

Managing Our Depressed Patients

Gold Standards vs Higher Standards

IN THIS ISSUE of the ARCHIVES, 2 very different articles add to the growing literature on the diagnosis and management of depression in primary care practice. The article by Klinkman et al¹ deals with the accuracy of diagnosis of depression when criteria (the so-called gold or criterion standard) developed in psychiatric populations are applied; the article by Lin et al² is the first to deal with relapse rates of major depressive disorder in a primary care population. These articles are of considerable interest to the family physician because so few data on depression are available from primary care populations. Despite the lack of data, family physicians were believed to underdiagnose and undertreat depressed patients, even though the nature of the illness and its optimal management were essentially unknown in primary care practice. The implication was that our patients were similar to psychiatric patients and should be referred to specialists who could take proper care of them. With the publication of a number of landmark studies, it became apparent that most patients with major depressive disorder are first seen in the medical and not the mental health sector, that the diagnosis is tricky because mood symptoms are rarely the chief complaint, and that the prevalence of depression among primary care patients equals that of common disorders such as hypertension.³⁻⁷ Family physicians began to get interested in depression: if we could diagnose and treat hypertension, we could diagnose and treat depression.

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In recent years, 2 events have conspired to intensify the efforts of family physicians to understand their own patients: one is the publication of the Agency for Health Care Policy and Research (AHCPR) guidelines^{8,9} that provide recommendations for diagnosis and treatment of depressed primary care patients and the other is the advent of managed care. The AHCPR formally urged primary care physicians to diagnose and treat depression. Managed care has raised new issues for our patients, creating changes in access to individual mental health care providers and constraints on types of treatment. Given the enormous prevalence of depressed patients in our practices, the primary care physician must be expert at diagnosis and must use medication and time-limited counseling effectively.

It is noteworthy that at the time of the publication of the AHCPR guidelines, "transfer of technology" studies such as the randomized clinical trial by Schulberg et al¹⁰ were in process and had yet to validate the recom-

mendations of the published guidelines. In other words, state-of-the-art treatment "technology" found to be effective in psychiatric patients had yet to be found effective—"transferred"—in our primary care patients. What was known was that the guidelines, when followed, were effective in psychiatric populations.¹¹⁻¹³ Concerns about generalizing conclusions from one group of patients to another rest on the differences in populations that include such characteristics as severity, prevalence, differences in symptoms, and natural course; moreover, the medical comorbidity of our patients may change the operating characteristics of screening instruments as well as the tolerance to and effectiveness of pharmacological therapy.

The articles herein deal with 2 issues addressed by the AHCPR guidelines, namely, diagnosis and relapse, both important in the successful treatment of our depressed patients; and both studies facilitate the transfer of technology because they deal with patients seen in routine primary care practice. Although Schulberg et al^{10,14} later confirmed the utility of acute-phase treatment of major depressive disorder in family practice and internal medicine patients, many questions remain about optimal diagnostic and treatment strategies. The study by Lin et al² is the first to explore relapse rates and thereby validate the continuation- and maintenance-phase pharmacotherapy recommended in the AHCPR guidelines, and the study by Klinkman et al¹ adds to the body of information regarding diagnosis. Let us deal first with the issue of diagnosis.

Klinkman et al¹ studied demographic and clinical factors associated with the detection of "depression" by 50 family physicians in private and academic practice in southeast Michigan. Physicians rated each patient immediately after the visit for their perception of level of depression and other factors, including a single yes/no question asking whether the patient had "clinically significant depression." Independently, each of these patients was interviewed and assigned a criterion standard psychiatric diagnosis on the basis of *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R)*¹⁵ criteria as determined by the Structured Clinical Interview for *DSM-III-R (SCID)*¹⁶ and an estimate of severity as determined by the Hamilton Rating Scale for Depression.¹⁷ These diagnoses were then compared with physician perception. When physician perception agreed with the SCID diagnoses, patients were labeled "true positive" and "true negative"; when there was disagreement, patients were labeled "false positive" and "false negative."

Seventy-seven percent of the sample (which was deliberately weighted to overselect for patients likely to have major depressive disorder) was either true positive or true negative; in other words, there was 77% concordance. Of the remainder where there was disagreement, another 9% were the “false positives,” identified by their family physicians as having “clinically significant depression” but not meeting SCID criteria for major depressive disorder. Of note, the majority of these false positives were patients currently receiving treatment for major depressive disorder who no longer met the criteria for “caseness” prescribed by the SCID criteria. For the patient to be a “case,” the patient must currently meet the SCID criteria for a mood disorder; fortunately, patients effectively treated no longer do so. Their family physicians, however, are likely to continue to apply the diagnostic label not in spite of but, perhaps, because they are under treatment. This false-positive group may, therefore, be an artifact of the study. In effect, this phenomenon brings the concordance rate of diagnosis in the study to more than 86%, not a bad rate of agreement.

There then remains about 14% of the sample of 372 patients, the so-called false negatives, labeled by the SCID as having a depressive disorder but not so labeled by their physicians. It is the group we worry about: is the family physician missing the diagnosis? The ongoing debate in the literature has been framed as, who is correct? But it is time to reframe the debate: trying to figure out who is right and who is wrong not only misses the point but also assumes perfection in the criterion measure. (A strong note of caution is raised by the results of the study by Schulberg et al in which 17% of criterion measure–positive patients did not have major depressive disorder.¹⁰) The real issue is that we use a different paradigm to determine “caseness”; knowledge of the patient over time is a fundamental component to our approach to diagnosis and treatment. If family physicians use diagnostic strategies not designed for their populations and not consistent with the family practice paradigm, they will have a hard time correctly diagnosing their patients.

The article by Lin et al² is the first to substantiate the risk of relapse of major depressive disorder in a primary care population. The authors looked at patients in 2 randomized trials who were prescribed antidepressants by their primary care physicians in a large staff model health maintenance organization. After 7 months of treatment, there were 251 patients of the original cohort who no longer met *DSM-III-R* criteria for major depression; in other words, they had lost their “caseness” as determined by independent assessment. A 12-month period between a baseline assessment at 7 months and another at 19 months was considered the relapse-risk period. Relapse was defined as (1) satisfying *DSM-III-R* criteria for major depression at 19 months or (2) reporting an interval episode of 2 weeks or more of depressed mood and symptoms between 7 and 19 months. With these criteria, more than 37% of patients were considered to have relapsed, a rate similar to that previously found in psychiatric populations, heretofore considered to have more severe disease. Not surprisingly, risk of relapse was associated with the per-

sistence of symptoms (subthreshold) at 7 months and history of 2 or more episodes of major depression or chronic mood symptoms for 2 years. Patients with both risk factors were 3 times more likely to relapse than patients with neither.

Two methodological issues are of concern in this study. First, the authors do not follow up treatment status throughout the relapse-risk period; in other words, the “at-risk” group included patients who had lost their “caseness” for whatever reason, including both effective treatment and spontaneous remission. The second methodological issue, acknowledged by the authors themselves, is that retrospective symptom report was used to determine the presence of an interval episode, while a structured interview was used at 19 months. Despite these limitations, the study provides important data on the natural course of major depressive disorder in primary care practice. These results are the first in a primary care population to support the AHCPR guidelines to continue and maintain treatment beyond the acute phase of the illness as well as the need to educate our patients about their risk of relapse and how to identify it so they will seek care.

These studies advance the literature on depressive disorders within our own discipline: they apply to the patients we see every day. We can use these data. Family physicians frequently see “distressed” patients, whom they describe as “depressed” without implying any specific diagnosis and often without implementing any specific therapy except, perhaps, supportive listening. In light of this phenomenon, it is interesting that each research group used a psychiatric criterion measure as well as a less standardized measure of depression. Lin et al² used retrospective symptom report to determine interval episodes, but a structured interview to determine episodes at the 19-month marker; and Klinkman et al¹ asked their physicians whether the patient had “clinically significant depression,” not whether the patient “currently meets criteria for *DSM-III-R* major depressive disorder,” which was their criterion standard. Interestingly, the stand-alone word *depression* (whether “clinically significant” or not) has no place in *DSM-III-R* and *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*¹⁸ terminology, which uses the terms *mood disorders*, *major depressive disorder*, *adjustment disorder with depressed mood*, *dysthymia*, *bereavement*, and the bipolar variants. Much of the early family practice literature on “depression” displays a lack of precision in terminology and classification; it was hard to tell whether researchers were describing symptoms or cases. We now know that there are a lot of symptoms in our patients that do not meet psychiatric standards of diagnosis, and we are beginning to see how family physicians understand “caseness.”

These studies contribute to the growing body of knowledge regarding patients who do not meet strict psychiatric definitions of depressive disorders, and they support the need to understand the natural course of both “distressed” and “depressed” patients. We need a model that permits us to view major depressive disorder as potentially chronic, albeit not always active, the way we view treated breast cancer or hypertension.

Agreeing on a criterion standard is less critical than holding ourselves to a high standard. This high standard must include precision in our diagnosis, the use of clinical acumen to complement standardized tests, and attention to follow-up as an integral part of our diagnostic paradigm.

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REFERENCES

1. Klinkman MS, Coyne JC, Gallo S, Schwenk TL. False positives, false negatives, and the validity of the diagnosis of major depression in primary care. *Arch Fam Med.* 1998;7:451-461.
2. Lin EHB, Katon WJ, VonKorff M, et al. Relapse of depression in primary care: rate and clinical predictors. *Arch Fam Med.* 1998;7:443-449.
3. Regier DA, Narrow WE, Rae DS, Manderscheid RW, Locke BZ, Goodwin FK. The de facto US mental health and addictive disorders service system: Epidemiologic Catchment Area prospective 1-year prevalence rates of disorders and services. *Arch Gen Psychiatry.* 1993;50:85-94.
4. Katon W, Schulberg H. Epidemiology of depression in primary care. *Gen Hosp Psychiatry.* 1992;14:237-242.
5. Wells K, Stewart A, Hays R, et al. The functioning and well-being of depressed patients. *JAMA.* 1989;252:914-919.
6. Schulberg H, Madonia M, Block M, et al. Major depression in primary care practice: clinical characteristics and treatment implications. *Psychosomatics.* 1995; 36:129-137.
7. Simon G, VonKorff M. Recognition, management, and outcomes of depression. *Arch Fam Med.* 1995;4:99-105.
8. Depression Guideline Panel. *Clinical Practice Guideline Number 5: Depression in Primary Care, 1: Detection and Diagnosis.* Rockville, Md: US Dept of Health and Human Services, Agency for Health Care Policy and Research; 1993. AHCPR publication 93-0550.
9. Depression Guideline Panel. *Clinical Practice Guideline Number 5: Depression in Primary Care, 2: Treatment of Major Depression.* Rockville, Md: US Dept of Health and Human Services, Agency for Health Care Policy and Research; 1993. AHCPR publication 93-0551.
10. Schulberg HC, Block MR, Madonia MJ, et al. Treating major depression in primary care practice: eight-month clinical outcomes. *Arch Gen Psychiatry.* 1996; 53:913-919.
11. Elkin I, Shea T, Watkins J, et al. National Institute of Mental Health Treatment of Depression Collaborative Research Program: general effectiveness of treatments. *Arch Gen Psychiatry.* 1989;46:971-982.
12. Shea MT, Elkin I, Stanley D, et al. Course of depressive symptoms over follow-up: findings from the National Institute of Mental Health Treatment of Depression Collaborative Research Program. *Arch Gen Psychiatry.* 1992;49: 782-787.
13. Kupfer DJ, Frank E, Perel JM, et al. Five-year outcome for maintenance therapies in recurrent depression. *Arch Gen Psychiatry.* 1992;49:769-773.
14. Schulberg HC, Block MR, Madonia MJ, Rodriguez E, Scoff CP, Lave J. Applicability of clinical pharmacotherapy guidelines for major depression in primary care settings. *Arch Fam Med.* 1995;4:106-112.
15. American Psychiatric Association, Committee on Nomenclature and Statistics. *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition.* Washington, DC: American Psychiatric Association; 1987.
16. Spitzer RL, Williams RJB, Gibbon M, Forst M. *Structured Clinical Interview for DSM-III-R-Nonpatient Edition (SCID-NP-9/1/89 Version).* New York, NY: Biometrics Research Division, New York State Psychiatric Institute; 1989.
17. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry.* 1960; 23:56-62.
18. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.* Washington, DC: American Psychiatric Association; 1994.

Clinical Pearl

Low-Dose Warfarin Therapy Plus Aspirin?

Adjusted-dose warfarin therapy (to an international normalized ratio of 2.0:3.0) was much better at preventing strokes in patients with atrial fibrillation than low-dose warfarin therapy, 0.5 to 3.0 mg/d, plus aspirin, 325 mg/d. The relative risk for stroke in the group receiving low-dose warfarin therapy plus aspirin was 301% (95% confidence interval, 113%-661%). (*Lancet.* 1996; 348:633-638.)