Compliance With Antidepressants in a Primary Care Setting, 2: The Influence of Gender and Type of Impairment

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Background: DSM-IV diagnosis of major depressive disorder includes a requirement that symptoms result in significant clinical distress or impairment. This criterion is difficult to assess and is often overlooked. This study examines the use of the Sheehan Disability Scale as a possible method of assessing impairment, as well as the relationship between functioning and discontinuation of antidepressant medication. ***Method:*** Patients (N = 272) receiving antidepressant therapy due to an episode of major depressive disorder were asked to complete an antidepressant compliance questionnaire. Patients were telephoned monthly while they continued on antidepressant therapy, up to 6 months. During each call, the Sheehan Disability Scale was administered. ***Results:*** Of patients referred to this study, 94.8% met DSM-IV criteria of at least 5 symptoms of major depressive disorder. Most patients had initial scores ranging from 5 to 8 on all 3 Sheehan disability subscales (occupational, social, and family functioning); 72% of patients had at least moderate impairment (scores ≥ 4) on all 3 subscales. After 8 weeks of treatment, 42% of patients had scores < 4 on all 3 subscales (recovery); after 24 weeks, 64% of patients had scores <4 on all 3 subscales. Dropout risk in men was related to improvement in occupational, social, and family functioning, whereas dropout risk in women was related only to improvement in family functioning. ***Conclusion:*** The Sheehan Disability Scale can be valuable in assessing impairment and thus in correctly diagnosing major depressive disorder. We suggest that scores of 4 or more (moderate impairment) on all 3 subscales indicate sufficient impairment for a strict diagnosis of major depressive disorder. Functional symptoms continued to improve for up to 24 weeks on antidepressant therapy, suggesting 6 months or more of therapy is necessary for maximum functional improvement. Premature discontinuation of antidepressant therapy is more likely to occur in women who experience significant improvement in family functioning or men who experience significant improvement in any functional area. *(J Clin Psychiatry 2001;62[suppl 22]:34–37)*

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The definition of mental disorder in the introduction to DSM-IV requires that there be clinically significant impairment or distress. To highlight the importance of considering this issue, the criteria sets for most disorders include a clinical significance criterion (usually worded ". . . causes clinically significant distress or impairment in social, occupational, or other important areas of functioning"). Assessing whether this criterion is met, especially in terms of role function, is an inherently difficult clinical judgment. Reliance on information from family members and other third parties (in addition to the individual) regarding the individual's performance is often necessary.[1]

Too often, scant attention is paid to this criterion in the research literature. Use of an assessment tool to measure such distress or impairment, in addition to an assessment of depressive symptoms, could allow differentiation between patients who meet the full diagnosis of a major depressive (having 5 or more symptoms, as well as clinically significant impairment or distress) and those patients

with the symptoms but with little or no impairment. This would be especially valuable because overdiagnosis of depression can be as much of a problem as underdiagnosis of depression, especially in primary care settings.[2,3] The Sheehan Disability Scale, which assesses impairment in occupational, social, and family functioning, may be an appropriate instrument.

The effect of patients' functional impairment on their compliance with antidepressant medication has also received little attention. Patients often prematurely discontinue their antidepressant medication because they are "feeling better."[4,5] However, that general term could encompass improvement in functional impairment as well as alleviation of depressive symptoms.

This study focuses on the use of the "clinically significant impairment" criterion, assessing outcome with a complementary "impairment" measure and investigating whether functional improvement (defined as a decrease in impairment) influences compliance. The degree of impairment was also used as a complementary outcome measure, i.e., response and recovery were defined analogously to the cutoffs often used for assessments of depressive symptoms.

MATERIALS AND METHODS

After receiving informed consent of the patients (N = 272), participating general practitioner physicians (GPs) (N = 91) sent the principal investigator (K.D.) a file for each patient, indicating the DSM-IV criteria for major depressive disorder, patient name and contact information, and the antidepressant described for that patient (fluoxetine, 221 patients; citalopram, 14 patients; paroxetine, 12 patients; sertraline, 9 patients; fluvoxamine, 5 patients; trazodone, 2 patients; venlafaxine, 2 patients; and moclobemide, 1 patient; missing values in 6 patients). Patients with major depressive disorder for whom an antidepressant was indicated were consecutively enrolled. Inclusion criteria were an episode of major depressive disorder and being at least 18 years old. The mean age of the patients was 43 ± 13 years; 72% were women.

Each patient was asked to complete and return the Antidepressant Compliance Questionnaire (ADCQ) and the Sheehan Disability Scale[6] and to indicate the hour and day when he or she preferred to get a monthly call at home. Patients were told they would receive a call each month for as long as they were on treatment, up to 6 months. During these phone calls, contact was limited to the administration of the Sheehan Disability Scale and some standard questions (Are you still taking the antidepressant medication? If not, when and for what reason(s) was the drug discontinued, and is the general practitioner informed about the discontinuation?).

The Sheehan Disability Scale

In this study, functional improvement ("feeling better") was assessed by the degree of impairment caused by the depressive symptoms. The Sheehan Disability Scale was used to measure this impairment. The Sheehan Disability Scale is a self-rated assessment of impairment in occupational, social, and family functioning, each rated from 0 to 10 (0–3: mild impairment; 4–6: moderate impairment; 7–10: severe impairment). Response was defined as a 50% decrease in initial impairment; recovery was defined as an impairment score of 3 or less (no more than mild impairment) on all 3 Sheehan subscales (occupational, social, and family functioning). Efficacy analyses were intent to treat and last patient observation carried forward.

Statistical calculations (t test, trend test, Pearson correlation coefficients) were carried out using the SAS package (SAS Institute, Inc., Cary, N.C., 1996). All results were considered to be significant at the 5% critical level.

Figure 1. Baseline Scores on the Occupational, Social, and Family Subscales of the Sheehan Disability Scale (N = 272)[a]

[a]Heights of the bars indicate the percentage of patients having each score.

RESULTS

Criteria For Major Depressive Disorder

Of the patients referred by their physician, 94.8% demonstrated the presence of at least 5 of the 9 symptoms for major depressive disorder, as required for a DSM-IV diagnosis of major depressive disorder. Of the remaining patients, 3.7% had only 4 symptoms, and 1.6% had only 3 symptoms.

No guidelines have been developed for the additional criterion "clinically significant impairment." It is therefore interesting to examine the distribution of patients' scores on the 3 Sheehan subscales (Figure 1). Most patients had initial scores ranging from 5 to 8 on all 3 subscales. Figure 2 shows the percentage of patients with scores > 6 (severe impairment) and > 3 (moderate or severe impairment) in 1, 2, 3, or no domains of the Sheehan Disability Scale.

Since we believe that major depressive disorder affects all 3 domains of functioning (occupational, social, family), we propose that *clinically significant impairment* be defined as at least moderate impairment (scores > 3) in all 3

Figure 2. Percentage of Patients (N = 272) With 1, 2, 3, or No Domains of Severe and Moderate Impairment

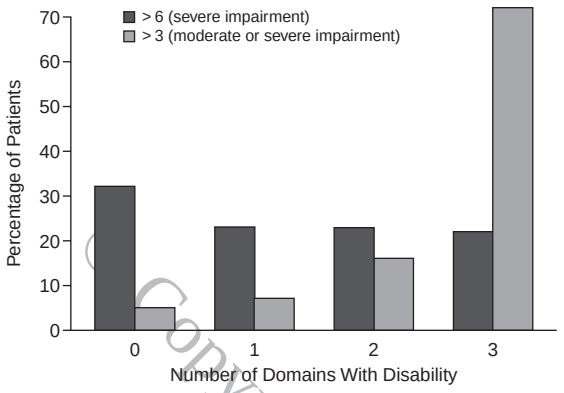
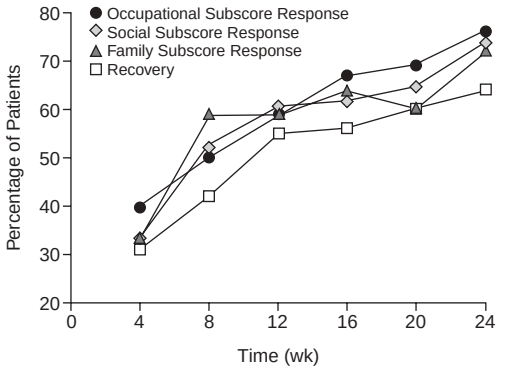


Figure 3. Percentage of Patients (N = 272) Meeting Criteria for Response (≥ 50% decrease in impairment) for Each Sheehan Subscale Score and for Recovery (a score of ≤ 3 on all subscores) Over Time



domains. Under that definition, 72% of the included patients would fulfill the DSM-IV criteria for major depressive disorder.

Some gender differences were found. In women, the mean disability scores at baseline for occupational, social, and family functioning were 5.8, 5.8, and 6.5, respectively, whereas in men they were 6.1, 5.3, and 5.6, respectively. The impairment in family functioning was significantly greater in women than in men ($p = .01$). In women, the impairment in family functioning was significantly greater than in social or occupational functioning ($p = .003$), whereas in men, there were no significant differences in impairment among occupational, social, or family functioning ($p = .19$). The impairment scores in occupational, social, and family functioning significantly but weakly correlated with the number of positive DSM-IV items (Pearson correlation coefficients [r] = 0.22, 0.21, and 0.23, respectively).

Efficacy of Antidepressant Treatment: Impairment as an Outcome Measure

A trend test demonstrated that, in men as well as in women, there was a highly significant improvement in functioning (as measured by a decrease in impairment) between baseline and 20 weeks of treatment ($p = .0001$). After 8 weeks of treatment, 50%, 52%, and 59% of patients met the criterion for response in occupational, social, and family functioning, respectively; 42% met the criterion for recovery. After 24 weeks of treatment, 76%, 74%, and 72% of patients responded for occupational, social, and family functioning, respectively; 64% recovered (Figure 3).

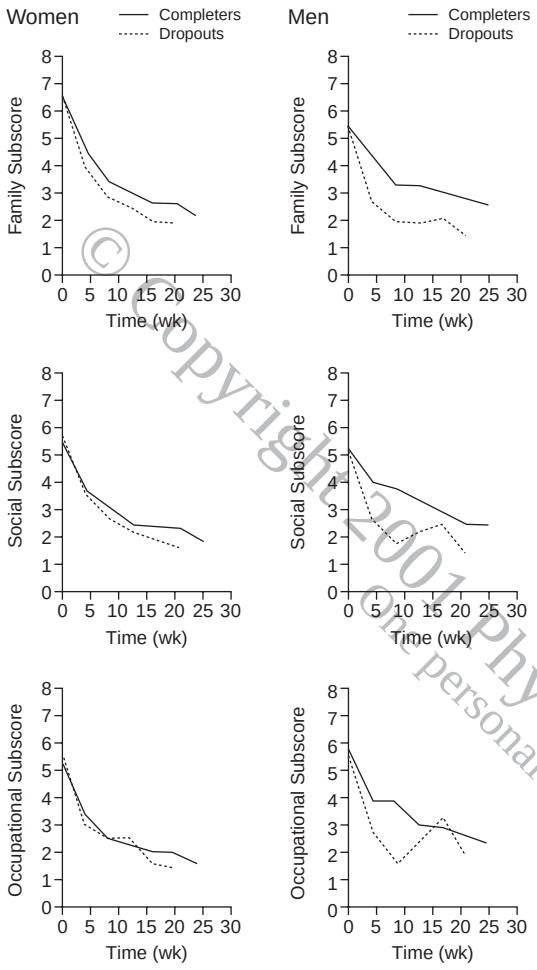
Compliance in Relation to Gender and Impairment

The dropout rate after 4, 8, 12, 16, 20, and 24 weeks was 12%, 22%, 32%, 42%, 48%, and 53%, respectively (median time to dropout was 22 weeks). The relation between impairment and dropout risk is gender specific (Figure 4). While in women the dropout risk was related only to improvement in family functioning, in men it was related to improvement in occupational, social, and family functioning. Men with a more significant improvement in functioning were especially likely to drop out. In women, dropouts had a more significant improvement in family functioning than completers ($p < .0001$ after 4, 8, 12, 16, and 20 weeks of treatment). In men, dropouts had a more significant improvement in family functioning ($p < .0001$ at weeks 4 through 24), social functioning ($p < .0001$ after 4, 8, and 12 weeks), and occupational functioning ($p < .0001$ after 4 and 8 weeks).

DISCUSSION

The use of the "clinically significant impairment" criterion could help the clinician to diagnose major depressive disorder (and all other Axis I diagnoses) more accurately. Moreover, this could probably help in decreasing the variance in prevalence rates between different studies. When applying DSM-IV criteria for major depressive disorder (5 of 9 symptoms) and defining *clinically significant impairment* as a score of 4 or more in each of the 3 major fields of functioning (occupational, social, family life), 28% of the patients in this study do not merit a diagnosis of major depressive disorder. A less severe cutoff for "clinically significant impairment" (at least a moderate impairment in 2 of the 3 major fields of functioning) would have excluded 12% of patients, and a very broad definition of *clinically significant impairment* (at least a moderate impairment in 1 of the 3 major fields of functioning) would have excluded 5% of patients. Since the available literature does not provide applicable guidelines and since a clinically meaningful depression usually interferes with all aspects of life, we propose the first definition (at least a moderate impairment in the 3 major fields of functioning). Indeed, we believe that depression is at risk of being overdiagnosed as well as being underdiagnosed. The Depression Research

Figure 4. Sheehan Subscale Scores Versus Time After Initiation of Antidepressant Medication[a]



[a]The left column shows results in women (N = 196), the right column shows results in men (N = 76). Family, social, and occupational subscores are shown in the top, center, and bottom rows, respectively.

in European Society (DEPRES) study[7] showed that, at least in a sample population, only 10% of depressed patients are treated with antidepressants, but other studies also showed that 13% to 40% of patients treated with antidepressants (for a depressive illness) should not have been treated with these drugs because they never fulfilled the criteria for this diagnosis.[8,9]

Although the most pronounced improvement occurred between 0 and 8 weeks of treatment, there was still further improvement in functioning between 8 and 24 weeks. This is in accordance with the work of Mintz and colleagues,[10] who reported that improvement in functioning occurs more slowly than improvement in depressive symptoms. After 8 weeks, the response rate was between 50% (for occupational impairment) and 59% (for impairment in family functioning), and the recovery rate was only 42%. After 24 weeks, the response rate was between 72% (for impairment in family functioning) and 76% (for occupational impairment), and the recovery rate was 64%. These data illustrate that, in addition to the well-established prevention of relapse,[11] improvement in functioning is another important reason for treating depressed patients for at least 6 months.

Some gender-specific issues emerged in this study. First, impairment in functioning caused by depressive symptoms is slightly different in men and women. Whereas women seem to experience impairment most seriously in their family life, men experience impairment evenly across all 3 categories. This finding should be interpreted carefully, however, since we did not collect sociodemographic data; some of this difference could be explained if significantly more women than men in this study did not have an occupation outside the home.

Second, the present study suggests that men are especially prone to prematurely stop taking antidepressants as soon as they feel less impaired by their depressive symptoms. Indeed, a significant improvement in occupational, social, or family functioning increased the dropout risk in men, whereas only a significant improvement in family functioning increased the dropout risk in women. The fact that "feeling better" (in this study, "feeling less impaired") is an important cause of discontinuation in antidepressant treatment is a confirmation of previously published data.[4,5] To the best of our knowledge, though, this is the first report of the gender specificity of this reason for dropout.

Drug names: citalopram (Celexa), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), trazodone (Desyrel and others), venlafaxine (Effexor).

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