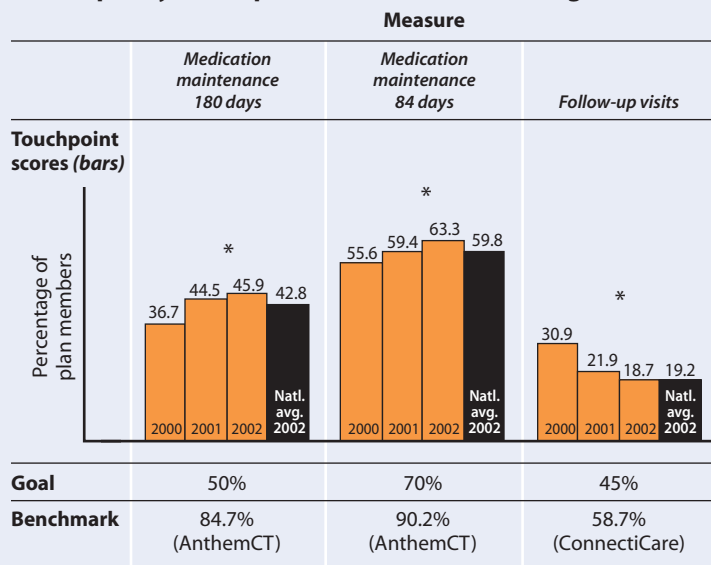
pression disease management or quality improvement programs. In randomized controlled trials, those patients with major depressive disorder who received collaborative treatment from both primary care physicians and mental health providers experience improved clinical outcomes in comparison with patients who receive usual care. How that collaborative care is operationally defined, however, is important. For example, in multivariable regression, the location of mental health providers' and primary care physicians' practices in the same building was strongly associated with increased interaction and collaboration (Valenstein 1999).

Observations by EWG adviser, Barbara Lennert, RN, CRRN, quality manager, Touchpoint Health Plan, are in accord with the findings of Valenstein et al. Figure 4 shows the performance of Touchpoint Health Plan over the course of a 3-year period on the three HEDIS Antidepressant Medication Management Measures and compares them with national averages and with the benchmark plans Anthem Blue Cross Blue Shield (BCBS) and ConnectiCare (Touchpoint Health Plan 2002).

When asked why she believed there was such a discrepancy among the plans' performances, Lennert described the situation at the benchmark plans: "They've been the benchmark for 2 years in a row, so we called them to attempt to understand their processes of care that have resulted in such exceptional scores. What we learned was that they [ConnectiCare] have behavioral health practitioners directly in their clinics. It makes an enormous difference. It comes down to this: They have a patient in one of their primary care physician's offices who has been diagnosed with depression. That patient is literally taken across the hall to the behavioral health care professional's office, where he or she is started on a collaborative care program immediately. Most clinics, including ours, simply are not set up that way."

In addition, the use of sample medications is not allowed in Anthem BCBS clinics. The physicians, therefore, write prescriptions for the medications at the time of diagnosis and do so for shorter periods of time, which is similar to providing sample medications. This ensures that patients return for follow-up visits and prescription refills. The added effect of this is that the HEDIS "clock" starts immediately at the time of diagnosis, not after completion of sample medications, inasmuch as these sample medications are not counted in the HEDIS measure.

**FIGURE 4 Touchpoint Health Plan  
HEDIS quality antidepressant medication management**



\* P-value not significant

AnthemCT=Anthem Blue Cross Blue Shield Connecticut

SOURCE: TOUCHPOINT HEALTH PLAN 2002

### The absence of depression care systems within primary care

"Usual care" in depression — if there is such a thing — rarely entails referral for cognitive or behavioral therapy. It sometimes involves a prescription for an antidepressant, while other types of self-management recommendations and support are rare. In one study, patient satisfaction with "usual care" was measured and found to be lackluster at best. Patient outcomes, as well as measured levels of satisfaction with care during a 3-month period after diagnosis, were "unimpressive." The study authors recommended that to improve both clinical outcomes and patient satisfaction, primary care physicians may need to adopt a more comprehensive and collaborative approach to care management. Expertise of other team members may need to be tapped to enable managed care to offer optimal care to patients with depression (Solberg 2003).

In a series of focus groups with primary care physicians and their staffs, researchers explored patterns of care and openness to adoption of new models of care for patients with depression. The key finding was considerable variation in care among practices. In addition, barriers to full-fledged adoption of a collaborative care model with mental health practitioners were identified. Participants did, however, support involvement of other office staff and recognized the need for more systematic follow-up for depressed patients.

Study participants indicated that they would be more

amenable to alternative care models if those models were introduced appropriately. The authors reported on at least two promising approaches to introducing such changes. One involves external feedback of performance data to the individual practices, offered in conjunction with a variety of systems, concepts, and tools. The second approach involves an internal change process in which a multiclinic improvement team collects and presents performance data and develops systematic solutions by using rapid-cycle testing (Solberg 1999).

With all these difficulties regarding the diagnosis of depression, primary care physicians' lack of time and managed health care policies act as major barriers to improving outcomes in patients with depression. "A potentially more effective approach to treating depression is health management, rather than traditional disease management. In this approach, the focus of care is patients' functional status and quality of life rather than the treatment of a specific health condition in isolation; patients are actively involved with care, and care choices are driven by competing demands. Another approach that may help improve outcomes in depression is the Recognize, Assess, Categorize, and Treat (ReACT) strategy, which is an efficient way to detect and triage patients with depressive disorders according to the severity of illness. Adjunctive aids, such as the use of support staff, monitoring systems, and collaborative care with mental health specialists, also have great potential for improving primary care physicians' effectiveness in treating depression." The ReACT strategy is described in detail in a supplement to the *American Journal of Managed Care* (Klinkman 1999).

Another author summed up recommendations nicely in his argument for collaborative care: "It is valuable for the physician to have psychiatrists he or she knows to facilitate consultation, communication, and coordination. The value of brief psychotherapy in the treatment of a depressive episode underlines the need for a psychiatrist with whom the physician can work collaboratively. The depressed patient presents the physician with a situation in which he or she can make a positive difference in the life of a person and his or her family. The need to model and teach the treatment of depression in primary care is evident, with the likelihood that this will be the arena in which these patients will continue to receive care" (Schuyler 2000).

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## **5 Guidelines stipulate discontinuation of therapy at a maximum of 6 months; some of my patients take antidepressants for years, however, and it is costing me a bundle.**

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In 1999, 6 years after publication of the Agency for Health Care Policy and Research (AHCPR, now AHRQ) *Depression in Primary Care* guideline, this issue was addressed in the *Journal of Clinical Psychiatry*: "Recent guide-

lines recommend that treatment with antidepressants should be continued for at least 4 to 6 months after the initial response and that long-term prophylactic treatment be given to patients who have experienced 2 or more depressive episodes. However, there is little consensus on the duration for which continuation or maintenance treatment should be given" (Keller 1999).

Today, 11 years after the guideline was released, there is still confusion as to its intent and a lack of consensus regarding what constitutes an appropriate length of therapy for a person suffering from major depressive disorder. Few primary care patients with recurrent or chronic depression are receiving adequate maintenance therapy (Katon 2001).

### **The meta-analysis**

In defense of researchers befuddled by the evidence, there was, until recently, little robust, peer-reviewed literature to document the benefits of antidepressant treatment extending beyond 6 months. Nevertheless, a study published in the *Lancet* provided a clearer idea of the benefits of longer-term therapy. The authors aimed to determine optimal duration of antidepressant therapy for the prevention of relapse. They pooled data from 31 randomized clinical trials involving 4,410 subjects. These patients had responded to therapy during the acute phase of treatment and were randomly assigned to a 6-, 12-, or 24-month continuation treatment phase (Geddes 2003).

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*"Physicians need computer-based support to follow guidelines and monitor patients' adherence to prescribed therapy."*

— WAYNE LEDNAR, MD, PHD

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The researchers found that patients who continued treatment with an antidepressant throughout the continuation phase reduced the odds of relapse by 70 percent, in comparison with patients who discontinued treatment. When patients were analyzed in cohorts, those taking antidepressants for 1 year, after a 2- to 4-month phase of acute therapy, had an 18 percent chance of relapse, in comparison with a 35 percent chance of relapse among patients who did not continue therapy. Those taking antidepressants for 2 years, after a 2- to 4-month phase of acute therapy, had a 24 percent chance of relapse, in comparison with a 62 percent chance of relapse among patients who did not continue therapy.

The message of this meta-analysis — that continued antidepressant therapy benefits patients with recurrent depressive disorder — should not be dismissed: "The treatment benefit for an individual patient will depend on their absolute risk of relapse with greater absolute benefits in those at higher risk" (Geddes 2003).

The patients who had responded to the acute phase of therapy were evaluated; however, according to another researcher, “Only about 25 to 35 percent of patients will achieve remission after 6 to 8 weeks of treatment; another 15 to 20 percent may remain depressed for months or years” (Thase 2001). Unfortunately, not all patients achieve remission in 6 to 8 weeks. For patients who may be resistant to treatment or for those who may be very seriously depressed, adherence to therapy is especially important. Inappropriate interpretation of the guidelines to assume the recommended discontinuation of therapy at or before 6 months can be harmful to all patients with depression but is especially dangerous in this high-risk group with greater severity of illness.

The section of the AHCPR depression guideline concerning the continuation or maintenance phase is provided here (see box at right). A careful reading reveals that there is no recommendation to discontinue therapy at 6 months or at any particular time *unless and until* full symptom remission is achieved.

### The cost of an adequate length of therapy

Although there is no large body of data regarding appropriate length of SSRI therapy and its effects on clinical outcomes and cost outcomes, an analysis of the Tennessee Managed Medicaid database demonstrated that longer length of therapy (>180 days on antidepressants) resulted in lower total overall health care costs (Figure 5). Findings from this study support the same economic trends reported earlier: Patterns of antidepressant use have a definitive influence on cost.

In summary, patients who are compliant with therapy for 3 months or longer have the lowest overall associated medical costs; costs are highest among patients who switched and/or augmented therapy or who discontinued it altogether (Thompson 1996).

### Conclusion

From the considerable body of literature just presented, it is safe to say that depression in America is seriously and even tragically underdiagnosed and undertreated. People are suffering needlessly, not only from their disease but also from the stigma associated with it. Much needs to be done to remove that stigma, by educating providers and health plans about optimal approaches to depression therapy; systems must be developed to support the efforts of the primary care physician, who remains the primary caregiver for the depressed population. Finally, costs associated with depression must not be viewed in isolation within the pharmacy budget alone but calculated with a macroperspective that encompasses all

### The Agency for Health Care Policy and Research Guideline Verbatim: Continuation/Maintenance Phase Management With Medication

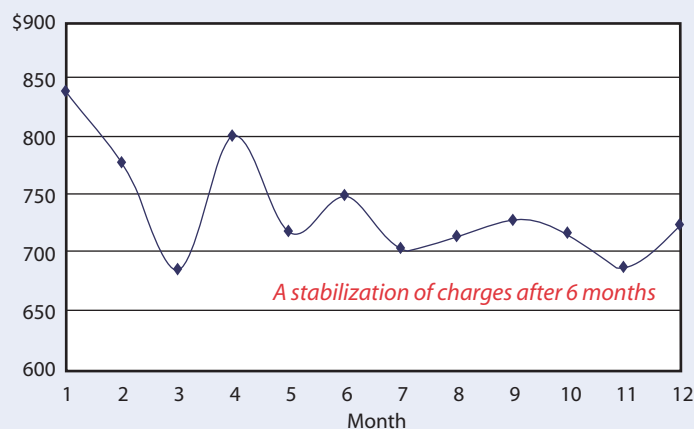
*Guideline:* There is very strong evidence that specific medications prevent relapse/recurrence in most patients with recurrent forms of major depressive disorder. Since the episode onset date may not be readily determined, particularly in first-episode patients, most patients should receive the full therapeutic dosage of antidepressant drug for 4 to 9 months (the average duration of a major depressive episode) of continuation therapy after symptom remission is achieved. In those for whom the onset date is known, a somewhat shorter continuation phase may be attempted, but it should not be less than 4 months. For those with episodes lasting 2 years or more, it may be wise to pursue a continuation period of at least 9 months. Patients who have a recurrence shortly after continuation therapy withdrawal may require long-term maintenance medication. (*Strength of Evidence = A.*)

SOURCE: AHCPR 1995–1997

medical, pharmaceutical, and hospital charges associated with an episode of major depression.

Although many managed care professionals are directly responsible for containing certain cost areas — such as pharmacy — administrators and medical executives alike must take a comprehensive look at *total* health care costs associated with depression; they must

**FIGURE 5 Economic trend results: >180-day cohort**  
Total monthly charges



SOURCE: EADDY 2003



appreciate the difference between a short-term cost-savings scheme and a longer-term cost-effectiveness intervention. This will not be accomplished easily, especially because of a lack of compelling data documenting cost effectiveness, let alone cost savings associated with disease management. Nevertheless, without a paradigm shift in the way that depression is diagnosed and treated in our society, costs will continue to escalate and patients with depression will continue to suffer needlessly from this debilitating and recurrent disease.

## LITERATURE REVIEW

### An Examination of the Effect of HEDIS On the Care of Patients With Depression

The basic question of whether the existence of HEDIS improves the care of patients with depression has an ambiguous answer: maybe and maybe not. As shown by the 2002 HEDIS Compass Results in Figure 6, as a nation, physicians' efforts to keep patients on antidepressant therapy are still extremely inadequate. In commercial Medicaid and Medicare plans, compliance rates for the acute phase are between 47 and 60 percent and in the continuation phase, between 32 and 43 percent. These statistics reflect poorly on the nation's health care in relation to this important proxy measure of quality.

*"The HEDIS measures have also evolved over the years, making them a moving target for the doctors and the plans."*

— BARBARA LENNERT, RN, CRRN

Nevertheless, the very existence of HEDIS is better than nothing at all, and HEDIS makes all stakeholders aware of the vital importance of quality measurement. Without any measurement, improvement or decline in the quality of care delivered to patients could never be quantified and, therefore, never changed.

### Limitations of HEDIS

HEDIS indicators measure processes of health care but not outcomes of treatment. Some clinicians, academicians, and scientists recommend use of a brief tool, such as the 21-point Patient Global Improvement Scale, to measure how much a condition — in this case, depression — has improved

or worsened since treatment was started, regardless of number of contacts within the health care system (see Figure 7 on page 17).

These professionals argue that measuring remission and response rates at 3, 6, and 12 months — in lieu of or in addition to HEDIS indicators — is more clinically relevant. From the literature, it is known that about 60 percent of all nonpsychotic outpatients with major depressive disorder taking an antidepressant "respond" to treatment. "Response" is equivalent to a 50 percent or greater improvement. This means that the other 40 percent continue to be burdened with symptoms of depression and are functionally impaired. Moreover, of those that do respond, only about half achieve remission from symptoms, equivalent to a 70 percent or greater improvement (Golden 2002).

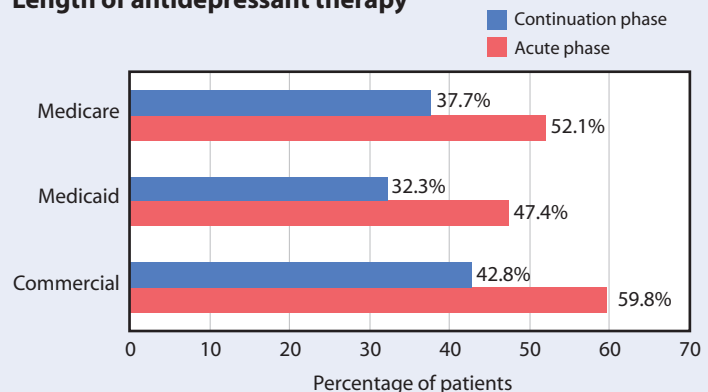
*"An optimal outcome measure for depression is lacking; the best-case scenario would be a very short, patient-rated global measure of improvement at 3, 6, and 12 months after starting antidepressant treatment."*

— DAVID V. SHEEHAN, MD, MBA

In almost every disease, with the exception of depression, patients have shown improvement in HEDIS scores over time. Relative to depression management measures, the reasons for this lack of improvement and poor performance on the HEDIS scores include medication switching, improper coding and/or documentation of a visit, miscounting visits, and use of medication samples that skew medication start dates.

**FIGURE 6 2002 HEDIS Compass results**

#### Length of antidepressant therapy



SOURCE: HEDIS 2002

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*Another limitation of HEDIS is its narrow definition of what a health care provider is. The fact that HEDIS only counts contacts with the prescribing professional does not fit well with newer models of disease and case management.*

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— BENJAMIN DRUSS, MD, MPH

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The reasons for poor performance on HEDIS scores were examined through a systematic chart review on a random sample of 249 HMO patients who failed one or more of the three HEDIS criteria (i.e., three follow-up visits or adequate duration of acute or continuation phase treatment) (Kobak 2002).

The most common reasons for lackluster performance were found to be as follows:

- The patient restarted a previously prescribed successful antidepressant.
- The patient did in fact have a visit with the prescribing provider, but mental health was not coded or documented in the patient's chart.
- Visits were undercounted.
- Use of medication samples skewed start dates to make them seem later than they actually were.
- Patient noncompliance was the most common reason for failure to achieve both acute and continuation phase duration of treatment.

Restarting a previous medication is common among patients and warrants discussion regarding requirements for visit frequency and perhaps an adjustment of the HEDIS indicators (Kobak 2002).

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## **FACULTY PRESENTATION**

### **Diagnosis and Treatment Outcomes Tracking: A Specialist's Perspective on the Mini International Neuropsychiatric Interview Assessment Tool**

DAVID V. SHEEHAN, MD, MBA

Diagnosis is best accomplished in psychiatry through structured diagnostic interviews, not scales. Scales generally are not intended for diagnostic purposes; unfortunately, in clinical practice, they are occasionally misused. Structured diagnostic interviews essentially take DSM-IV or ICD-10 criteria and operationally define them. Structured interviews are designed with decision-tree logic. Therefore, if answers to the initial two or three questions are negative, a clinician in a busy office practice does not need to go further with the interview. On the other hand, if patients answer "yes," then the clinician

goes on to ask additional questions along the decision tree that will more fully confirm or invalidate a diagnosis. Progressing through the interview increases the sensitivity of the line of questions.

After the primary diagnosis has been made, severity of illness is measured by means of psychiatric rating scales. This is a system that is in place in all clinical research studies and is used in psychiatric treatment; it is also becoming common in the primary care clinical setting.

Although there are many structured interviews, three are frequently described in the literature. The Composite International Diagnostic Interview (CIDI), developed by the World Health Organization, is widely used in Europe and is very good for epidemiological studies but is not practical in clinical settings, because it takes more than 2 hours to implement. The Structured Clinical Interview for DSM-IV (SCID) is a U.S.-based questionnaire that takes about 1 hour and 15 minutes to implement. It is also very good for research and epidemiology studies but is time consuming and awkward to navigate in a clinical setting. These limitations led to the development of the Mini International Neuropsychiatric Interview (MINI), a structured interview that can be completed in less than 15 minutes and has the same sensitivity, specificity, and psychometric properties of the CIDI and the SCID. The MINI covers the 17 most common disorders in psychiatry and is now the most widely used structured diagnostic interview in the world. It has been translated into 44 languages and can be administered to approximately 70 percent of the world's population.

To track disease progression accurately, one measure is needed for identification of symptoms, another measure for disability (severity of symptoms), and a third measure for global improvement — a brief patient-rated treatment outcome tracking scale that asks, in essence, "How much has your condition improved or worsened since you started treatment?" All good tracking systems contain these elements. But why should there be separate measures for symptoms and disability? Because these characteristics change desynchronously from each other. Disability can be lessened and symptoms may not, and vice versa; they do not change necessarily in tandem. It is important, however, to influence both, and sometimes the global scale identifies change that is not captured by the other two instruments.

If the score on the Patient Global Improvement Scale (Figure 7) is 5 or 6, it is considered a response; a score of 7 to 9 is equivalent to a remission; a score of 10 is defined as recovery, which, unfortunately, is rare. At a minimum, clinicians are aiming for remission of symptoms, and that goal can be traced with this particular instrument.

### **Computerizing the MINI**

Computerization of the original paper-based MINI has undergone many revisions. The latest version is on

a tablet personal computer that contains the diagnosis and treatment-outcome tracking system. The personal computer has a touch-sensitive screen that allows data to be entered with a pen.

In contrast to the paper version of the structured interview, the decision tree is computerized and the calculations are run in the background, bypassing areas that do not need to be investigated.

With the tablet personal computer, data on patient compliance with medication therapy can be captured as well. Another application is data export. Because the system is wireless, data can be exported in a variety of formats to be read and/or stored by any computer. This feature enables printing of prescriptions, patient information sheets, and the rating scales as they appeared on the screen.

### Further applications for the computerized MINI

A kiosk version of the MINI with a touch-sensitive screen is under development for the city of New York. This version will enable screening of all Medicare and Medicaid disability benefit recipients throughout the next year, amounting to several hundred thousand evaluations. If a patient is illiterate, he or she will be given headphones and will listen to a spoken version of the MINI, which is also available in Spanish. Completion of these MINI surveys will yield a large database of diagnostic information on this patient population over the next year.

GlaxoSmithKline is putting up a version of the MINI on its Web site. Also in development is a personal digital assistant version that will allow physicians to work with the survey in a wireless capacity. In addition, patients can complete the computerized MINI in the waiting room, from home on their computers, or over the telephone with office staff.

A logical extension of the MINI is inclusion of treatment protocols. Once a diagnosis is made — major depressive disorder, for example — the MINI could be programmed to suggest treatment with a particular drug or drug class. The physician could then click a button to see which of these are included on formulary. Prices could be listed for each, along with efficacy information, safety data, and so forth. The physician could then write an appropriate prescription, which would print out from the wireless system. A patient information sheet also could be printed to help reinforce the information given to the patient by his or her physician.

The current and future applications are a robust means of readily diagnosing disease, assessing severity of illness, and tracking change, both positive and negative. Programmed tools, such as the MINI, hold promise for ultimately delivering more appropriate and timely care for all patients suffering from mental illness.

### FACULTY PRESENTATION

#### The MacArthur Initiative on Depression In Primary Care

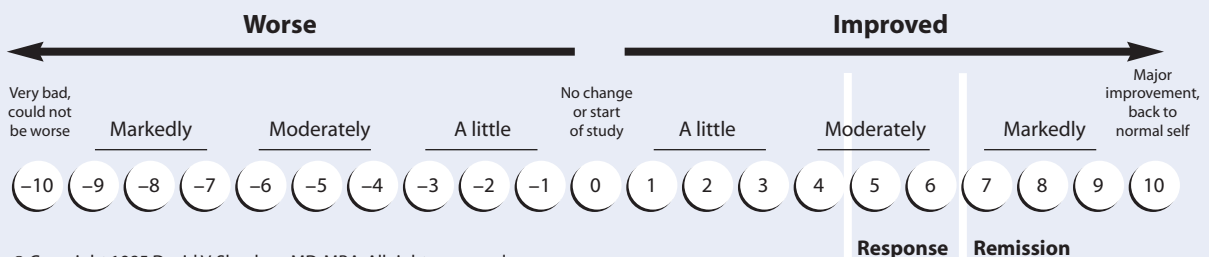
JOHN WILLIAMS, MD, MHS

The MacArthur Initiative is a chronic care collaborative model that focuses on productive interactions between patients and provider teams to improve outcomes (Figure 8). It builds on 13 randomly controlled trials that support the superiority of collaborative care over usual care in terms of reduction of symptoms and adherence to therapy. Integral to this model is training for all team members: the care manager, the mental health specialist, and the primary care physician.

Key elements of the initiative include clinician training designed to develop a new skill set that enables the team members to use this new management model ef-

**FIGURE 7 Patient Global Improvement Scale**  
A brief patient-rated treatment-outcome tracking scale

**How much has your condition improved or worsened since starting this study or treatment?**  
(Mark the circled number that rates your change compared to the start of the study or treatment)



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fectively. The most critical aspect of the model is systematic follow-up care that includes symptom monitoring with standardized measurement instruments and adherence monitoring enhanced by care manager follow-up telephone calls.

Resources are a part of the model and include patient-education handouts, physician-education tools and materials, reproduction of clinical practice guidelines on the optimal treatment of depression, and the Patient Health Questionnaire diagnostic tool. Care managers support physician initiated treatment, and the model is designed to engender a high degree of collaboration and communication with behavioral health specialists.

Over a 9-month period, five visits with the primary care physician are recommended, in addition to five telephone follow-up calls with the care manager. During these acute and continuation phases of treatment, the major functions of the primary care physician include diagnosis, development of a care plan that takes patient preferences into consideration, use of a one-page tool that enables patients to set self-management goals, monitoring of symptom response, and communication with other team members.

Care manager functions include development and maintenance of rapport with patient and provider, education of the patient, monitoring of symptoms and communication of those findings to the primary care physician, development and maintenance of a self-care action plan for the patient, and maximization of adherence through negotiation of solutions to treatment-emergent problems. The role of the behavioral health specialist (usually a supervising psychiatrist) is to provide consultation to the primary care physician, supervise the care manager, and provide interventions for high-risk or treatment-resistant patients.

The MacArthur Initiative *suggests* increased functionality and enhanced quality of life for patients and improved productivity for employers. The evidence that these models work is compelling (at least with regard to clinical outcomes). What is needed is better dissemination of the evidence and programs to help physicians incorporate the models into their everyday practice.

In addition, new models of optimal depression care must be flexible enough to apply to the user's own environment, and they must be built on credible data with 12 to 18 months of follow-up care to demonstrate positive effects on employee productivity. Tolerability and *efficacy* are the wrong indicators; researchers should be measuring tolerability and *effectiveness*.

## FACULTY PRESENTATION

### The Quality Partnership Program: Improving the Quality of Depression Management

TIMOTHY S. REGAN, RPH, CPH, AND

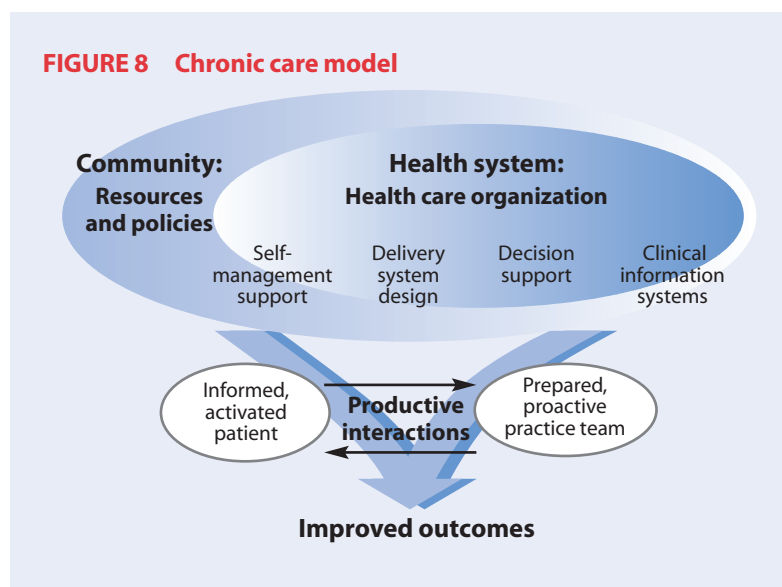
BARBARA LENNERT, RN, CRRN

The Quality Partnership Program (QPP) in Depression is a comprehensive assessment, education, and outcomes research program that was developed collaboratively by GlaxoSmithKline and Applied Health Outcomes. It is a systematic approach to improve the quality of depression management. With a plan's own administrative claims data, the QPP is used to examine the key issues of tolerability, compliance, quality of care, and costs associated with utilization of antidepressants. The effect of length of therapy is measured in conjunction with evidence-based guidelines, and prevalence of anxiety is highlighted as a comorbid condition with depression (Figure 9).

The QPP is regionally diverse and involves MCOs, behavioral health organizations, and state Medicaid agencies. Its findings will be publicized in the medical literature, in poster presentations at health care symposia, and in summary reports to key customers. Initial data findings should be available in the second quarter of 2004.

**Method:** With a plan's own medical, pharmacy, and behavioral health administrative claims data, a baseline assessment (phase 1) is conducted. This assessment comprises the elements represented in Figure 9. With the results of that initial assessment as a guide, a pro-

**FIGURE 8 Chronic care model**



gram of data-driven, evidence-based education ensues. Elements of the intervention/educational program (phase 2) include:

- One-on-one and small-group academic detailing
- Provider-specific reports
- Continuing medical education programs
- MindSET educational tools (Figure 10)
- Letters from the health plan to individual providers
- Publication of planwide newsletters
- Teleconferences
- Dissemination of patient-education materials
- Introduction of disease management programs such as the MacArthur Initiative, screening tools, and severity-of-illness scales

Phase 3 involves further analysis and follow-up to determine the effect of the intervention at least 6 months after the completion of phase 2.

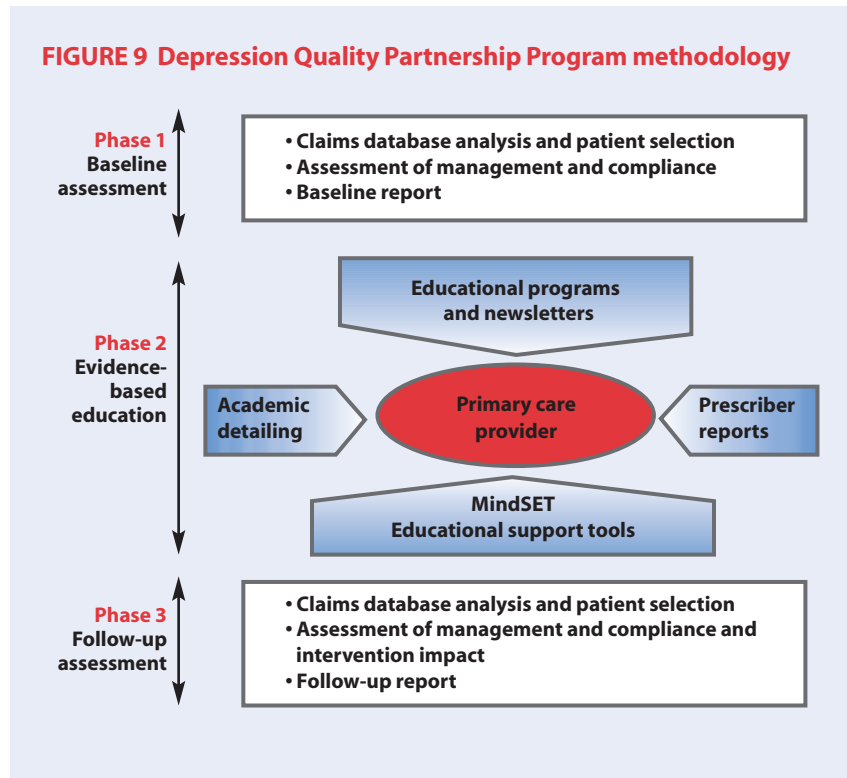
### Depression QPP case study with Touchpoint Health Plan

As was demonstrated in Figure 4 on page 12, Touchpoint's HEDIS scores in depression have mirrored the national average in medication management for both the chronic and the acute phases, as well as in rate of follow-up visits after diagnosis (3 in 12 weeks). This performance is in sharp contrast to their "best performing plan in the nation" on the overall HEDIS effectiveness of care measures for 2 consecutive years. Especially impressive have been their effectiveness-of-care scores for their patients with diabetes, for whom they set national benchmarks in three of the six measures for the 2002 reporting year. Touchpoint's performance on the depression measures, however, fell far short of bench-

mark, and the organization decided to participate in the Depression QPP as a means of changing that.

### The beginnings of a solution

As mentioned earlier, the benchmark plans utilize behavioral health specialists who have their offices adjacent

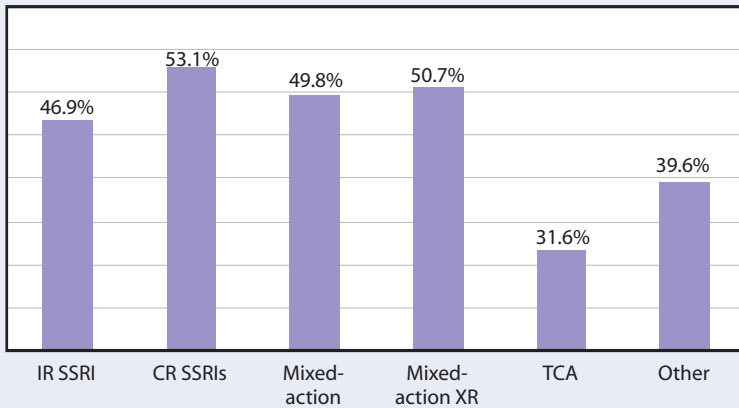


**FIGURE 10 The MindSET educational tool kit**

Patient Brochures and "At-a-Glance" fact sheets	Physician/provider support tools	Member outreach resources	Employer group/workplace programs
<ul style="list-style-type: none"> <li>• Depression Awareness</li> <li>• Anxiety Disorders – OCD, GAD, PTSD, SAD, Panic Disorder</li> <li>• Stress Management</li> <li>• Older Adults and Depression</li> <li>• On the Job With Depression</li> <li>• Many other titles</li> </ul>	<ul style="list-style-type: none"> <li>• Depression Symptoms</li> <li>• Medication Adherence – How Your SSRI Works – Towards Feeling Better – Making the Most of Treatment</li> <li>• MINI Patient Health Survey Screening</li> <li>• CME Programs</li> <li>• Many other tools and resources for providers</li> </ul>	<ul style="list-style-type: none"> <li>• Six member-letter templates</li> <li>• Program announcement letter</li> <li>• News article program</li> <li>• Many additional customizable tools and resources</li> </ul>	<ul style="list-style-type: none"> <li>• Employer Resource Guide</li> <li>• PowerPoint "Lunch and Learn"</li> <li>• At-a-Glance Sheets</li> <li>• Depression Awareness</li> <li>• MindSET in the Workplace Actuarial Model</li> </ul>

CME=continuing medical education; GAD=generalized anxiety disorder; MINI=Mini International Neuropsychiatric Interview; OCD=obsessive-compulsive disorder; PTSD=post-traumatic stress disorder; SAD=social anxiety disorder; SSRI=selective serotonin reuptake inhibitor.

**FIGURE 11 Preliminary Quality Partnership Program phase 1 results**  
**Percentage of patients remaining on therapy for 180 days or more**



CR=controlled-release; IR=immediate-release; SSRI=selective serotonin reuptake inhibitor; TCA=tricyclic antidepressant; XR=extended-release.

SOURCE: TOUCHPOINT HEALTH PLAN 2002

to the primary care clinics. Proximity and utilization of behavioral health specialists increase the rate of proper coding and thus accounts for most depressed patients in the HEDIS denominator. (Touchpoint is able to account for only about 10 percent of its population with the diagnosis of depression and/or one or more prescriptions for antidepressant medication in its denominator, because of the exclusionary criteria used by HEDIS regarding prior diagnosis or prescription use). Utilization of medication samples further contributes to the problem of improper coding.

While continuing to provide the best “usual” care for their patients with depression, Touchpoint has initiated a bonus program for primary care physicians who improve their patients’ HEDIS depression scores. It is hoped that the bonus program, as well as the collaboration with Applied Health Outcomes, will enable providers at Touchpoint to improve HEDIS scores and the quality of care for their patients with depression significantly. Preliminary data, as seen in Figure 11, mirror results to date in the NMCD.

## FACULTY PRESENTATION

### Diagnosis of Anxiety and Depression: Point-of-System Entry – A Managed Behavioral Health Organization Perspective

JONATHAN BOOK, MD

The objective of this synthesis is to provide a managed behavioral health organization (MBHO) descriptive view regarding the varied points of entry in managed care

systems through which individuals pass to obtain a diagnosis and treatment of depression and anxiety.

It is still true that there are numerous variations in MCOs. There are also numerous organizational structures with regard to how MBHOs work with their customers, which are often, but not exclusively, health plans. Some MBHO customers are large self-insured employers who may contract with one or multiple health plans and who then carve out the management of behavioral health services; some customers are government agencies.

### At the organizational level

The following list provides an overview of what an MBHO provides to an MCO:

- Consultation to MCO medical leadership on behavioral health practice and management (primary care physician behavioral health assessment, treatment, and referral)
- Contribution of behavioral health expertise to pharmacy review, policy, and decisions (pharmacy and therapeutics committee involvement)
- Behavioral health clinical policy, practice guidelines, and tools
- Education of primary care physicians and other specialists
- Management of behavioral health specialty networks and services
- Coordination of behavioral health and medical care
- Behavioral health prevention activities

The overarching perspective of MBHOs is that clinicians diagnose and treat depression and anxiety; MBHOs and MCOs do not. If an MBHO’s services work well, they provide structures, capability, and resources to help clinicians in the field provide effective and efficient care.

There are three primary points of entry into an MBHO system: the primary care physician, a behavioral health care specialist, and the MBHO itself.

### Point of entry: the primary care physician

The majority of individuals who seek professional care for a behavioral health disorder do so through their primary care physician. Very few contracts actually have primary care physicians as gatekeepers to specialty behavioral health practice; that trend was common 10 or 12 years ago, when more primary care physician groups were capitated for all medical care, including behavioral health.

In view of how limited a primary care physician's time is and how complex or difficult it might be for him or her to treat patients with depression and/or anxiety, patients were expected to overwhelm the system when physicians were no longer gatekeepers with economic incentives to keep them in their practices. That has not happened, perhaps because primary care physicians have difficulty with diagnosing patients whose complaints could indicate a need for behavioral health expertise versus those who have many complaints — fatigue, pain, and poor sleep — that might or might not be related to behavioral health. In addition, patients presenting with these intermediate symptoms can make up as much as 60 percent of a primary care physician's day-to-day work.

A further consideration is the patient's dealings with depression and anxiety, which involve two important dynamics. First is the economic incentive: often there is a higher copayment for accessing behavioral health benefits than for accessing general medical benefits. Therefore, the patient has a financial incentive to stay in primary care rather than move to a behavioral health specialist. The second issue is the stigma. There is still less stigma for the patient to stay within the primary care practice than to see a behavioral health specialist.

Another aspect about the primary care physician point of entry is that MBHOs provide the MCO with prevention activity specific to behavioral health disorders, the most common ones being designed for depression in general and depression in identified subpopulations. Common examples of these subgroups are patients with cardiac disease, patients with diabetes, postpartum mothers, and families of patients who have depression. The MBHO is the source of the screening tools — often direct to the patients — and then manages by triage those with positive screening results, providing referral into treatment and feedback to the primary care physician.

### **Point of entry: the behavioral health specialist**

In a second point of entry, an individual goes directly to a behavioral health specialist. The clinician evaluates the individual's needs and then calls the MBHO to seek authorization for the proposed treatment. Rather than an excessive number of referrals from primary care physicians to specialists, the increase in numbers of patients in managed behavioral health care has represented largely those who go directly to behavioral health specialists. Consequently, there are more patients in this specialty treatment than there were 10 years ago.

When a psychotherapist is involved and medication is being prescribed, a primary care physician prescriber and a psychotherapist commonly work across systems and need to collaborate and communicate across those systems.

### **Point of entry: the MBHO**

A third point of entry into the system is the MBHO itself. This is when an individual calls an MBHO directly to request care. There are four ways in which this happens within MBHOs:

- **Employee Assistance Program:** Through an arrangement between the MBHO and an employer, individuals may contact an Employee Assistance Program to obtain information, assessment, and referral for employees or their family members.
- **Case management:** Individuals may call their MBHO directly and obtain guidance and referral from a clinical case manager.
- **Disease management:** The MBHO may reach out to individuals and provide tools for screening and guidance for referral and further interventions if indicated.
- **Self-referral:** Individuals may use provider lists and educational material provided by the MBHO to make their own connections with additional behavioral health services.

The last point, the self-referred entry to the MBHO system, is particularly interesting. The themes driving this point of entry are consumer empowerment, prevention, and demand management through mechanisms such as member access to assessment tools or education about depression or anxiety; reminder tools to help patients comply with treatment plans by using technology available through their MBHO's Web site; interactive voice response technology; or, less technologically oriented, a direct mailing to members. An interesting aspect of self-referral is that it provides services to some individuals who are unable or unwilling to seek traditional face-to-face help. It is not yet clear whether these individuals will subsequently seek additional, traditional help. At this point, it appears that excessive self-referrals for professional services are not common. From the industry perspective, MBHOs are not observing many "worried well" persons seeking behavioral health care services.

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*From the provider perspective, our experience is that we are seeing patients who are quite ill; we're not seeing mild cases.*

— SABAH CHAMMAS, MD

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The multiple points of entry into managed behavioral health have enabled an increasingly large number of patients in need to receive the assessment and treatment they require.

## DEVELOPING EVIDENCE-BASED PROTOCOLS

### The Sequenced Treatment Alternatives To Relieve Depression Study: Background and Rationale

The Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) Study, supported in part by the National Institutes of Mental Health, “attempts to fill in major clinical information gaps and to evaluate the theoretical principles and clinical beliefs that currently guide pharmacotherapy of major depressive disorder” (Fava 2003). The study is designed so that results can be translated readily to real-world clinical situations, in both primary and specialty care settings. It is being conducted with representative patient groups and typical settings through the use of common clinical management tools. Study outcomes of interest include key clinical indicators, health care resource utilization, and attendant cost estimates.

#### Design and methods

In the STAR\*D, a prospective design protocol is used to assess the differential effectiveness of various anti-depression treatment options. Citalopram is the initial SSRI utilized in this study. A multilevel treatment algorithm is applied when, and if, citalopram therapy fails to produce improvement. The primary and secondary instruments used to measure symptom improvement are the Hamilton Rating Scale for Depression and the 16-item Quick Inventory of Depressive Symptomatology Self-Report, respectively. The primary instrument used to measure functionality is the Medical Outcomes Study Short-Form 12 (SF 12); the secondary instruments are the six-item Work Productivity and Activity Impairment Questionnaire and the five-item Work and Social Adjustment Scale. The 16-item Quality of Life Enjoyment and Satisfaction Questionnaire is used to assess quality of life. Side effect burden is measured by both the Frequency and Intensity of Side Effect Rating and the Global Rating of Side Effect Burden. A short, two-item Patient Satisfaction Inventory is used to measure satisfaction with treatment and the medical personnel administering that treatment. Health care utilization and cost data are derived from the 15-item Modified Utilization and Cost Patient Questionnaire (see box).

STAR\*D will be populated with 4,000 adult (ages 18 to 75) outpatients with nonpsychotic major depressive disorder. Those in whom citalopram therapy fails will be randomly assigned to a level 2 treatment protocol. In all, four levels of treatment are specified for patients whose current level fails; failure is defined as insufficient achievement of symptom relief. Monitoring this large

#### Screening tools available for the detection and diagnosis of depression

- Behavior And Symptom Identification Scale–32 (BASIS-32)/Outcome Questionnaire-45 (OQ-45)/Hopkins Symptom Checklist-90 (HSCL-90)
- Beck Depression Inventory/Zung Self-rating Depression Scale/Hamilton Rating Scale for Depression
- Center for Epidemiologic Studies-Depression (CES-D)
- DSM/Primary Care Version
- Edinburgh Postnatal Depression Scale
- Mini International Neuropsychiatric Interview (MINI)
- Patient Health Questionnaire-9 (PHQ-9)
- Primary Care Evaluation of Mental Disorders (PRIME-MD)
- Whooley Depression Screen

number of patients through various levels of treatment and analyzing which treatment protocols produce the most optimal outcomes will enable study authors to develop an evidence-based treatment algorithm. This algorithm may form the cornerstone of a sequenced approach to therapy for patients with major depressive disorder.

#### Dissemination of findings

The authors pointed out: “No studies have evaluated the acceptability of different treatment options in broadly defined participant groups treated in diverse care settings” (Fava 2003). In other words, no studies have captured accurately a real-world scenario. Because of this lack of robust, reliable data, it is no wonder that significant variation in care exists. Yet, when data are available and are crafted into scientifically based recommendations regarding the treatment sequence for depression, the dissemination of such guidelines will be the next challenge.

Numerous studies cite insufficient application of research findings in the routine care of patients with depression, and the STAR\*D authors recognized that finding effective methods of disseminating empirically based evidence continues to be a considerable challenge.

The authors concluded that with dissemination *and implementation* of the STAR\*D algorithm, quality of patient care should improve. They were also sanguine about reductions in the cost of treating patients with depression. Results of the STAR\*D study will be published as soon as they become available (Fava 2003).



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