

A Record-Based Analysis of 803 Patients Treated for Depression in Psychiatric Care

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Background: New antidepressants emerged and became widely used during the 1990s. The present study investigated quality-of-care problems in the treatment of depression in a current psychiatric setting.

Method: We investigated the treatment received for depression by all 803 inpatients or outpatients with a clinical diagnosis of ICD-10 depressive episode or recurrent depressive disorder in 1996 in the Peijas Medical Care District, which provides psychiatric services for citizens of Vantaa, a city in southern Finland.

Results: Most patients (84%) in the sample were found to have received antidepressants, generally in adequate, albeit low, doses. Inadequate antidepressant treatment was common only with tricyclic antidepressants. Most patients received a single antidepressant for extended periods; only 22% had 2 or more antidepressant trials. During the treatment period, disability pension was granted to 19% of those not already pensioned, two thirds (67%) of whom had received only 1 antidepressant trial prior to being granted a pension.

Conclusion: The present study supports the emerging perception of improved quality of pharmacotherapy in psychiatric settings, with the exception of treatment with tricyclic antidepressants. Problems of quality of care now appear to be related to the suboptimal intensity and monitoring of the treatment provided, which may eventually result in considerable costs to society due to permanent disability.

(*J Clin Psychiatry* 2001;62:701–706)

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In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Drs. Rytsälä, Melartin, Leskelä, Lestelä-Mielonen, Sokero, and Isometsä have no significant commercial relationships to disclose relative to the presentation.

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Besides being a substantial cause of human suffering, unipolar major depression exerts the fourth largest impact among illnesses worldwide in terms of functional disability.¹ Despite the central role of major depression in public health, even the most recent general population epidemiologic studies find that the majority of people suffering from major depression in the United States² as well as Europe³ still fail to receive appropriate treatment. From an epidemiologic perspective, only a minority of all individuals seeking medical treatment for depression receive psychiatric care. However, the individuals treated in psychiatric settings are likely to suffer from the most severe, long-lasting, incapacitating, and comorbid depressions, with the highest likelihood of completed suicide or permanent functional disability. Thus, from a tertiary prevention viewpoint, psychiatric care holds a key position.

According to studies conducted in the 1980s,^{4–7} patients receiving no specific treatment for depression, or inadequate treatment, seemed to have been the rule even among subjects attending psychiatric facilities. Does this alarming situation still prevail in psychiatric settings today, with the expansive growth of antidepressant sales and increasing awareness among psychiatrists of the importance of depression during the last decade? While most published studies still find nontreatment or undertreatment of depression to be a problem,^{8–12} some recent reports^{13–15} have noted improved quality of antidepressant treatment of patients with depression in psychiatric care. Because quality-of-care problems seem to be particularly related to inadequate treatment with tricyclic antidepressants (TCAs),^{12,16–20} much of the possible improvement in quality of antidepressant treatment might be explained by the fact that selective serotonin reuptake inhibitors (SSRIs) and other new antidepressants have attained a position of first-line treatment in many clinical settings. These new compounds appear to be used more often in adequate doses than TCAs, both in primary health care¹⁷ and in psychiatric care.¹³

The aim of this study was to investigate the adequacy of the treatment of depression in 1996 in a psychiatric secondary care setting providing treatment for a well-defined catchment area. We expected to find better coverage and a higher proportion of adequate antidepressant treatment

than were found in the earlier studies.^{4-7,21-23} We also compared the treatment provided for those with better and worse clinical outcomes, particularly those returning to work and those granted a disability pension.

METHOD

The Vantaa Depression Study (VDS) is a collaborative depression research project involving the Department of Mental and Alcohol Research of the National Public Health Institute, Helsinki, and the Department of Psychiatry of the Peijas Medical Care District (PMCD), Vantaa, Finland. The catchment area of the Peijas Medical Care District comprises the cities of Vantaa (population = 166,500 in 1996) and Kerava (population = 29,400); however, the VDS only includes subjects living in the city of Vantaa. The facilities of the Department of Psychiatry of the PMCD provide secondary care psychiatric services for all citizens of Vantaa and include a 50-bed psychiatric inpatient unit, a general hospital outpatient clinic, 6 community mental health care centers, each covering a specified catchment area, and 2 day hospitals. The VDS includes both a naturalistic prospective major depressive disorder cohort study and a quality-of-care study. The baseline findings from the quality-of-care study are reported here.

Data for this study were collected from a computerized patient database incorporating all outpatient visits as well as treatment periods at the inpatient unit. We included all patients aged 20 to 59 years who had been assigned a clinical diagnosis of depressive episode (F32.xx) or recurrent depressive disorder (F33.xx) according to ICD-10 criteria²⁴ and who had at least 1 outpatient visit or day of inpatient treatment in the PMCD during the study period January 1, 1996, to December 31, 1996. We excluded all those with an earlier diagnosis of schizophrenia, other nonaffective psychosis, or bipolar disorder. Also excluded were patients treated in the somatic departments of Peijas Hospital and those who had consulted but not received treatment from the psychiatric consultation services.

The first author (H.J.R.) reviewed the psychiatric records of the 803 included patients and completed a structured form with 57 items for each case. These items comprised (1) sociodemographic characteristics (including age, sex, marital status, occupational status, and work status at both the beginning and end of treatment) and clinical features (including severity of depression as classified in the clinical ICD-10 diagnosis) and (2) treatment received during the whole treatment period (including psychopharmacologic treatment, number of visits to psychiatrists and other health professionals, inpatient treatment, and refusal of antidepressant treatment) in the PMCD, irrespective of the year it began. Treatment provided was reviewed up to the end of 1997. Patients treated at the PMCD inpatient unit at least once were classified as inpatients. The adequacy of dose of antidepressant was

defined as the usual adult dose in the APA Practice Guidelines,^{25,26} and the length of treatment with antidepressant medications was recorded. Antidepressants available in Finland in 1996 comprised most of those in the APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder (Revision)²⁶ and, in addition to these, mianserin. Desipramine, protriptyline, amoxapine, bupropion, phenelzine, and tranylcypromine were not available in Finland at the time.

For statistical analyses of treatment received, we employed logistic regression models using stepwise backward elimination with the likelihood ratio test as the criterion for removal to control for age, sex, and other possible confounding factors. These are specified for each model separately (see Results). Variables were dichotomized if needed. The chi-square test was used with Yates correction. The Kruskal-Wallis test was used to test differences in duration of use of antidepressants. For comparing the groups granted disability pension and not granted pension, we employed 1-way analysis of variance (ANOVA). SPSS software²⁷ was used.

RESULTS

Sample and Treatment Characteristics

The study sample comprised 290 male and 513 female patients, whose characteristics are shown in Table 1. The sexes differed significantly only in the prevalence of alcohol misuse. During the treatment period, the depressed patients averaged only a few visits to psychiatrists (median = 2; range, 1-52), but more to other health professionals including psychiatric nurses, social workers, and psychologists (median = 7; range, 1-148). One fifth (20%) of both sexes were inpatients, with a mean of 1.8 inpatient treatment periods (median = 1, range 1-20) during the overall treatment period investigated. The median length of a hospital stay was 14 days.

Antidepressant Treatment

Most (675/803 [84.1%]) of the patients received antidepressants, including a minority (11.3%) on treatment with clearly subtherapeutic low doses. The prevalence of antidepressant treatment by degree of severity of depression is shown in Table 2. TCAs were used in inadequate doses in about half of the cases (78/148 [52.7%]), whereas inadequate treatment with SSRIs and other newer antidepressants was rare (13/527 [2.5%]; $\chi^2 = 245.7$, $p < .0001$). The antidepressants used are shown in Table 3. In a logistic regression model with stepwise backward elimination, use of TCAs was significantly associated with older age (odds ratio per year of age = 1.06, Wald $\chi^2 = 19.92$, $df = 1$, $p < .0001$, 95% confidence interval [CI] = 1.03 to 1.08), previous psychiatric care (odds ratio = 1.58, Wald $\chi^2 = 4.52$, $df = 1$, $p = .03$, 95% CI = 1.04 to 2.42), and use of neuroleptics (odds ratio = 2.57, Wald $\chi^2 = 17.70$,

Table 1. Sociodemographic Characteristics of the 803 Psychiatric Patients in the Peijas Medical Care District of Vantaa, Finland

| Characteristic | Men (N = 290) | Women (N = 513) | Total (N = 803) |
|---|------------------|--------------------|--------------------|
| Age, y, mean \pm SD | 43 \pm 9.3 | 43 \pm 10.2 | 43 \pm 9.9 |
| Marital status, % | | | |
| Married | 42 | 41 | 41 |
| Cohabiting | 12 | 11 | 11 |
| Divorced | 29 | 31 | 31 |
| Widow(er) | 1 | 4 | 3 |
| Unmarried | 16 | 13 | 14 |
| Occupational status, % | | | |
| Entrepreneur | 10 | 3 | 5 |
| White-collar worker | 26 | 36 | 33 |
| Blue-collar worker | 57 | 50 | 52 |
| Pensioned | 3 | 4 | 4 |
| Student | 4 | 4 | 4 |
| Other | 0 | 3 | 2 |
| Work status at the beginning of the treatment, % | | | |
| Unemployed | 27 | 20 | 22 |
| Sick leave | 20 | 20 | 20 |
| Pensioned, psychiatric reason | 14 | 14 | 14 |
| Pensioned, somatic reason | 6 | 3 | 4 |
| Employed | 30 | 33 | 32 |
| Student | 3 | 4 | 4 |
| Other | 0 | 4 | 3 |
| Not known | 0 | 1 | 1 |
| Work status at the end of the treatment, % | | | |
| Unemployed | 22 | 13 | 16 |
| Sick leave | 10 | 8 | 8 |
| Pensioned, psychiatric reason | 30 | 28 | 29 |
| Pensioned, somatic reason | 7 | 3 | 5 |
| Employed | 27 | 37 | 34 |
| Student | 2 | 5 | 4 |
| Other | 0 | 3 | 2 |
| Not known | 0 | 2 | 1 |
| Dead | 2 | 0 | 1 |
| Severity of depression, % | | | |
| Mild | 7 | 10 | 9 |
| Moderate | 35 | 37 | 36 |
| Severe | 29 | 29 | 29 |
| Severe with psychotic features | 11 | 9 | 10 |
| Not specified | 18 | 15 | 16 |
| Misuse of alcohol, % ^a | | | |
| No alcohol misuse | 61 | 80 | 73 |
| Alcohol misuse | 39 | 20 | 27 |
| Previous psychiatric care, % | | | |
| No | 52 | 49 | 50 |
| Yes | 48 | 51 | 50 |
| Quartiles of duration of current treatment period, wk | | | |
| 25 | 16 | 23 | 21.0 |
| 50 | 60 | 65 | 63.0 |
| 75 | 119 | 121 | 120.1 |

^aMen vs. women, $\chi^2 = 33.4$, $df = 1$, $p < .0001$.

$df = 1$, $p < .0001$, 95% CI = 1.65 to 3.98). The model also included sex, living alone or together, occupation, alcohol misuse, use of anxiolytics, use of hypnotics, and degree of severity of depression as covariates.

Sequential Use of Antidepressants

The first antidepressant had been switched to another compound in only about one fifth (174/803 [22%]) of pa-

Table 2. Prevalence of Antidepressant Use by Severity of the Clinical Diagnosis of Depression

| Depression Severity | Men (N = 290) | | Women (N = 513) | | Total (N = 803) | |
|---------------------|------------------|------|--------------------|------|--------------------|------|
| | N | % | N | % | N | % |
| Mild | 14 | 70.0 | 35 | 67.3 | 49 | 68.1 |
| Moderate | 93 | 90.3 | 158 | 83.6 | 251 | 86.0 |
| Severe | 75 | 90.4 | 136 | 91.3 | 211 | 90.9 |
| Psychotic | 31 | 93.9 | 39 | 83.0 | 70 | 87.5 |
| Not specified | 39 | 76.5 | 55 | 72.4 | 94 | 74.0 |
| Total | 252 | 86.9 | 423 | 82.5 | 675 | 84.1 |

Table 3. Characteristics of Antidepressant Treatment Periods by Type of Antidepressant^a

| Antidepressant | N | % | Mean Dose (mg) ^b | Dose Range (mg) | Median Duration (wk) ^{c,d} |
|---------------------|-----|-------|-----------------------------|-----------------|-------------------------------------|
| Tricyclics | | | | | |
| Amitriptyline | 70 | 10.4 | 93 | 25–250 | 96 |
| Clomipramine | 33 | 4.9 | 120 | 10–250 | 51 |
| Doxepin | 30 | 4.4 | 85 | 25–250 | 67 |
| Imipramine | 2 | 0.3 | 138 | 125–150 | 5 |
| Nortriptyline | 1 | 0.1 | 100 | 100 | 163 |
| Trimipramine | 12 | 1.8 | 92 | 50–150 | 70 |
| SSRIs | | | | | |
| Fluoxetine | 184 | 27.3 | 26 | 8–60 | 34 |
| Fluvoxamine | 26 | 3.9 | 102 | 50–300 | 35 |
| Citalopram | 138 | 20.4 | 28 | 10–60 | 63 |
| Paroxetine | 16 | 2.4 | 23 | 20–40 | 28 |
| Sertraline | 16 | 2.4 | 84 | 50–200 | 44 |
| Tetracyclics | | | | | |
| Maprotiline | 6 | 0.9 | 81 | 38–150 | 89 |
| Mianserin | 54 | 8.0 | 54 | 10–90 | 29 |
| Trazodone | 12 | 1.8 | 208 | 100–300 | 74 |
| NaSSA | | | | | |
| Mirtazapine | 6 | 0.9 | 30 | 15–45 | 21 |
| SNRI | | | | | |
| Venlafaxine | 1 | 0.1 | 75 | 75 | ... |
| RIMA | | | | | |
| Moclobemide | 68 | 10.1 | 417 | 150–600 | 32 |
| Total | 675 | 100.0 | | | 44 |

^aAbbreviations: NaSSA = noradrenergic and specific serotonergic antidepressant, RIMA = reversible inhibitor of monoamine oxidase A, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

^bMeans of the highest daily doses used during the treatment period.

^cExact duration of treatment not known in 59 cases.

^dDuration of use was significantly longer (Kruskal-Wallis test, $\chi^2 = 11.68$, $df = 3$, $p = .009$) for tricyclics vs. SSRIs, tetracyclics, and others.

tients (Table 4), and only 2 patients had received up to 5 antidepressant trials. During the whole treatment period reviewed, TCAs only were received by 113 patients (14.1%), SSRIs only by 307 patients (38.2%), and other antidepressants only by 106 patients (13.2%). Antidepressants of at least 2 different types were received by 149 patients (18.6%). The median duration of the first antidepressant trial was about 10 months (median = 44 weeks; range, 0.4–524 weeks). Forty-seven patients (7% of those prescribed any antidepressant) received 2 antidepressants simultaneously. There were no statistical differences between the sexes in terms of receiving only 1 or 2 antide-

Table 4. Antidepressants Administered in First and Second Antidepressant Trials^a

| | Second Antidepressant | | | | | | | |
|----------------------|-----------------------|------|----------|------|----------|-----|-------------------|------|
| | TCA | | SSRI | | Other | | None ^b | |
| | (N = 54) | | (N = 71) | | (N = 49) | | (N = 629) | |
| First Antidepressant | N | % | N | % | N | % | N | % |
| TCA (N = 148) | 3 | 2.0 | 24 | 16.2 | 11 | 7.5 | 110 | 74.3 |
| SSRI (N = 380) | 42 | 11.1 | 18 | 4.7 | 30 | 7.9 | 290 | 76.3 |
| Other (N = 147) | 9 | 6.1 | 29 | 19.7 | 8 | 5.5 | 101 | 68.7 |

^aAbbreviations: SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

^bThis total includes the 128 patients who never received an antidepressant.

pressants. None of the patients were prescribed any other augmentation medication.

Patient Dropout and Refusal of Treatment

Refusing antidepressant treatment was the most common explanation for not receiving antidepressants; it was markedly more common among those with mild than those with more severe degrees of depression (8.0% vs. 3.5%, $\chi^2 = 5.182$, $df = 1$, $p = .03$) and also associated with younger age and being employed after treatment. About one fifth (22%) of all outpatients who had at least one outpatient visit dropped out from their scheduled further visits. In the logistic regression model with stepwise backward elimination and including age, sex, living alone versus cohabiting, occupation, being employed at the beginning of treatment, being employed at the end of treatment, and severity of depression as the covariates, dropping out was significantly predicted by younger age (odds ratio per year of age = 1.03, Wald $\chi^2 = 7.72$, $df = 1$, $p = .006$, 95% CI = 1.01 to 1.05), being employed at the beginning of treatment (odds ratio = 1.60, Wald $\chi^2 = 4.81$, $df = 1$, $p = .03$, 95% CI = 1.05 to 2.44), and milder severity of depression (odds ratio = 2.35, Wald $\chi^2 = 17.83$, $df = 1$, $p < .0001$, 95% CI = 1.58 to 3.49). Whether or for how long those who dropped out as outpatients continued antidepressant treatment is unknown. Less than half of the patients received medications other than antidepressants. These included anxiolytics (41.6%), hypnotics (35.2%), and neuroleptics (34.0%). There were no statistical differences between the sexes in the use of these medications. A great majority (85%) of psychotic patients and over one fourth (28%) of nonpsychotic patients received neuroleptics.

Treatment and Work Status

At the end of the treatment period, the proportion of employed patients was nearly identical to that at the beginning (Table 1). During the treatment period, 125 patients (19% of those not already receiving disability pension) were granted disability pension due to psychiatric illness. These patients were significantly older than those receiving no pension (mean ages = 48.5 and 39.7 years,

Table 5. Number of Antidepressant Trials Prescribed in Psychiatric Care Before Granting of Disability Pension Among Patients Granted a Disability Pension During the Study Period

| No. of Trials | N | % |
|-------------------------|-----|-------|
| No antidepressant trial | 8 | 6.4 |
| 1 | 76 | 60.8 |
| 2 | 29 | 23.2 |
| 3 | 9 | 7.2 |
| 4 | 3 | 2.4 |
| Total | 125 | 100.0 |

respectively; $p < .0001$, 1-way ANOVA). There were no differences between the sexes in either group. The new pension recipients were also more severely ill than those receiving no pension: more (58% vs. 42%, $p = .0001$) suffered from severe or psychotic depression. The new pension recipients also had significantly more visits to professionals than did those receiving no pension (mean = 15.1 vs. 9.4; median = 11 vs. 7; $p = .0003$, 1-way ANOVA) and received significantly more concomitant medications: 53% versus 36% received anxiolytics ($p = .001$), 43% versus 33% received hypnotics ($p = .03$), and 42% versus 29% received neuroleptics ($p = .007$), respectively.

Antidepressant Treatment and Disability Pensions

Despite their obvious lack of response, two thirds (67%) of the patients granted a disability pension during the study period had received only a single antidepressant trial or none at all (Table 5); the figure was 82% for all other patients. The median length of the first antidepressant trial did not differ significantly between the groups (44 vs. 45 weeks, NS). More of the patients granted a disability pension for major depression than those with no pension received TCAs (31% vs. 11%). Thus, being granted a disability pension was significantly associated with receiving TCAs ($\chi^2 = 29.49$, $df = 1$, $p < .0001$). This finding remained significant after adjusting for possible confounding factors (age, sex, living with a partner, occupation, work status at the beginning of treatment, severity of depression, alcohol misuse, and use of anxiolytics, hypnotics, and neuroleptics) in the logistic regression model with stepwise backward elimination (odds ratio = 2.17, Wald $\chi^2 = 7.39$, $df = 1$, $p = .007$, 95% CI = 1.24 to 3.78).

DISCUSSION

The vast majority of psychiatric patients treated in psychiatric settings are likely to receive antidepressants in doses found effective in clinical trials, indicating that current quality-of-care problems are different from past quality-of-care problems.

Before discussing our findings, some methodological aspects of the present study should be noted. The major

strength of the study is that it was based on a large patient population representing psychiatric secondary care in Finland's fourth largest city. We could not include patients who had visited private psychiatrists outside the PMCD, or the very few treated at Helsinki University Central Hospital. Based on another study²⁸ and an unpublished epidemiologic survey of the city of Vantaa, we estimate our sample to represent two thirds of all depressed subjects in the general population of Vantaa seeking treatment from psychiatrists (E.T.I., J. Lönnqvist, M.D., Ph.D., unpublished data, 1999). Thus, we expect our findings to be generalizable to Finland's entire population¹³ in secondary care settings in the latter half of the 1990s and, given their similarities to findings from some other recent studies,^{21–23,29} to psychiatric settings in other Western countries as well. The data were collected from a computerized database comprising the full psychiatric patient records of the catchment area. We consider the quality of these comprehensive records available to us to be good, which allowed us to investigate the clinical characteristics and the treatments received in more detail than in previous investigations. Nevertheless, record-based studies also have their well-known limitations. Our study was based on clinical diagnoses of depression, the validity of which are unknown. The possibility of false-negative, undiagnosed cases cannot be excluded. We investigated psychiatric records carefully to exclude false-positive cases likely to have had some other psychiatric disorder. Since our study population was based on the 12-month prevalence of depression in the PMCD, inclusion of cases in the study was influenced by both the incidence of depression and the duration of treatment period, which enriches chronic patients in the population. However, as such, the population accurately represents the caseload of the attending personnel.

In the earlier studies of antidepressant treatment received by psychiatric patients in the 1980s, treatment was generally found to be absent or inadequate.³⁰ Some recent smaller studies¹³ have indicated improvement in the quality of care during the last decade. Our main finding was that the large majority of depressed patients received adequate antidepressant treatment, although often in low doses. Inadequate treatment was common only among those receiving TCAs, whereas treatment with newer antidepressants almost always occurred with doses found to be effective in clinical trials. It should be noted that mirtazapine and venlafaxine entered the Finnish market in 1996, so only a few patients in our study received them. The median duration of the treatment period was found to be over 1 year; thus, acute, continuation, and maintenance treatment phases were probably included in most cases. The modest intensity of the treatment provided, largely due to limited resources in terms of monitoring antidepressant treatment as well as psychosocial treatments, is clearly a problem. Most patients visited psychiatrists only

1 to 3 times. However, even considering this, we found the psychiatrists to have been quite conservative in switching antidepressants. This was true even when poor response was obvious, e.g., in those granted a disability pension.

Depression-related functional disability^{31–32} and the necessity of disability pensions³³ due to depression are major losses to both the individual and society. Treatment of depression has been shown to markedly reduce depression-related disability.³⁴ In our sample, one fifth of those not already receiving a disability pension were granted one during the treatment period investigated. Patients in this subgroup were considerably older and more severely ill, used more concomitant psychotropic medication, and had slightly more visits to professionals than patients in other subgroups. Nevertheless, about two thirds of these patients (67%) received a disability pension after only a single trial of an antidepressant. We have also made a similar finding in another, nationally representative study of patients with major depression who were granted a disability pension in Finland.³³ Furthermore, use of TCAs, often in inadequately low doses, was more common (31% vs. 11%) among patients granted a disability pension during the study period than among the other patients. While it remains unknown whether more intensive pharmacotherapy or psychosocial treatment could have prevented their permanent disability, it is at least obvious that more intensive treatment efforts are warranted. Our concern is that cutting costs in the quality of care may result in much higher permanent costs to society.

The present study supports the emerging perception of improved quality of pharmacotherapy in psychiatric settings, with the exception of treatment with TCAs. Problems in the quality of care for depression in psychiatric settings are more likely to be related to suboptimal intensity and monitoring of treatment than to mere lack of treatment. Too few visits to psychiatrists and other professionals to allow systematic follow-up and psychosocial treatments, exclusive reliance on the low end of the dose range of antidepressants, limited number of antidepressant trials or augmentations, and acceptance of permanent disability without first pursuing vigorous treatment are all likely to be major problems in current psychiatric settings. These problems may eventually result in considerable human and economic costs to both the patient and society.

Drug names: amitriptyline (Elavil and others), bupropion (Wellbutrin and others), citalopram (Celexa), clomipramine (Anafranil and others), desipramine (Norpramin and others), doxepin (Sinequan), fluoxetine (Prozac), fluvoxamine (Luvox and others), mirtazapine (Remeron), nortriptyline (Pamelor and others), paroxetine (Paxil), phenelzine (Nardil), protriptyline (Vivactin), sertraline (Zoloft), transylcypromine (Par-nate), trazodone (Desyrel and others), trimipramine (Surmontil), venlafaxine (Effexor).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, mianserin and moclobemide are not approved by the U.S. Food and Drug Administration for use in the United States.

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