Best Clinical Practice: Guidelines for Managing Major Depression in Primary Medical Care

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Practice guidelines such as those of the United States Public Health Service Agency for Health Care Policy and Research have been instrumental in addressing the significant problem of how best to manage major depression in primary medical care settings. Since this set of guidelines was published in 1993, new findings from randomized clinical trials and extensive clinical experience permit us to reevaluate trends in treatment of major depression in primary medical care. This review suggests guidelines for achieving best clinical practice given current knowledge.

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Continuing advances in our knowledge about the etiology, diagnosis, and treatment of major depression have led to the formulation of guidelines for best clinical practice in managing this disorder. Some guidelines represent the consensus of experts pooling their clinical experiences, others emanate from professional organizations expressing their particular discipline-based perspectives, while still others constitute the thinking of governmentally sponsored panels drawing upon meta-analyses restricted to randomized controlled trials (RCTs). Such guidelines typically address the management of all depressed populations,[1,2] but it also is known that particular treatment issues pertain specifically to the depressed patients managed by primary care physicians.[3,4] In either instance, however, a consensus exists that while major depression usually is a recurrent or chronic disorder[5] with a poor prognosis,[6] its clinical course can be markedly improved with timely, scientifically validated interventions.

Given this progress, we offer recommendations for best clinical practice in managing the depression experienced by primary care patients. We draw heavily on the principles presented in the 1993 Agency for Health Care Policy and Research (AHCPR) Depression Guideline Panel Report,[4] but we also consider the findings from primary care sector RCTs published between 1993 and 1998.[7] This synthesis permits us to address the broad questions of concern to physicians as well as the treatment decisions about which the AHCPR Panel could only express tentative recommendations.

ANTIDEPRESSANT MEDICATIONS

Visits to primary care physicians for the treatment of depression continue to constitute about 35% of all such quests for professional help.[8] Drawing upon the 1993–1994 National Ambulatory Medical Care Surveys, Pincus et al.[8] determined that 60% of depressed patients were prescribed an antidepressant upon meeting with primary care physicians. Approximately 60% of these medications were selective serotonin reuptake inhibitors (SSRIs) and 40% were non-SSRI type antidepressants. This extensive prescribing volume and uncertainty by the AHCPR Depression Guideline Panel[4] as to whether antidepressants are as efficacious for depressed primary care patients as for psychiatric patients experiencing a mood disorder poses the question, What presently is known about the outcomes of pharmacotherapy in the ambulatory medical sector?

Efficacy

As knowledge about the basic psychopharmacology of antidepressants has grown,[9] so has information about their efficacy when prescribed to primary care patients. The AHCPR Depression Guideline Panel[4] identified only 7 primary care RCTs whose findings were in a format suitable for meta-analyses, but Trivedi et al.[10] identified 28 such

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RCTs published between 1975 and 1995. Their meta-analysis of this larger literature used the confidence profile method to calculate the percentage of intent-to-treat samples whose baseline Hamilton Rating Scale for Depression (HAM-D) score improved by at least 50%, or whose Clinical Global Improvement score indicated marked or extensive improvement during acute phase treatment. Trivedi et al. found overall efficacy rates to be 64.4% for tricyclics, 65.4% for heterocyclics, and 53.7% for SSRIs. These rates from primary care studies somewhat exceed those obtained for the 3 drug classes in RCT intent-to-treat samples of psychiatric patients, i.e., 51.5% for tricyclics, 62.3% for heterocyclics, and 47.4% for SSRIs.[4] Trivedi et al.[10] conjectured that these differences in efficacy possibly reflected the fact that primary care patients often experienced mild-to-moderate rather than severe episodes of a mood disorder, they were less often treatment resistant, and those with significant psychiatric or medical comorbidity were excluded from the clinical trial.

Additional support for the findings of Trivedi et al.[10] about the efficacy of antidepressants when prescribed for primary care patients is evident in the several RCTs conducted with this population since the earlier report of Trivedi et al.[10] Moon and Vince[11] found 6-week Montgomery-Asberg Depression Rating Scale (MADRS) scores decreased by at least 50% in 63% of patients prescribed paroxetine and in 54% of those prescribed lofepramine. Ravindran et al.[12] reported similar MADRS score decreases in 69% of patients with depression and associated anxiety who were prescribed paroxetine and among 67% of such patients prescribed clomipramine. Schulberg et al.[13] found that 54% of depressed patients prescribed nortriptyline by primary care physicians within standardized procedures experienced a 50% reduction at 4 months in 17-item HAM-D scores; at 8 months, 48% were recovered (HAM-D score $\leq$ 7). Simon et al.[14] found that 48% to 55% of patients with initial HAM-D scores of 15 or greater who were treated by primary care physicians with fluoxetine, imipramine, or desipramine under "usual care" conditions scored < 7 on the 17-item HAM-D at 6 months.

Since antidepressant medications achieve the same 50% to 60% response rate when prescribed for primary care and psychiatric patients, it is justifiable to implement similar pharmacotherapy protocols with both populations. An example of such a protocol is that produced by the Texas Medication Algorithm Project (TMAP),[15] which builds upon and updates the treatment principles proposed by the AHCPR Depression Guideline Panel.[4] Of particular interest in the TMAP algorithm is its detailed specifications of pharmacotherapy strategies pertinent to a patient's stage of depressive illness and the clinical decisions to be made in relation to whether or not the patient is improving.

First-Line Pharmacotherapy

The prescribing of tricyclic antidepressants (TCAs) by primary care physicians has diminished markedly since the advent of SSRIs in the early 1990s, and the latter drug class now constitutes first-line pharmacotherapy in the ambulatory medical sector. Is this change justified by efficacy differences among the drug classes, differences in patient compliance with the various drug classes, and/or other factors? Using data from studies with psychiatric patients, the AHCPR Panel's meta-analysis[4] found virtually equivalent efficacy among different antidepressant classes in outpatients with nonpsychotic major depressive disorder. The exception was a series of comparisons evaluating the response of atypical depression to placebo, phenelzine, or another monoamine oxidase inhibitor or tricyclic agent. Subsequent analyses of large pharmacologic prescription databases from the United Kingdom[16] and Scotland[17] found dosage levels for SSRIs more adequate than those for TCAs, but both drug types were prescribed for an inadequate duration.

Examining whether patient compliance with a medication's dosage and duration differs by drug class, Katon et al.[18] found depressed primary care patients treated in routine practice conditions somewhat more likely to stop using TCAs than SSRIs over a 6-month period. The randomized trial conducted by Simon et al.[19] in a routine practice setting similarly found patients more likely to discontinue desipramine or imipramine compared with fluoxetine. In contrast, the Trivedi et al.[10] meta-analysis of primary care RCTs conducted under more stringent experimental conditions found equivalent attrition by drug class: 15.9% for TCAs (16 treatment cells), 13.3% for heterocyclics (14 treatment cells), and 15.0% for SSRIs (1 treatment cell). The varied findings regarding adherence to SSRIs and TCAs in primary care resemble inconsistent findings from meta-analyses of psychiatric RCTs where, possibly because of differences in drug classification and research procedures, the odds ratio of discontinuing an SSRI rather than a TCA ranged from 0.70 (CI = 0.61 to 0.79)[20] to 0.90 (CI = 0.84 to 0.97)[21] to 0.95 (CI = 0.86 to 1.07).[22] Thus, Hotopf et al.[23] determined that when SSRI discontinuation rates were compared with those of the older TCA compounds (amitriptyline and imipramine), the SSRIs show a significant advantage at the .05 level (odds ratio = 0.82; CI = 0.72 to 0.92). This advantage is lost when SSRI discontinuation rates are compared with those of newer tricyclics and heterocyclics.

Another reason for variability in discontinuation rates across drug classes is the interaction between treatment setting, prescribing physician, and medication type. Attrition rates were found to be highest for health maintenance organization (HMO) patients prescribed tricyclic and heterocyclic drugs, and lowest for fee-for-services patients prescribed SSRIs.[24] Furthermore, among tricyclic-treated patients, those prescribed this medication by a psychiatrist

were significantly more likely to continue its use for at least 1 month compared to patients so treated by a nonpsychiatric physician.[25]

Even when the clinical factors affecting the choice of first-line pharmacotherapy are resolved, the primary care physician must still consider economic ones. Given higher acquisition costs for SSRI antidepressants, formulary directors and pharmacy benefit managers question whether SSRIs produce sufficiently superior clinical outcomes to justify their added expense. This issue has been addressed in various ways. Simulations employing decision-analytic models[26–30] and observational, nonrandomized studies comparing SSRIs and TCAs[31–33] have found no differences in overall treatment costs. In a prospective randomized trial, Simon et al.[14] compared clinical outcomes and treatment costs for HMO patients initially prescribed fluoxetine or 1 of 2 tricyclic drugs. Initial prescription of fluoxetine resulted in fewer side effects, a lower rate of medication switching, and no difference in clinical outcomes, quality-of-life outcomes, or overall treatment costs. We conclude, therefore, that while SSRI acquisition costs are higher, total treatment costs per depressive episode are similar for patients treated with SSRI or TCA medications.

Finally, when selecting an initial medication, the physician hopes to avoid unsuccessful pharmacotherapy and to persevere with medications likely to produce a positive outcome. The AHCPR Panel[4] recommended represcribing a previously well-tolerated, effective medication based on clinical case reports and clinician consensus. No subsequent trials have used this predictor in a randomized comparison with alternative treatments, e.g., an efficacious but untried medication that may have better pharmacoeconomic, side effect, tolerability, or safety characteristics. The Panel's recommendation, therefore, should continue as current practice based on face validity rather than empiric support.

Monitoring Treatment

The majority of patients prescribed an antidepressant medication improve sufficiently within 6 to 12 weeks to progress from pharmacotherapy's acute phase to the continuation phase. Nevertheless, a sizeable minority of patients starting this treatment will be unable to tolerate the medication's side effects or will display inadequate symptomatic improvement, or both. The determination of whether and when treatments are to be switched, modified, or augmented has great significance, but few empirical data are available to guide these clinical decisions.

An initial step in this process is monitoring patient reaction to the initially prescribed medication. Such monitoring optimally would be conducted by the primary care physician through patient visits weekly or every 2 weeks during the first 6 weeks of pharmacotherapy, as was recommended by the AHCPR Depression Guideline Panel.[4] However, the current managed care practice environment in the United States renders frequent monitoring impractical. The inadequate time available for follow-up monitoring also typically precludes a standardized assessment such as that conducted with the HAM-D. The TMAP[15] recommends, therefore, that a clinician's global impression of change in the patient's depressive severity serve as a proxy index of clinical course. This impression may be formed through phone contact with the patient or when he/she makes an office visit.

Regarding when the physician should judge that a patient is displaying a full, partial, or no response to treatment, the AHCPR Depression Guideline Panel[4] recommended that clinical course be evaluated within 4 to 6 weeks. It also indicated that a 25% or greater reduction in baseline symptom severity constitutes a meaningful criterion for extending the initial treatment. This AHCPR recommendation was tenuously based on earlier literature from pharmacotherapy RCTs conducted in psychiatric tertiary care settings. More recent studies continue to be conducted in these settings. Quitkin et al.[34] and Nierenberg et al.[35] determined that medication response ascertained at 4 weeks provided useful information about the likelihood of subsequent response, and Katz et al.[36] found that drug response could be predicted as early as 2 weeks after starting medication. While these findings are intriguing, there currently is no basis for revising the Guideline Panel's recommendation about the value of monitoring a medication's impact for a full 4 to 6 weeks before judging its efficacy. This is particularly true among patients with concurrent general medical illnesses that may impede clinical response.

Modifying Treatments

As was previously noted, approximately 40% to 50% of patients prescribed an antidepressant medication will not take it for the minimum period needed to achieve therapeutic gains or will fail to improve even when adhering to prescribed dosages. The significance of this problem has stimulated strategies for helping nonresponders. These strategies include switching the initial medication or augmenting it with an additional medication.[37] The latter approach may involve 2 antidepressants that act on different neurotransmitter systems (e.g., serotonin and norepinephrine), target different aspects of neurotransmission (e.g., reuptake transporters and receptors), or combine these actions. Another augmentation approach is the use of 2 agents indicated for different disorders (e.g., an antidepressant and an antipsychotic).[38–40]

The decision as to whether monotherapy should be continued by switching from the initially prescribed medication to a different one or to augment it in the ways described above is a complex one. The benefits of switching monotherapies include lower medication-related costs, fewer potential side effects, and increased patient adherence. It is also possible to produce symptomatic improve-

ment in 50% of patients assessed as nonresponders to the initial medication by switching them to an alternative one. The benefits of augmentation include maintaining patient optimism about clinical improvement, maintaining the partial response achieved with the initial medication, and converting partial responders (or even nonresponders) to full remitters. The TMAP[15] has recommended that patients with no history of prior treatment failures and those quickly developing an intolerance to the initial medication be switched to an alternative monotherapy. However, augmentation is preferable for patients with a history of prior treatment failures.

Continuation and Maintenance Pharmacotherapy

Patients whose symptoms have remitted during acute phase pharmacotherapy remain at substantial risk for relapse during the subsequent 12 months. Data from primary care treatments trials for major depression found that 37% of such patients again experience depressive symptoms during this follow-up time period.[41] Various studies have demonstrated the value, therefore, of continuation pharmacotherapy of 6 months duration in reducing relapse rates.[4,42] It is especially important that patients whose depressive symptoms persist at subthreshold levels 7 months after initiating pharmacotherapy and those with a history of 2 or more episodes of major depression or chronic mood symptoms receive continuation therapy, given these patients' particularly high risk of relapse.[41]

Primary care physicians increasingly are aware of the standards for prescribing antidepressant medications during the acute and continuation phases of pharmacotherapy. Most remain unaware, however, that the AHCPR Depression Guideline Panel[4] recommended maintenance pharmacotherapy for patients with histories of 3 or more depressive episodes and for those with 2 past episodes and vulnerability to future recurrences because of associated risk factors. We would note that the AHCPR recommendation was based on several studies of psychiatric patients (for example, Kupfer et al.).[43] There have been no comparable clinical trials of maintenance treatment's efficacy in reducing recurrence of the depression in primary care. The need for such research is emphasized by the fact that antidepressants can lose their efficacy during maintenance therapy, with recurrence rates ranging from 9% to 57%.[44] The possible causes of real or apparent medication tolerance are unclear, but may include altered antidepressant pharmacokinetics associated with the primary care patient's existing or newly emerging physical illness.

PSYCHOTHERAPY

More than 250 psychosocial treatments have been described in the literature, but relatively few are designed specifically to reduce and resolve the symptoms of a mood disorder. Furthermore, the psychotherapies directed at depression were largely developed and validated with psychiatric patients. Meta-analyses of studies conducted with this population led the AHCPR Depression Guideline Panel[4] to estimate efficacy rates of 46% for cognitive therapy, 55% for behavioral therapy, and 52% for interpersonal psychotherapy. In the absence of methodologically sound, randomized, controlled trials of such interventions with primary care samples, the AHCPR Panel concluded that depression-specific psychotherapies are similarly efficacious when treating ambulatory medical patients experiencing major depression.

In the years following publication of the AHCPR report, several studies were completed that provide firmer support for the Panel's conclusions about the transferability of psychotherapy. Scott and Freeman[45] found that mean HAM-D scores for primary care patients treated with cognitive therapy dropped from 18.3 at baseline to 6.7 at 16 weeks. Mynors-Wallis et al.[46] reported a 60% recovery rate (i.e., HAM-D of 7 or less) at 12 weeks among primary care patients participating in at least 4 sessions of problem-solving therapy, a briefer and more focused form of cognitive therapy developed to treat major depression in primary care.[47,48] In a sample of primary care patients with major depression randomly assigned to acute and continuation phase interpersonal psychotherapy, Schulberg et al.[13] found 46% of the intent-to-treat sample and 72% of the treatment-completer subgroup recovered (HAM-D $\leq$ 7) at 8 months. The preceding studies suggest that depression-specific psychotherapies (cognitive-behavioral, interpersonal, and problem-solving) are more similar than different in overall efficacy during the acute phase of treatment and in their impact on targeted symptoms, despite varied theoretic principles and therapeutic foci.

When selecting formal psychotherapy as the sole acute phase treatment, clinicians should apply the following principles: (1) the time-limited psychotherapy should focus on current problems and aim at symptom reduction rather than personality reconstruction; (2) the therapist should be skilled in providing the psychotherapy to patients who have a major depression; and (3) symptomatic response should be monitored and medication considered for patients failing to show any improvement by 6 to 8 weeks or nearly full remission by 12 weeks. Equally significantly in the present era of managed care, clinicians should ascertain that the patient's insurance plan will pay for the 8 to 20 psychotherapy sessions typically necessary to achieve recovery from the depressive episode.

Monitoring Treatment

The monitoring of a patient's clinical progress when treated with a depression-specific psychotherapy should be pursued much in the manner described previously for patients prescribed an antidepressant medication. The psychotherapist, who typically will be a mental health specialist rather than a primary care physician, should deter-

mine at frequent intervals whether severity of the patient's presenting depressive symptoms is being reduced, whether functioning is improving, and so on. Such assessments can be made through administration of brief self-report instruments such as the Beck Depression Inventory and the Medical Outcomes Study Short Form 12 or through administration of clinician-rated instruments such as the HAM-D, the Clinical Global Improvement scale and the Inventory of Depressive Symptomatology.

When judging whether psychotherapy is ineffective or requires augmentation with an antidepressant, we would note that partial and full remission of a mood disorder is thought to occur more slowly when treated with psychotherapy than with pharmacotherapy. Earlier reports by Watkins et al.[49] and Schulberg et al.[13] determined that clinical improvement for the former intervention may not be evident until 6 to 8 weeks after treatment's start, rather than during the 4- to 6-week period required for a medication. Thus, a delayed response to psychotherapy should not necessarily be judged as indicating the need to modify, augment, or drop it.

Continuation and Maintenance Psychotherapy

In contrast to the numerous studies of continuation pharmacotherapy and the initial such study of maintenance pharmacotherapy by Kupfer et al.,[43] there have been virtually no studies of psychotherapy's ability to prevent or reduce recurrence when extended beyond treatment's acute phase.[50] The primary care study by Schulberg et al.[13] was the only one in which patients were provided psychotherapy for 8 months rather than for the 2 to 4 months typifying such treatment in both psychiatric and primary care research. In a somewhat different study of psychiatric patients, Fava et al.[51] reduced the recurrence of depression among patients who were provided cognitive-behavioral therapy following a partially successful course of pharmacotherapy. Thus, extended psychotherapy possibly prevents recurrence, but few data are available to advocate such interventions in the face of managed care restrictions on more-than-brief psychotherapeutic treatments.

SELECTING FIRST-LINE TREATMENT: PHARMACOTHERAPY OR PSYCHOTHERAPY?

The preceding reviews indicate that both pharmacotherapy and psychotherapy effectively treat major depression when provided in the ambulatory medical care sector. Is there any evidence, then, as to whether one is superior, particularly with regard to specific subgroups of depressed primary care patients? The AHCPR Depression Guideline Panel[4] concluded from its review of earlier RCTs of each treatment type that antidepressant medication rather than psychotherapy alone should be selected as the initial acute phase intervention for more severely depressed patients. Either medication or psychotherapy could serve as the initial treatment for patients with depressions of mild or moderate severity.

Two recent randomized trials conducted in primary care practices have directly compared pharmacotherapy and depression-specific psychotherapy as first-line treatments. Mynors-Wallis et al.[46] found comparable efficacy at 12 weeks for pharmacotherapy and psychotherapy among patients with major depression, with remission rates (HAM-D $\leq$ 7) of 52% for amitriptyline, 60% for problem-solving therapy, and 27% for pill placebo. No demographic, clinical, or personality variables predicted outcome in relation to treatment type.[52] Schulberg et al.[13] similarly determined that guideline-driven pharmacotherapy and interpersonal psychotherapy produced equivalent 8-month recovery rates (48% for nortriptyline and 46% for interpersonal psychotherapy among intent-to-treat samples). Their secondary analysis of the relationship between baseline severity and treatment selection[53] did not confirm earlier reports[54] of better outcomes with pharmacotherapy among the small minority of primary care patients who are severely symptomatic (baseline HAM-D > 20). These recent findings are consonant with those of Blackburn et al.[55] and Kovacs et al.,[56] in which the presence of endogenous symptom features appeared not to differentially affect response to antidepressant medication or cognitive therapy. We conclude, therefore, that the primary care physician can select either medication or a depression-specific psychotherapy as the initial intervention for treating major depression. When clinically and practically feasible, the patient's preference should also be considered in this decision. In either case, symptomatic outcome should be monitored.

With regard to the relative efficacy of combined treatment compared with monotherapy, little new evidence is available from primary care settings. Katon et al.[57] found that brief psychotherapy incorporating elements of both social cognitive and social learning theories, combined with education about the value of staying on a prescribed medication, significantly improved antidepressant adherence and increased the proportion of patients experiencing a 50% or greater improvement on a 20-item Symptom Checklist-90 depression scale compared with those receiving usual care. Following a "mega-analysis" of studies of psychiatric patients with recurrent depression, Thase et al.[58] concluded that combined therapy has a significant advantage over psychotherapy alone in the treatment of more severe episodes. Nevertheless, we retain the same uncertainty expressed in the 1993 AHCPR Guidelines as to whether combination treatment is a first-line treatment. It may specifically benefit patients who have not recovered with monotherapy or those with more complicated morbidity (e.g., concomitant Axis II disorders, complex psychosocial circumstances, chronic course of illness).

We would note that while complementary and alternative therapies for depression have been used by 20% of

those suffering from depression,[59] few rigorous scientific data are available to support the efficacy of such interventions. A review by Ernst et al.[60] of this literature led them to conclude that the therapies with the most evidence for beneficial effects are exercise, herbal therapy (*Hypericum perforatum*), and, to a lesser extent, acupuncture and relaxation therapies. Thus, pending further randomized controlled trials, complementary and alternative treatments of depression remain intriguing and provocative rather than scientifically founded first-line interventions.

Finally, our analysis of optimal initial treatments of major depression must consider the economic as well as clinical factors affecting such choices in primary care settings.[61] In the present era of cost savings and managed care, policy makers expect first-line treatments to improve clinical outcomes with little additional resource expenditures and perhaps even cost saving. How realistic is this expectation?

Several primary care, randomized, controlled trials have analyzed the cost-effectiveness of treatments of major depression.[62–64] Each determined that improved clinical outcomes could be achieved with guideline concordant services compared to usual care. However, costs of the former exceeded those of the latter by $300 to $1500 per enhanced treatment episode.[7] Thus, improved clinical outcomes are costly. Can the increased costs of first-line treatment choices be justified, however, by their ability to reduce the other health-care costs incurred by a depressed patient? It is tempting to suggest that the cost-offset does occur and that significant savings can be reaped, at least among selected patient subgroups who adhere to antidepressant therapies.[65] Nevertheless, we conclude that such a cost-offset remains to be proven in true experiments. A particularly vital design element in such future research is the determination of how managed care mechanisms affect the magnitude of the cost-offset.[66]

MENTAL HEALTH SPECIALIST REFERRALS

The health care environment in the United States encourages, if not pressures, the primary care physician to treat most forms of major depression in the ambulatory medical sector. While it appears fiscally advantageous to do so, particularly for patients whose care is funded by a capitated mechanism, the clinical benefits in doing so remain unclear. Scott and Freeman[45] found similar reductions in severity of symptomatology among patients treated for major depression by either primary care physicians or mental health specialists. However, the costs were higher for the latter providers. Conversely, Katon et al.[67] demonstrated that collaboration between mental health specialists and primary care physicians significantly improved clinical outcomes over the generalist's usual care. Again, however, this benefit was achieved at a higher cost.[62]

Given the potential clinical benefits but higher fiscal costs of referring depressed primary care patients to a mental health specialist, efforts have been undertaken to expand upon or refine the collaborative model devised by Katon et al.[67] These efforts often involve creating new roles for nurses or social workers who function as "depression specialists" within the primary care practice. These roles presently are being tested for their utility in identifying and treating older depressed patients presenting to primary care physicians. As these collaborative roles expand, it will be ever more crucial to distinguish the respective responsibilities of the generalist and mental health specialist. Another strategy for involving the mental health specialist in the treatment of a depressed primary care patient is through a step-care arrangement, wherein patients who fail to remit after 8 weeks of treatment by the primary care physician are provided additional visits with a mental health specialist.[68] This strategy has been found to significantly improve the clinical and functional outcomes of high utilizers of medical care.[69]

The preceding studies did not identify specific patient subgroups requiring early referral for specialist treatment. The AHCPR Guidelines[4] enumerated (with no particular priority or empiric justification) and the University of Minnesota Consensus Guidelines[70] reiterated clinical indicators that suggest the need for mental health specialist care: severe symptoms; suicide risk; comorbid medical, psychiatric, or substance use disorder; and failure to respond to appropriate treatment. The merit of these clinical indicators and their economic justification remain uncertain, but we continue to endorse them, given their face validity.

CONCLUSION

Guidelines published by the AHCPR in 1993 for the management of major depression in primary care practice are still valid today. New data from RCTs of antidepressants and psychotherapies conducted in such a setting show that SSRIs and TCAs are both efficacious treatments for depression. However, primary care patients are more likely to discontinue TCAs compared with SSRIs. Analyses of overall treatment costs with TCAs and SSRIs suggest that despite the lower acquisition costs of the former, total treatment costs per depressive episode are similar for the 2 medications. Psychotherapy has demonstrated efficacy and may be of particular benefit for patients who do not wish to be administered medication. Thus, the primary care physician should consider patient treatment preferences when selecting a first-line intervention.

Drug names: amitriptyline (Elavil and others), clomipramine (Anafranil), desipramine (Norpramin and others), fluoxetine (Prozac), imipramine (Tofranil and others), paroxetine (Paxil), phenelzine (Nardil), nortriptyline (Pamelor and others).

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