

Continuity Is the Main Challenge in Treating Major Depressive Disorder in Psychiatric Care

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Objective: Several evidence-based treatment guidelines for major depressive disorder (MDD) have been published. However, little is known about how recommendations for treatment are adhered to by patients in current usual psychiatric practice.

Method: The Vantaa Depression Study is a prospective, naturalistic cohort study of 269 psychiatric patients with a new episode of DSM-IV MDD who were interviewed with the Schedules for Clinical Assessment in Neuropsychiatry and Structured Clinical Interview for DSM-III-R Personality Disorders between February 1, 1997, and May 31, 1998, and again at 6 and 18 months. Treatments provided, as well as adherence to and attitudes toward both antidepressants and psychotherapeutic support/psychotherapy, were investigated among the 198 unipolar patients followed for 18 months.

Results: Most depression patients (88%) received antidepressants in the early acute phase, but about half (49%) terminated treatment prematurely. This premature termination was associated with worse outcome of major depressive episodes, and with negative attitudes, mainly explained by fear of dependence on or side effects of antidepressants. Nearly all patients (98%) received some psychosocial treatment in the acute phase; about one fifth (16%) had weekly psychotherapy during the follow-up. About a quarter of patients admitted nonadherence to ongoing treatments.

Conclusion: Problems of psychiatric care seem most related to continuity of treatment. While adequate treatments are provided in the early acute phase, antidepressants are terminated too soon in about half of patients, often following their autonomous decisions. From a secondary and tertiary preventive point of view, improving continuity of treatment would appear a crucial task for improving the outcome of psychiatric patients with MDD.

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Several sets of evidence-based treatment guidelines have been published to improve detection and treatment of major depressive disorder (MDD).^{1–5} Effective treatments documented include antidepressant medications (administered in acute, continuation, and maintenance phases) and cognitive-behavioral, interpersonal, and psychodynamic psychotherapies.^{1–5} The guidelines also suggest that treatment be continued until remission of symptoms and a normal level of functioning are achieved.^{1–5}

Primary care^{6–9} and retrospective database studies^{10,11} have reported frequent shortcomings in depression treatment, including inadequate follow-up dosage and monitoring of antidepressant treatment. However, few recent psychiatric care studies have investigated how treatment recommendations, especially after the immediate acute phase, are carried out.^{12–16} Treatment received, and predictors of treatment inadequacy and premature termination, are rarely reported even though premature termination of treatments is a great concern for clinicians. According to a review, only 1% to 2% of all publications on treatment of affective disorders explore factors associated with medication adherence (how closely a person's behavior conforms to medical advice).¹⁷ Part of this neglect is explained by the unresolved confusion about terminology, and the highly variable methods used in measuring nonadherence.^{8,17–19} Recent studies, although limited in number, show increasing attention being focused on various risk factors for nonadherence, such as stigma, health beliefs, and negative attitudes toward psychiatric treatments.^{8,10,17,19–23} However, to what extent

patients' negative treatment attitudes, fear of side effects, perceived side effects per se, comorbidity, and severity of depression influence premature terminations of treatments, or nonadherence, is still poorly understood.¹⁷⁻¹⁹

In the present prospective naturalistic follow-up study, our aims were to describe (1) the quality and continuity of psychotherapeutic and antidepressant treatments received in acute, continuation, and maintenance phases of MDD, (2) patients' self-reported level of adherence and treatment attitudes, and (3) factors explaining these items among depressive patients in psychiatric care. We hypothesized that factors associating with premature termination of treatments and self-reported nonadherence would include preexisting negative treatment attitudes, perceived side effects, less severe depression, and more current comorbidity, and that negative treatment attitudes would be more common among those with current comorbidity, especially personality and alcohol use disorders.

METHOD

The background and methodology of the Vantaa Depression Study (VDS) have been described in detail elsewhere.^{24,25} In brief, the VDS is a collaborative depression research project between the Department of Mental Health and Alcohol Research of the National Public Health Institute, Helsinki, and the Department of Psychiatry of the Peijas Medical Care District (PMCD), Vantaa, Finland. Vantaa is Finland's fourth-largest city, with a population of 169,000 in 1997, and the PMCD provides psychiatric services free of charge to all its citizens.

Screening and Baseline Evaluation

The first phase of patient sampling for the VDS involved screening all patients (N = 806) in the PMCD for a possible new episode of DSM-IV MDD between February 1, 1997, and May 31, 1998, in Vantaa.^{24,25} After a positive screen, patients were fully informed about the study project and their participation was requested. Of the 703 eligible patients, 542 (77.1%) agreed and gave their written informed consent. Those 161 (22.9%) who refused to enter the study did not differ significantly ($p > .05$) in age or gender from those who consented.

In the second phase of sampling, the 542 consenting patients were interviewed face-to-face by a researcher (U.S.L., P.S.L.-M., T.K.M., H.J.R., or T.P.S.) using the World Health Organization (WHO) Schedules for Clinical Assessment in Neuropsychiatry (SCAN) 2.0,²⁶ for which all had received training through a WHO certified training center. Thereby, 269 patients were diagnosed with DSM-IV MDD and included in the study. Diagnostic reliability was investigated using 20 videotaped diagnostic interviews; the kappa coefficient for MDD was 0.86 (CI = 0.58 to 1.0), with 95% observed agreement rate.²⁴ The Structured Clinical Interview for DSM-III-R Person-

ality Disorders (SCID-II)²⁷ was used to assess diagnoses on Axis II. In addition to SCAN 2.0 and SCID-II, the cohort baseline measurements included the 17-item Hamilton Rating Scale for Depression²⁸ and Scale for Suicide Ideation.²⁹ The self-report scales included the 21-item Beck Depression Inventory,³⁰ Beck Anxiety Inventory,³¹ and Interview Measure of Social Relationships.³²

Treatments Provided and Their Continuity

Treatments provided were investigated at baseline and both follow-up interviews. Psychotherapeutic support comprised regular appointments with a mental health professional aimed at helping the patient by discussing his or her problems (weekly psychotherapy excluded). Weekly psychotherapy was defined as weekly therapy sessions for ≥ 4 weeks with a qualified, certified therapist (usually with psychodynamic, or sometimes cognitive-behavioral, training). The adequacy of antidepressant dosage was defined as the usual adult doses in the American Psychiatric Association (APA) Practice Guideline.¹ Continuity of psychotherapeutic and antidepressant treatment was assessed by interviewing patients and investigating all clinical information on treatment, including medical and psychiatric records. Treatment was defined as ongoing as long as it was provided or prescribed according to psychiatric records, while termination was the date when treatment was first documented as not ongoing (or reportedly terminated by the patient if no later contact with a professional). Here, sequential antidepressant trials and their intermediate short washout periods were classified as 1 continuous treatment period.

Patients were asked their subjective reasons for discontinuing antidepressants, with the following alternatives: (1) poor/no response, (2) side effects, (3) too-expensive medication, (4) no need for treatment because of recovery, (5) patient's autonomous decision, or (6) could not answer.

Self-Reported Treatment Adherence

Self-reported treatment adherence concerning the treatments provided was investigated by interviewing patients at the follow-ups using a Likert scale with the following response items: the patient has come to sessions/been on antidepressants (1) regularly, treatment compliance adequate with respect to treatment goals; (2) somewhat irregularly, it is unclear whether this would affect treatment goals; (3) very irregularly, the treatment did not proceed according to plan; or (4) not at all, the provided treatment could not be implemented.

Attitudes

Attitudes toward antidepressant and psychotherapeutic treatments at baseline were assessed separately by interviews and rated on a Likert scale with the following items: patient (1) actively wants treatment, (2) passively accepts treatment, (3) has reservations about treatment, (4) has

definitely negative attitudes toward treatment, or (5) could not answer. At the follow-ups, patients were interviewed with scales with the following items: attitudes toward treatment are (1) very positive, (2) positive, (3) neutral, (4) negative, (5) very negative, or (6) could not answer.

At baseline, patients with reservations about or definitely negative attitudes toward treatments were also asked their subjective reasons for these attitudes, with the following alternatives: (1) generally negative attitudes toward treatment, (2) fear of side effects (antidepressants)/not wanting to confide in stranger (psychotherapeutic treatments), (3) fear of dependence, (4) not knowing enough about treatment, (5) patient's/other's negative earlier experiences in treatment, (6) negative information from media, (7) no belief that treatment will help, (8) too-expensive treatment, or (9) could not answer.

Follow-Up

Of the total of 269 subjects with current MDD initially included in the study, 40 subjects were missing ($N = 229$) at 6 months, and 207 patients were interviewed at the 18-month follow-up.²⁵ Patients whose diagnosis was switched to bipolar disorder during the follow-up (13/269, [5%]) were excluded from the analyses, and 8 patients died during the follow-up. The study cohort includes the 198 unipolar MDD patients who were followed for 18 months. They were mostly women (72%), outpatients (85%), currently employed (65%), and married/cohabiting (54%), with a mean (\pm SD) age of 41.0 (\pm 11.1) years.²⁵ Employment status of 5 subjects was unknown. The dropouts (bipolar cases excluded) were significantly younger (mean \pm SD = 35.7 \pm 10.2 vs. 41.0 \pm 11.1 years, $t = 3.24$, $df = 254$, $p = .001$), were significantly more often unemployed (31/58 [53%] vs. 68/193 [35%], $\chi^2 = 6.20$, $df = 1$, $p = .013$), and had current comorbid psychiatric DSM-IV disorders (mean \pm SD = 3.5 \pm 2.0 vs. 3.0 \pm 1.7, $t = -2.08$, $df = 254$, $p = .038$), panic disorder (15/58, [26%] vs. 26/198 [13%], $\chi^2 = 5.41$, $df = 1$, $p = .020$), and social phobia significantly more often (17/58 [29%] vs. 34/198 [17%], $\chi^2 = 4.14$, $df = 1$, $p = .042$) than those attending the 18-month follow-up. When baseline treatments were compared, the only significant finding was that dropouts were without antidepressants more often (13/58 [22%] vs. 24/198 [12%], $\chi^2 = 3.84$, $df = 1$, $p = .050$).

During the follow-up, a detailed life chart was created.²⁵ We used 2 alternative definitions for duration of index episode after the first baseline interview: (1) uninterrupted duration of major depressive episode (MDE) (time with full MDE criteria), and (2) time to first onset of state of full remission lasting at least 2 consecutive months (time to full remission). As a categorical variable, remission was defined as in the DSM-IV as at least 2 consecutive months in which criteria were not met for an MDE. Recurrence was defined as in the DSM-IV as return of symptoms sufficiently severe to satisfy criteria for MDE

after at least 2 consecutive months of partial or full remission. Based on the life chart, time during follow-up was classified into acute, continuation, or maintenance phases in accordance with the APA Practice Guideline.¹ The patient was in the acute phase for as long as he or she had not achieved full remission.

Statistical Analyses

The Pearson χ^2 test was used to evaluate categorical and nonparametric data, the Mann-Whitney or Kruskal-Wallis test to compare continuous variables not normally distributed, and the 2-sample t test or the 1-way analysis of variance for continuous variables normally distributed. Logistic regression (LR) models were used to adjust for confounding factors. The probability of remaining on first antidepressants administered was estimated by Kaplan Meier survival curve. Cox proportional hazards models³³ were used in the analyses for predicting time to full remission. SPSS software, version 11.0.1,³⁴ was used. Treatment received was reported separately for patients with full, partial, or no remission from the index episode because of a tendency for more severely ill patients to receive more treatment in a naturalistic study.³⁵ The level of significance was set at $p < .05$.

RESULTS

Treatment Received in the Early Acute Phase

At baseline, most patients (174/198 [88%]) received antidepressants, and for the majority (154/198 [78%]), the dosage level was adequate for the acute phase. More than half (112/198 [57%]) of the study cohort patients received selective serotonin reuptake inhibitors (SSRIs) alone at baseline; about one fifth (36/198 [18%]), newer antidepressants (tetracyclics, a noradrenergic and specific serotonergic antidepressant, a serotonin-norepinephrine reuptake inhibitor (SNRI), a reversible inhibitor of monoamine oxidase A); 8% (15/198), tricyclic antidepressants (TCAs); and 6% (11/198), combination treatment, usually SSRI and TCA. While SSRIs and newer antidepressants were used inadequately in the acute phase in only about a tenth of cases (7% and 11%, respectively), TCAs were used inadequately in about half (47%) ($\chi^2 = 20.08$, $df = 2$, $p < .001$) of cases. Nearly all patients (98%) received psychotherapeutic support. However, only a few, and none of those without remission, received weekly psychotherapy (16%) or augmentation of pharmacotherapy (e.g., lithium or buspirone). Only 3% received electroconvulsive therapy (Table 1).

Continuity of Antidepressant Treatment

In contrast to generally adequate treatment in the early acute phase, the continuity of antidepressant treatment provision was far less complete, particularly in the continuation and maintenance phases (Table 2, Figure 1).

Table 1. Antidepressant and Psychosocial Treatments Received and Highest Level of Remission Achieved From the Index Episode of the Vantaa Depression Study MDD Patients Followed for 18 Months

Variable	Full Remission (N = 122)	Partial Remission (N = 61)	MDD (N = 15)	Total (N = 198)	Statistic	p
Antidepressant treatment, N (%)						
Antidepressant at baseline	101 (83)	58 (95)	15 (100)	174 (88)	$\chi^2 = 8.01$.018
Adequacy of first antidepressant trial ^a						
Adequate	86 (71)	53 (87)	15 (100)	154 (78)	$\chi^2 = 11.79$.019
Inadequate	15 (12)	5 (8)	0 (0)	20 (10)		
No antidepressant	21 (17)	3 (5)	0 (0)	24 (12)		
≥ 3 Trials on antidepressants	13 (11)	15 (25)	10 (67)	38 (19)	$\chi^2 = 28.68$.001
Antidepressant combination treatment	17 (14)	12 (20)	5 (33)	34 (17)		NS
Buspirone augmentation	7 (6)	4 (7)	0 (0)	11 (6)		NS
Lithium augmentation	0 (0)	0 (0)	0 (0)	0 (0)		NS
Psychosocial treatments						
Psychotherapeutic support, N (%)	119 (98)	60 (98)	15 (100)	194 (98)		NS
Weekly psychotherapy, N (%)	20 (16)	11 (18)	0 (0)	31 (16)		NS
No. all psychotherapeutic sessions, mean (SD) ^b	16.9 (15.7)	24.6 (26.6)	38.3 (17.6)	21.1 (20.7)	F = 9.13	< .001
Duration of psychotherapeutic treatment, mean (SD), mo ^c	9.4 (6.5)	11.5 (6.0)	17.5 (3.6)	10.7 (6.5)	F = 11.93	< .001
Visits to psychiatrist, mean (SD) ^d	2.9 (3.0)	5.3 (5.9)	8.6 (4.5)	4.1 (4.5)	$\chi^2 = 29.69$	< .001
Electroconvulsive therapy, N (%)	1 (1)	3 (5)	1 (7)	5 (3)		NS

^aAntidepressant(s) at adequate dosage level for at least 4 weeks in acute phase.^bData missing for 4.0% of patients; N = 190.^cData missing for 3.5% of patients; N = 191.^dKruskal Wallis test.

Abbreviations: MDD = major depressive disorder, NS = nonsignificant.

Table 2. Continuity of Antidepressant Treatment in the Index Episode and Lifetime Number of MDEs Prior to Entry Among Vantaa Depression Study MDD Patients Followed for 18 Months

Variable	Single Episode (N = 66)		2 Episodes (N = 65)		≥ 3 Episodes (N = 67)		Total (N = 198)		χ^2	p
	N	%	N	%	N	%	N	%		
No antidepressant (baseline)	16	24	2	3	6	9	24	12	14.73	.001
Antidepressant (baseline)	50	76	63	97	61	91	174	88		
Antidepressant ongoing for the index episode	15	23	26	40	35	52	76	38	8.60	.014
In acute phase	8	12	14	22	21	31	43	22		NS
In continuation phase	1	2	1	2	1	2	3	2		NS
In maintenance phase	6	9	11	17	13	19	30	15		NS
Antidepressant discontinued	35	53	37	57	26	39	98	50	8.60	.014
In MDE	4	6	6	9	5	8	15	8		NS
In partial remission	17	26	17	26	8	12	42	21	6.98	.030
In continuation phase	7	11	9	14	7	10	23	12		NS
In maintenance phase	7	11	5	8	6	9	18	9		NS
Antidepressant discontinued and restarted	6	9	6	9	7	10	19	10		NS

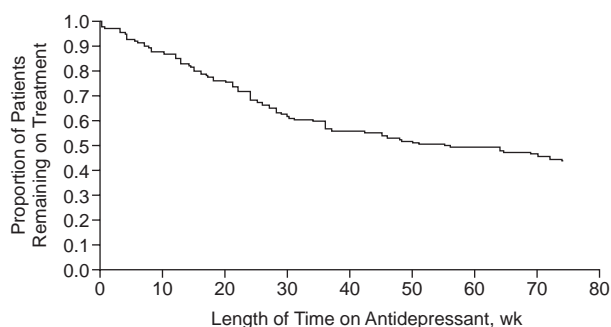
Abbreviations: MDD = major depressive disorder, MDE = major depressive episode, NS = nonsignificant.

Although the median time on antidepressant treatment was 55 weeks (95% CI = 34.7 to 75.3) (Figure 1), premature termination of treatment was common. In about half of the patients (86/174 [49%]), antidepressant treatment was terminated before completion of a continuation phase, or in the early maintenance phase for those with ≥ 3 lifetime episodes. One third of antidepressants were terminated in the acute phase (57/174 [33%]), i.e., while the patient was still in MDE or partial remission. About a quarter of the patients (49/174 [28%]) completed a continuation phase lasting at least 4 months. Only about a fifth (13/67 [19%]) of those with ≥ 3 lifetime episodes proceeded to a maintenance phase.

Predictors of Premature Termination

In stepwise backward LR analyses with premature termination of antidepressant treatment as a dependent variable, and factors significant in univariate analyses as independent variables, premature termination was significantly predicted by no earlier antidepressant treatment (OR = 2.1, 95% CI = 1.10 to 4.16, $p = .026$), and less severe depression (OR = 1.6, 95% CI = 1.00 to 1.13, $p = .049$). Premature termination also was associated with negative treatment attitudes during the follow-up: 86% (18/21) of the patients with negative attitudes at 6 months and 74% (20/27) at 18 months had premature termination of antidepressant treatment.

Figure 1. Probability of Remaining on Antidepressant Estimated by Survival Curve in the Vantaa Depression Study



Consequences of Premature Termination of Antidepressants

Patients whose antidepressant treatment was terminated during the MDE or partial remission achieved full remission more rarely (24/57 [42%] vs. 77/117 [66%], $\chi^2 = 8.85$, $df = 1$, $p = .003$), took longer to do so (mean \pm SD = 14.0 ± 5.6 vs. 9.7 ± 6.8 months, OR = 2.2, 95% CI = 1.37 to 3.44, $p = .001$), and spent less time without any depressive symptoms (median = 2.1 vs. 6.5 months, $z = -2.96$, $p = .003$). About a fifth (19/98 [19%]) of those who discontinued treatment had a new antidepressant trial during the follow-up, most of them for a recurrence (14/19 [74%] vs. 56/155 [36%], $\chi^2 = 9.93$, $df = 1$, $p = .002$).

Self-Reported Reasons for Terminating Antidepressants

The most frequent self-reported reason for discontinuing the first antidepressant trial among those who dropped out of antidepressant in the acute phase was “autonomous decision,” which was the main reason for terminating treatment in 40% (21/52, missing N = 5) of the patients. Other common self-reported reasons were side effects in 25% (13/52), poor response (11/52 [21%]), and subjective recovery (6/52 [12%]).

Self-Reported Antidepressant Adherence

Of 142 patients interviewed, 29 (20%) reported non-adherence at both follow-ups. The majority of patients (109/142 [77%]) reported taking antidepressants regularly when treatment was ongoing, about a tenth (16/142 [11%]) somewhat irregularly, and a similar proportion (17/142 [12%]) very irregularly or never.

In stepwise backward LR models adjusting for age, gender, and severity of MDD, having no avoidant personality (OR = 4.8, 95% CI = 1.33 to 17.48, $p = .017$), or no anxiety disorder (OR = 2.4, 95% CI = 1.01 to 5.71, $p = .047$) remained significant predictors for continued nonadherence. Two thirds (74/124 [60%]) of patients with no ongoing psychiatric treatment and almost all (68/74

[92%]) of those who had remained in treatment answered questions about adherence at 18 months.

Psychosocial Treatments

Most depressive patients were provided psychotherapeutic support in the acute phase, and those with poorer outcome, not unexpectedly, received it longer (Table 1). However, only two thirds (44/76 [58%]) of the patients without full remission remained in psychiatric care for 18 months, and a third of them (24/76 [32%]) were without any follow-up treatment at 18 months. Only 16% (31/198) of the patients received weekly psychotherapy during the follow-up. Most of the patients were already receiving psychosocial support at baseline, but weekly psychotherapy began about 3 months later (mean \pm SD = 2.9 ± 4.0 months) and lasted for about 1 year (mean \pm SD = 11.0 ± 6.0 months).

In stepwise backward LR analyses with receiving weekly psychotherapy as a dependent variable, and factors significant in univariate analyses as independent variables, the most significant predictors for having psychotherapy were fewer DSM-IV current comorbid psychiatric disorders (OR = 1.4, 95% CI = 1.02 to 1.82, $p = .034$), larger social network (OR = 1.1, 95% CI = 1.00 to 1.25, $p = .046$), and more severe suicidality (OR = 1.1, 95% CI = 1.02 to 1.14, $p = .004$).

Self-Reported Psychosocial Treatment Adherence

About two thirds (69/124 [56%]) of those without ongoing treatment and 92% of those (68/74) still in psychiatric care answered questions about adherence at 18 months. Nearly all who had received weekly psychotherapy (27/28 [96%]) reported attending sessions regularly. Most patients (82/109 [75%]) with psychotherapeutic support also reported attending sessions regularly, about one fifth (19/109 [17%]) somewhat irregularly, and 7% (8/109) very irregularly or never.

Attitudes Toward Antidepressant and Psychosocial Treatments

At baseline, the majority (223/262 [85%]) and two thirds (164/268 [61%]) of patients, respectively, had positive attitudes toward psychosocial and antidepressant treatments. Among study cohort patients, attitudes toward psychosocial treatments remained positive, and in most (56/68 [82%]) cases, negative attitudes toward antidepressants became positive during the follow-up. The factors explaining negative attitudes at baseline are shown in Table 3. Among those with reservations or negative attitudes about antidepressants, the most frequently reported reasons for these attitudes were fears of dependence and side effects, which were reported by nearly half of the patients (43% and 41%, respectively) at baseline. No belief that treatment will help (43%) and unwillingness to confide in a stranger (33%) were the most frequently reported

Table 3. Factors Associated With Negative Attitudes Toward Antidepressants (N = 97)^a and Psychosocial Treatment (N = 27)^b Among Vantaa Depression Study MDD Patients at Baseline^c

Factor	β	Wald χ^2	df	Odds Ratio	95% Confidence Interval	p
Negative attitudes toward antidepressants						
Younger age, y	-0.03	4.65	1	1.03	1.00 to 1.05	.031
Lower score on Beck Anxiety Inventory	-0.04	5.55	1	1.04	1.01 to 1.07	.019
Lower score on HAM-D	-0.76	8.88	1	1.08	1.03 to 1.14	.003
Longer duration of MDE prior to entry, mo	0.05	3.85	1	1.05	1.00 to 1.10	.050
No current comorbid alcohol use disorder	0.69	3.86	1	2.00	1.00 to 3.99	.050
Negative attitudes toward psychosocial treatment						
Male gender	1.45	11.50	1	4.25	1.84 to 9.80	.001
Dysthymia	-1.17	5.59	1	3.22	1.22 to 8.48	.018

^aData missing for 0.5% of patients, N = 268.^bData missing for 3% of patients, N = 262.^cTwo stepwise backward logistic regression models with negative attitudes (negative or very negative) toward antidepressant and psychosocial treatment as dependent variables and univariately significant factors, as well as age and gender, as independent variables.

Abbreviations: HAM-D = Hamilton Rating Scale for Depression, MDD = major depressive disorder, MDE = major depressive episode.

reasons for negative attitudes toward psychotherapeutic treatments. Patients with negative attitudes about antidepressants at entry tended to terminate medications in the acute phase more often than patients with positive or neutral attitudes (22/51 [43%] vs. 34/119 [29%], $df = 1$, $\chi^2 = 3.43$, $p = .064$). Those with negative attitudes to antidepressants or psychosocial treatments at 18 months also reported nonadherence to them more often than patients with positive or neutral attitudes (19/24 [79%] vs. 26/130 [20%], $\chi^2 = 34.29$, $df = 1$, $p < .001$, and 6/8 [75%] vs. 33/140 [24%], $\chi^2 = 10.31$, $df = 1$, $p = .001$), respectively).

DISCUSSION

We found most depressive patients in psychiatric care to be receiving adequate antidepressant and psychotherapeutic treatments in the early acute phase and to have favorable attitudes toward them. Over time, however, antidepressants were terminated too early in about half of the patients, often following their autonomous decisions. However, as long as pharmacologic and psychosocial treatments were ongoing, the majority of patients perceived themselves as adherent to them. Negative treatment attitudes at baseline were more common toward antidepressants than psychosocial treatments and tended to predict premature termination.

This study involved a relatively large cohort (N = 269) of both outpatients and inpatients with MDD, effectively representing psychiatric patients with a new episode of MDD in a Finnish city. On the basis of an epidemiological survey, we have estimated that two thirds of all depressed subjects in the general population of Vantaa seeking psychiatric treatment are treated in the PMCD.¹² Patients were carefully diagnosed using structured interviews with excellent reliability (kappa 0.86) for the diagnosis of MDD.²⁴ Other methodological issues are discussed in earlier reports.^{24,25} The VDS took place during the era of modern antidepressants in 1997 to 1999 in a community psychiatric setting. Before our study in late 1996, a re-

gional practice guideline for the treatment of MDD was implemented, and education was provided to all mental health professionals in the PMCD. In the regional practice guideline, and in our study protocol, it was recommended that suicidal patients should receive weekly follow-ups until they were not suicidal. It is probable that education and these recommendations, as well as the follow-up study per se, influenced treatments, and patients in our study cohort did receive somewhat more intensive treatment than usual. However, visits to psychiatrists (mean = 4), and augmentation medication were as rare as reported earlier in our record-based study on the PMCD, and also replicated was the finding of more inadequate use of TCAs.¹² Continuity of psychosocial and antidepressant treatment was assessed by investigating all clinical information, including medical and psychiatric records, and interviewing patients at the follow-ups, interviewers thus being aware of patient treatment status. The study dropouts (23%) are likely to have somewhat biased our findings toward better adherence to treatments. The PMCD provides psychiatric outpatient services free of charge, and the National Insurance Institution reimburses about 50% of antidepressant costs for depression. The generalizability of our findings to psychiatric care systems with different organization and funding is unknown. Our finding that patients without full remission had more intensive treatment as measured by frequency of psychotherapeutic sessions, visits to psychiatrists, and duration of treatment is a well-known tendency in naturalistic studies,³⁵ and suggests that poor outcome does not predominantly reflect inferior treatment.

In contrast to generally adequate treatment in the early acute phase, continuity of antidepressant treatment was far less complete in the later acute, continuation, and maintenance phases. About half (49%) of the patients terminated antidepressant treatment prematurely, and only about a quarter (28%) completed a continuation phase of at least 4 months. Patients with less severe depression and without previous antidepressant treatment terminated medication prematurely more often. Those who did so while still in the

acute phase achieved full remission significantly less often (42% vs. 66%) and in a longer time than other patients. Premature termination of antidepressants was predicted by negative attitudes. Underlying these attitudes were most frequently fears of dependence (43%) or side effects (41%). Many depression patients also reported having taken an active, autonomous role in the decision to terminate antidepressants. "Patient's autonomous decision" was a more common reason than all perceived side effects of antidepressants, poor response, or subjectively perceived recovery. So, it seems that premature termination of antidepressants not only associates with patients' negative attitudes, fears of addiction, and side effects, but also reflects their demands or willingness to cope alone without medicine. Patients may deny need for treatment and fear facing their illness as a chronic condition. Antidepressants might also be seen as an unnatural way to recover. These results among depression patients accord with findings in the population of the U.K. Defeat Depression campaign,³⁶ as well as with other recent studies, which reported factors such as stigma, health beliefs, and negative attitudes to be an important risk factors for nonadherence.^{8,10,17,19-23} Providing information on antidepressants, not only their side effects but also their nonaddictiveness during treatment, might prove an effective way to improve continuity of treatments and outcome of depression. Antidepressants with fewer side effects, however otherwise desirable, are unlikely alone to solve the problem of continuity, as side effects appear less important as causes of premature termination.

Continuity of psychotherapeutic treatments was associated with severity and more prolonged depressive symptoms. Noteworthy, however, was the finding that about one third (32%) of the patients not achieving full remission during the follow-up were without any psychosocial treatment at 18 months. Less than a fifth (16%) of the patients received weekly psychotherapy, which was somewhat surprising because about one third (34%) of the attending professionals in the PMCD were qualified and certified therapists in specific psychotherapy, and the mean number of sessions was high enough for brief psychotherapy. The patients who received psychotherapy were either those able to form a good treatment alliance and thus probably more able to benefit from therapy, or suicidal patients who needed more intensive treatment in the acute phase. Despite recommendations in practice guidelines^{4,5} for more intensive treatment, patients with personality disorders were most unlikely to receive weekly psychotherapy.

Negative treatment attitudes at baseline were more common toward antidepressants than psychotherapeutic treatments, but in most cases (82%), these attitudes became positive during the treatment. This change in attitude emphasizes the importance of motivating patients to at least try antidepressants. It also seems important to

ask about patients' treatment attitudes in order to recognize depressive patients at risk for nonadherence. Against our hypothesis, MDD patients with negative attitudes were not those with comorbid personality and alcohol use disorder. On the contrary, patients with alcohol use disorders had more positive attitudes about antidepressants. We also found that men and MDD patients with dysthymia (double depression) needed more encouragement before accepting psychotherapeutic treatments. The main reasons given for negative attitudes about psychosocial treatments were unwillingness to confide in a stranger and patients believing they would not be helped by the treatment. Younger age, less severe and longer-lasting depression, and milder anxiety symptoms also were associated with negative treatment attitudes.

Nonadherence is rarely an "on-off" phenomenon. Treatments may occur more or less irregularly, and it may be unclear whether this significantly affects achieving treatment goals or not. In contrast to our hypotheses, those with continued self-reported nonadherence to antidepressants were more often those without comorbidity, especially those without anxiety and avoidant personality disorders. It seems that presence of perceived distress is another major factor that motivates continuing in treatment. Nevertheless, both professionals and patients face difficulties in complying with treatment guidelines, and the treatment eventually provided is the result of their interaction and compromises.

Overall, our main finding is that problems of psychiatric care in MDD are mostly related to continuity of treatment. While adequate treatments are provided in the early acute phase, over time, in about half of the patients antidepressants are terminated too early, often because of the patients' autonomous decisions. From a secondary and tertiary preventive point of view, improving continuity of treatment appears a crucial task in improving the outcome of psychiatric patients with MDD.

Drug names: buspirone (BuSpar and others), lithium (Eskalith, Lithobid, and others).

REFERENCES

1. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder [Revision]. *Am J Psychiatry* 2000;157(suppl 4):1-45
2. Bauer M, Whybrow PC, Angst J, et al. WFSBP Task Force on Treatment Guidelines for Unipolar Depressive Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of unipolar depressive disorders, pt 1: acute and continuation treatment of major depressive disorder. *World J Biol Psychiatry* 2002; 3:5-43
3. Anderson IM, Nutt DJ, Deakin JFW, on behalf of the British Association for Psychopharmacology. Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 1993 British Association for Psychopharmacology guidelines. *J Psychopharmacol* 2000;14:3-20
4. Schulberg HC, Katon W, Simon GE, et al. Treating major depression in primary care practice: an update of the Agency for Health Care Policy and Research Practice Guidelines. *Arch Gen Psychiatry*

- 1998;55:1121–1127
5. Isometsä E, Lindfors O, Pirkola S, et al. The National Finnish Current Care Guidelines for the Treatment of Depression: an overview. *Psychiatria Fennica* 2003;34:181–196
6. Katon W, Von Korff M, Lin E, et al. Collaborative management to achieve treatment guidelines: impact on depression in primary care. *JAMA* 1995;273:1026–1031
7. Lin EH, Katon WJ, Simon GE, et al. Low-intensity treatment of depression in primary care: is it problematic? *Gen Hosp Psychiatry* 2000;22:78–83
8. Demyttenaere K, Enzlin P, Dewe W, et al. Compliance with antidepressants in a primary care setting, 1: beyond lack of efficacy and adverse events. *J Clin Psychiatry* 2001;62(suppl 22):30–33
9. Von Korff M, Katon W, Unutzer J, et al. Improving depression care: barriers, solutions, and research needs. *J Fam Pract* 2001;50:E1
10. Melfi CA, Chawla AJ, Croghan TW, et al. The effects of adherence to antidepressant treatment guidelines on relapse and recurrence of depression. *Arch Gen Psychiatry* 1998;55:1128–1132
11. Claxton AJ, Li Z, McKendrick J. Selective serotonin reuptake inhibitor treatment in the UK: risk of relapse or recurrence of depression. *Br J Psychiatry* 2000;177:163–168
12. Rysälä HJ, Melartin TK, Leskelä US, et al. A record-based analysis of 803 patients treated for depression in psychiatric care. *J Clin Psychiatry* 2001;62:701–706
13. Simon GE, Von Korff M, Rutter CM, et al. Treatment process and outcomes for managed care patients receiving new antidepressant prescriptions from psychiatrists and primary care physicians. *Arch Gen Psychiatry* 2001;58:395–401
14. Cuffel BJ, Azocar F, Tomlin M, et al. Remission, residual symptoms, and nonresponse in the usual treatment of major depression in managed clinical practice. *J Clin Psychiatry* 2003;64:397–402
15. Sirey JA, Myers BS, Bruce ML, et al. Predictors of antidepressant prescription and early use among depressed outpatients. *Am J Psychiatry* 1999;156:690–696
16. Kennedy N, Abbot R, Paykel ES. Remission and recurrence of depression in the maintenance era: long-term outcome of a Cambridge cohort. *Psychol Med* 2003;33:827–838
17. Lingam R, Scott J. Treatment non-adherence in affective disorders. *Acta Psychiatr Scand* 2002;105:164–172
18. Pampallona S, Bollini P, Tibaldi G, et al. Patient adherence in the treatment of depression. *Br J Psychiatry* 2002;180:104–109
19. Demyttenaere K. Risk factors and predictors of compliance in depression. *Eur Neuropsychopharmacol* 2003;13:S69–S75
20. Lin EHB, Von Korff M, Ludman EJ, et al. Enhancing adherence to prevent depression relapse in primary care. *Gen Hosp Psychiatry* 2003;25:303–310
21. Sirey JA, Bruce ML, Alexopoulos GS, et al. Perceived stigma as a predictor of treatment discontinuation in young and older outpatients with depression. *Am J Psychiatry* 2001;158:479–481
22. Demyttenaere K, Haddad P. Compliance with antidepressant therapy and antidepressant discontinuation symptoms. *Acta Psychiatr Scand* 2000;101(suppl 403):50–56
23. Keller MB, Hirschfeld RMA, Demyttenaere K, et al. Optimizing outcomes in depression: focus on antidepressant compliance. *Int Clin Psychopharmacol* 2002;17:265–271
24. Melartin TK, Rysälä HJ, Leskelä US, et al. Current comorbidity of psychiatric disorders among DSM-IV major depressive disorder patients in psychiatric care in the Vantaa Depression Study. *J Clin Psychiatry* 2002;63:126–134
25. Melartin TK, Rysälä HJ, Leskelä US, et al. Severity and comorbidity predict episode duration and recurrence of DSM-IV major depressive disorder. *J Clin Psychiatry* 2004;65:810–819
26. Wing JK, Babor T, Brugha T, et al. SCAN: Schedules for Clinical Assessment in Neuropsychiatry. *Arch Gen Psychiatry* 1990;47:589–593
27. Spitzer RL, Williams JBW, Gibbon M, et al. Instruction Manual for the Structured Clinical Interview for DSM-III-R (SCID, 5/1/89 Revision). New York, NY: Biometrics Research; 1989
28. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56–62
29. Beck AT, Kovacs M, Weissman A. Assessment of suicidal intention: the Scale for Suicide Ideation. *J Consult Clin Psychol* 1979;47:343–352
30. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–571
31. Beck AT, Brown G, Epstein N, et al. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol* 1988;56:893–897
32. Brugha TS, Sturt E, MacCarthy B, et al. The Interview Measure of Social Relationships: the description and evaluation of a survey instrument for assessing personal social resources. *Soc Psychiatry* 1987;22:123–128
33. Cox DR. Regression models and life-tables (with discussion). *J R Stat Soc B* 1972;34:541–554
34. Statistical Package for the Social Sciences for Windows [computer program]. Release 11.0.1. Chicago, Ill: SPSS Inc; 1989–2001
35. Sturm R. Instrumental variable methods for effectiveness research. *Int J Methods Psychiatr Res* 1999;7:17–26
36. Paykel ES, Hart D, Priest R. Changes in public attitudes to depression during the Defeat Depression Campaign. *Br J Psychiatry* 1998;173:519–522