Medication and Psychotherapy in the Treatment of Bulimia Nervosa

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Objective: Two treatments for bulimia nervosa have emerged as having established efficacy: cognitive-behavioral therapy and antidepressant medication. This study sought to address 1) how the efficacy of a psychodynamically oriented supportive psychotherapy compared to that of cognitive-behavioral therapy; 2) whether a two-stage medication intervention, in which a second antidepressant (fluoxetine) was employed if the first (desipramine) was either ineffective or poorly tolerated, added to the benefit of psychological treatment; and 3) if the combination of medication and psychological treatment was superior to a course of medication alone. Method: A total of 120 women with bulimia nervosa participated in a randomized, placebo-controlled trial. Results: Cognitive-behavioral therapy was superior to supportive psychotherapy in reducing behavioral symptoms of bulimia nervosa (binge eating and vomiting). Patients receiving medication in combination with psychological treatment experienced greater improvement in binge eating and depression than did patients receiving placebo and psychological treatment. In addition, cognitive-behavioral therapy plus medication was superior to medication alone, but supportive psychotherapy plus medication was not. Conclusions: At present, cognitive-behavioral therapy is the psychological treatment of choice for bulimia nervosa. A two-stage medication intervention using fluoxetine adds modestly to the benefit of psychological treatment.

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When bulimia nervosa was first identified, it was viewed as "extremely difficult to treat" (1). Since that time, a variety of treatment approaches have been explored, and two interventions have emerged as having established efficacy. One is cognitive-behavioral therapy, which was originally developed by Fairburn (2). The outcome of patients treated with cognitive-behavioral therapy has been clearly shown to be superior to that of patients assigned to a waiting list or a delayed treatment condition, and it appears that the benefits of cognitive-behavioral therapy are often well maintained at follow-up (3). Cognitive-behavioral therapy has been shown to be superior to alternative forms of psychological treatment in some but not all controlled trials (4–7).

The other major intervention currently employed in the treatment of bulimia nervosa is antidepressant medication. Since 1979, over 15 placebo-controlled studies have documented that the short-term outcome of patients receiving antidepressant medication is superior to that of patients receiving placebo (8). However, the utility of antidepressants as the sole treatment for bulimia nervosa has been questioned because of the frequency of side effects of some agents and concerns about long-term outcome (9, 10).

Not surprisingly, the emergence of cognitive-behavioral therapy and of antidepressant medication as leading treatments for bulimia nervosa has raised questions about their comparative efficacy and about the advantages of combining them. The results of some studies examining these issues indicate that cognitive-behavioral therapy alone is generally superior to a trial of a single antidepressant agent and suggest that there may be some advantage to combining cognitive-behavioral therapy with antidepressant

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TABLE 1. Design of Study of Medication and Psychotherapy in the Treatment of Bulimia Nervosa

	Psychological Treatment		
Medication	Cognitive-Behavioral Therapy	Supportive Psychotherapy	None
Placebo	Cognitive-Behavioral Therapy + Placebo	Supportive Psychotherapy + Placebo	
Medication	Cognitive-Behavioral Therapy + Medication	Supportive Psychotherapy + Medication	Medication

medication (9, 11–13). However, several important clinical questions were not completely resolved by the available data. One is how the efficacy of more traditional, psychodynamically oriented, supportive psychotherapy compares to that of cognitive-behavioral therapy. Second, does a more sophisticated two-stage medication intervention, in which a second antidepressant is employed if the first is either ineffective or poorly tolerated, add to the benefits of psychological treatment? And third, is the combination of psychotherapy and medication superior to a course of medication alone? This article describes the short-term results of a randomized, placebo-controlled study of 120 women with bulimia nervosa that was designed to address these questions.

METHOD

Patient Selection

To participate in this study, patients were required to meet DSM-III-R criteria for bulimia nervosa for at least 1 year. Only patients who used self-induced vomiting as a primary method of compensating for binge eating were included. Patients were also required to be women between the ages of 18 and 45 years whose weights were between 80% and 120% of ideal. Patients were excluded if they were medically ill, had evidence of cardiac conduction disease, were pregnant, had abused drugs or alcohol within the past year, were judged to be acutely suicidal, or had previously had an adverse reaction to either desipramine or fluoxetine.

Patients were recruited through advertisements in local media. Individuals who seemed eligible for the study on the basis of a telephone screening were invited to an evaluation appointment, in which a research assistant assessed the eating disorder through use of the Eating Disorder Examination (14) and other axis I psychiatric disorders through use of the Structured Clinical Interview for DSM-III-R (15). Candidates who appeared to meet the entry criteria returned 1 week later to meet with a psychiatrist who confirmed the diagnoses, obtained a medical history, and conducted a physical examination. A complete blood count, serum chemistries, and an ECG were also obtained. After providing written informed consent, eligible patients entered a single-blind placebo washout phase lasting 7–10 days. Following this phase, individuals who continued to meet the study entry criteria were randomly assigned to one of five treatment groups (table 1).

A total of 209 patients were seen for the initial evaluation; 149 returned for the second assessment. One hundred twenty individuals were eventually randomly assigned to treatment. The most common reason for attrition during the evaluation phase was failure to return for the subsequent appointment; other reasons included failure to meet diagnostic criteria for bulimia nervosa and improvement during the single-blind placebo washout. This study was reviewed and approved by the New York State Psychiatric Institute/Columbia University Institutional Review Board.

Treatment

In four of the five treatment groups, patients received a psychological treatment (cognitive-behavioral therapy or supportive psychotherapy). Approximately half of the patients receiving psychological treatment were assigned to medication and half to placebo; in these four groups, medication assignment was unknown to both patients and staff (double-blind). Patients assigned to the fifth group received medication but no formal psychological treatment and were informed that they were receiving medication. Thus, the study included a 2×2 factorial design to compare cognitive-behavioral therapy with supportive psychotherapy and to examine the benefit of medication versus placebo among patients receiving psychological treatment. In addition, by comparing the outcome of patients receiving medication only to that of patients receiving cognitive-behavioral therapy or supportive psychotherapy and medication, we planned to determine the benefit of adding each of these forms of psychological treatment to a course of medication.

TABLE 2. Data on Characteristics of Patients With Bulimia Nervosa at Time of Evaluation and on Treatment Received

	Cognitive-Behavioral Therapy						Supportive Psychotherapy					
Variable	+ Medication (N=23)			+ Placebo (N=25)			+ Medication (N=22)			+ Placebo (N=22)		
	Mean	*SD*	*Range*	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*
Age (years)	26.1	5.7	19–38	25.8	4.4	18–38	28.0	5.3	18–39	26.9	4.3	21–37
Duration of bulimia nervosa (years)	7.26	5.8	1–20	8.00	4.0	1–16	9.55	5.3	1–20	7.55	3.7	1–18
Body mass index (kg/m^2)	21.6	2.2	18.5–27.5	22.1	2.1	17.5–26.7	21.7	2.3	17.8–26.2	21.7	2.2	18.5–26.5
Number of treatment sessions	16.8	5.2	1–20	16.5	5.0	4–20	17.8	4.3	7–20	17.7	4.6	4–20
Duration of treatment (weeks)	17.6	6.9	0–26.7	16.2	6.6	1.3–27.3	16.9	5.7	4.3–27.0	17.4	5.6	3.3–25.0
	N	*%*		*N*	*%*		*N*	*%*		*N*	*%*	
Current major depression	4	17		6	24		5	23		2	9	
Past anorexia nervosa	4	17		9	36		7	32		6	27	
Premature termination	8	35		9	36		6	27		6	27	
Received second medication	12	52		11	44		18	82		14	64	

Cognitive-behavioral therapy. This treatment was based on a manual (G.T. Wilson, 1989) derived from the treatment approach of Fairburn et al. (4). Stage 1 (sessions 1–8) consists of the following components: an overview and explanation of the philosophy and goals of the treatment program; the use of daily self-monitoring homework to identify high-risk situations that trigger binge eating and purging; introduction of cognitive restructuring strategies in which patients learn to identify and challenge dysfunctional cognitions related to their disorder; instruction and guidance in learning to normalize eating patterns (e.g., eat three meals a day); and an emphasis on alternative, more constructive strategies for coping with high-risk situations for binge eating. Patients are given information about weight regulation and about how dieting is linked to the development and maintenance of binge eating. Stage 2 (sessions 9–16) emphasizes problem-solving strategies for coping with high-risk situations for binge eating and purging. Cognitive restructuring is focused on specific concerns about body weight and shape. Flexible eating habits are emphasized, and patients are helped to incorporate previously avoided foods into their diet. Stage 3 (sessions 17–20) continues to emphasize the strategies acquired in stage 2. The major focus of treatment is on the maintenance of improvement and on relapse prevention.

Supportive psychotherapy. This treatment was a manual-based, modified version of the short-term psychotherapy used in the Fairburn et al. study (4). Our treatment differed from that of Fairburn et al. in at least two important respects: 1) we eliminated elements that overlap with the putative active therapeutic ingredients of cognitive-behavioral therapy, such as patient self-monitoring of eating and the conditions that trigger binge eating, as well as instruction and implicit advice on necessary changes in diet and eating patterns; and 2) supportive psychotherapy was less directive and focal in nature. In stage 1 (sessions 1–8), therapists obtained a comprehensive description of the eating problem and its development, as well as a detailed personal and family history, and helped patients identify underlying problems that might be responsible for the eating disorder. Stage 2 (sessions 9–16) had the following aims: to encourage patients to explore underlying emotional problems, to facilitate self-disclosure and expression of feelings, and to foster independence and raise the issue of termination of treatment. Stage 3 (sessions 17–20) continued the exploration of underlying issues and how they might affect future adjustment. Termination of therapy was also addressed.

Supportive psychotherapy in the present study was designed to control for nonspecific therapeutic influences inherent in cognitive-behavioral therapy. In contrast to cognitive-behavioral therapy, supportive psychotherapy was nondirective and emphasized patient self-exploration and understanding. It was intended to represent the type of treatment that outpatients might typically receive from psychodynamically oriented psychotherapists providing short-term supportive therapy.

Therapist background and orientation. Cognitive-behavioral therapy and supportive psychotherapy were provided by three therapists (one psychiatrist, one doctoral-level psychologist, and one master's-level psychologist obtaining a doctoral degree). Each therapist provided both cognitive-behavioral therapy and supportive psychotherapy. All three therapists considered themselves eclectic in orientation and were trained to implement the manual-based treatments employed in this study. Therapists received biweekly group supervision in cognitive-behavioral therapy and supportive psychotherapy that was provided, respectively, by an expert in cognitive-behavioral therapy for eating disorders (G.T.W.) and by a psychoanalyst with extensive experience in the treatment of patients with eating disorders (S.P.R.).

Medication. Patients randomly assigned to receive medication first received desipramine for 8 weeks. If binge frequency had not declined by at least 75% or if intolerable side effects occurred, the desipramine was tapered and discontinued over the succeeding 2 weeks, and patients then received fluoxetine. Patients randomly assigned to placebo first received desipramine placebo and, following the same criteria, were then given fluoxetine placebo.

Patients met weekly with a psychiatrist. During these brief visits, the psychiatrist collected binge/purge diaries and assessed medication response and side effects. The psychiatrist inquired briefly about developments since the previous session, provided basic education concerning medical aspects of eating disorders, and supported whatever attempts the patient was making to improve without specifically endorsing any particular approach.

During the first week after randomization, the dose of desipramine was raised to 200 mg/day, and, if tolerated, this dose was continued for the next 3 weeks. The dose could then be raised to 300 mg/day if improvement was not satisfactory. Fluoxetine was initiated at 60 mg/day. The dose of medication could be lowered to minimize side effects.

Assessment

Throughout the study, patients were asked to record the number of daily binge eating and vomiting episodes in a diary, which was collected by the psychiatrist weekly. Patients were asked to complete the following self-report questionnaires during the initiation phase, at specified intervals during the study, and at termination: the Body Shape Questionnaire (16), the Eating Attitudes Test (17), the Beck Depression Inventory (18), the SCL-90 (19), the Three-Factor Eating Questionnaire (20), and a visual analogue scale to rate the treatment's logic and relevance. At termination of treatment, the patient's status was assessed by an interviewer who was unaware of the patient's treatment assignment, through use of the Eating Disorders Examination. All treatment sessions were audiotaped, and randomly selected tapes were rated by an advanced doctoral candidate in clinical psychology.

Statistical Analysis

Data from all 120 patients randomized were included in the analyses. Response to treatment was evaluated by using termination data; for patients who discontinued treatment prematurely, data from the last visit were carried forward, with the exception of one patient who attended only the first session. For continuous variables, the difference between post- and pretreatment levels was calculated and used as the dependent variable. Logarithmic transformations were used to reduce excessive skewness in the following variables: binge and vomiting frequencies; Beck inventory; Eating Disorders Examination eating concern subscale; SCL-90 obsessive-compulsive, interpersonal sensitivity, anxiety, anger-hostility, and paranoid ideation subscales; and the body mass index. Effects of treatments were estimated by using analysis of variance (ANOVA) for continuous variables and logistic regression for categorical variables. Odds ratio values were tested with likelihood chi-square tests, with 1 degree of freedom. Other comparisons were analyzed by using ANOVA or the chi-square statistic.

The primary outcome measures were the frequencies of binge eating and of vomiting recorded in patient diaries at the end of treatment. Data from other, secondary measures are presented to provide a more complete description of patient outcome; except when noted, significance levels are reported without correction for multiple comparisons, and, because of the number of secondary measures examined, these results should be interpreted with caution.

Medication Only (N=28)			Combined (N=120)		
Mean	*SD*	*Range*	*Mean*	*SD*	*Range*
24.3	4.5	19–39	26.1	4.9	18–39
7.36	4.3	1–18	7.91	4.7	1–20
22.3	2.1	18.4–26.5	21.9	2.2	17.5–27.5
11.5	4.5	3–16	15.8	5.3	1–20
12.5	5.6	2.0–23.0	16.0	6.3	0–27.3

N	%	*N*	%
8	29	25	21
9	32	35	29
12	43	41	34
19	68	74	62

TABLE 3. Pre- and Posttreatment Measures for Patients With Bulimia Nervosa

	Cognitive-Behavioral Therapy								Supportive Psychotherapy							
	+ Medication (N=23)				+ Placebo (N=25)				+ Medication (N=22)				+ Placebo (N=22)			
	Pre		Post		Pre		Post		Pre		Post		Pre		Post	
Measure	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Binges per week (diary)	7.29	4.8	0.95[a]	1.6	7.22	4.0	2.56[a]	3.3	7.92	5.6	3.57[a]	3.1	6.18	3.6	3.32[a]	4.0
Vomiting episodes per week (diary)	10.8	13	1.1[a]	2	10.8	12	5.6[a]	15	10.6	9	5.5[a]	5	11.9	13	7.5[a]	10
Body Shape Questionnaire	137	29	87[a]	36	132	32	94[a]	36	132	30	94[a]	35	127	31	104[a]	39
Eating Attitudes Test	45.0	13	19.1[a]	12	42.3	16	24.5[a]	17	45.8	16	28.1[a]	13	39.9	16	28.7[a]	23
Beck Depression Inventory	10.9	6	4.4[a]	5	11.7	10	6.8[a]	7	15.9	12	6.7[a]	7	14.3	9	10.2[a]	11
Eating Disorder Examination																
Binges per month	28.8	23	2.5[a]	5	28.1	22	6.6[a]	14	33.4	21	13.2[a]	15	21.8	12	10.6[a]	18
Vomiting episodes per month	38.7	27	3.4[a]	6	45.9	69	7.6[a]	17	39.3	29	16.8[a]	16	41.6	48	25.4[a]	43
Importance of shape and weight	8.43	2.4	7.11	3.2	8.56	2.9	6.81[a]	3.6	9.45	2.5	6.25[a]	3.3	8.95	2.5	7.71	3.2
Shape concern subscale	3.74	1.2	2.18	1.4	3.59	1.3	2.27	1.3	3.78	1.4	2.47	1.5	3.52	1.2	2.52	1.5
Weight concern subscale	3.53	1.1	2.06	1.4	3.47	1.4	1.99	1.4	3.69	1.5	1.98	1.5	3.36	1.2	2.38	1.7
Restraint subscale	3.21	1.2	1.15[a]	1.2	3.13	1.2	1.43[a]	1.4	3.28	1.3	2.06[a]	1.6	2.93	1.5	1.68[a]	1.6
Overeating subscale	3.26	0.5	1.37	1.1	3.18	0.6	1.73	1.3	3.32	0.7	2.17	1.3	2.99	0.6	1.91	1.2
Eating concern subscale	2.45	1.6	0.84[a]	1.0	2.36	1.4	0.77[a]	0.9	2.49	1.3	1.36[a]	1.6	2.31	1.3	1.32[a]	1.4
Global score	3.23	0.7	1.52[a]	0.9	3.15	0.7	1.65[a]	0.9	3.31	0.9	2.01[a]	1.1	3.02	0.7	1.96[a]	1.2
Three-Factor Eating Questionnaire																
Restraint	13.3	3.6	11.0[a]	4.3	13.7	4.1	13.6	4.5	13.0	4.0	12.8	4.9	12.4	3.5	11.8	3.9
Disinhibition	13.3	2.1	7.3[a]	4.8	13.5	1.6	10.2[a]	4.8	13.1	1.9	9.5[a]	4.5	12.0	2.5	9.6[a]	3.5
Hunger	8.26	2.9	5.05[a]	3.1	9.60	3.1	7.09[a]	3.4	8.59	3.4	6.00[a]	3.8	7.00	3.8	6.53	4.5
SCL-90																
Global symptom index	1.83	0.6	1.39[a]	0.4	1.69	0.5	1.47[a]	0.5	1.88	0.6	1.51[a]	0.5	1.66	0.3	1.51	0.5
Depression	2.16	0.8	1.47[a]	0.5	2.01	0.8	1.74	0.7	2.38	0.9	1.75[a]	0.7	2.07	0.6	1.83	0.8
Somaticism	1.72	0.8	1.37[a]	0.5	1.46	0.4	1.27	0.4	1.49	0.5	1.27[a]	0.3	1.33	0.4	1.28	0.4
Obsessive-compulsive	1.90	0.7	1.45[a]	0.5	1.83	0.7	1.59[a]	0.6	2.01	0.8	1.61[a]	0.6	1.67	0.5	1.52	0.6
Interpersonal sensitivity	2.09	0.8	1.58[a]	0.6	1.97	0.8	1.75	0.8	2.31	1.0	1.83[a]	0.8	1.92	0.5	1.75[a]	0.7
Anxiety	1.83	0.7	1.31[a]	0.4	1.57	0.6	1.37	0.5	1.66	0.6	1.37[a]	0.5	1.56	0.5	1.41	0.5
Anger-hostility	1.83	0.9	1.37[a]	0.5	1.46	0.4	1.39	0.5	1.63	0.8	1.36[a]	0.6	1.65	0.5	1.47[a]	0.7
Phobic anxiety	1.35	0.5	1.17	0.3	1.27	0.3	1.22	0.3	1.27	0.4	1.13	0.2	1.20	0.2	1.29	0.4
Paranoid ideation	1.65	0.7	1.34[a]	0.5	1.56	0.7	1.36	0.5	1.90	0.9	1.54[a]	0.7	1.60	0.5	1.65	0.5
Psychosis	1.56	0.5	1.26[a]	0.3	1.46	0.5	1.31	0.4	1.73	0.7	1.29[a]	0.4	1.51	0.3	1.31[a]	0.3
Weight (lb.)	126	15	125	15	130	11	133[a]	11	133	17	131[a]	18	130	15	133	13
Body mass index (kg/m^2)	21.6	2.2	21.5	2.1	22.1	2.1	22.6[a]	2.3	21.7	2.3	21.2[a]	2.5	21.7	2.2	22.1	2.2

[a]Significant difference between pre- and posttreatment ($p<0.05$, ANOVA).

RESULTS

Pretreatment Characteristics

The clinical characteristics of the patients treated in this study are presented in tables 2 and 3. On average, patients were 26.1 years old, were of normal body weight (mean body mass index=21.9 kg/m^2), and had had bulimia nervosa for 7.91 years. Of the 120 patients, 100 (83%) were white, seven (6%) were black, seven (6%) were Hispanic, and six (5%) were Asian. Twenty-one percent were currently in an episode of major depression, and 29% had a history of anorexia nervosa. Twenty-one patients (18%) had previously taken fluoxetine, and four (3%) had previously taken desipramine. The five treatment groups did not differ significantly on any of these characteristics.

Description of Treatments

Both cognitive-behavioral therapy and supportive psychotherapy were designed to be administered in 20 sessions over 16 weeks; the average number of psychotherapy visits attended was 17.2 (SD=4.8) over an average of 17.0 weeks (SD=6.2). Neither the number of visits nor the duration of treatment differed between the two forms of psychological treatment. Patients assigned to receive only medication were expected to attend a total of 16 sessions over 16 weeks; the average number of visits attended was 11.5 (SD=4.5) over 12.5 weeks (SD=5.6). Both the number of visits and the duration of treatment for patients assigned to medication only were significantly less than those for patients receiving psychological treatment (number of visits: $F=30.9$, $df=1, 118$, $p=0.0001$; duration: $F=11.8$, $df=1, 118$, $p=0.0008$). This reflects the planned length of the treatments, the slightly higher rate of dropout in the medication only condition, and the fact that for patients receiving medication only, premature discontinuation of medication because of side effects shortened the overall length of treatment. For patients who were also receiving psychological treatment, the full course of cognitive-behavioral therapy or supportive psychotherapy was offered regardless of changes in medication status.

Medication Only (N=28)				Combined (N=120)				ANOVA											
								Cognitive-Behavioral Therapy Versus Supportive Psychotherapy			Medication Versus Placebo			Cognitive-Behavioral Therapy + Medication Versus Medication Only			Supportive Psychotherapy + Medication Versus Medication Only		
Pre		Post		Pre		Post													
Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	df	p	F	df	p	F	df	p	F	df	p
8.32	7.5	2.59[a]	3.5	7.43	5.3	2.60[a]	3.3	12.98	1, 87	0.0005	3.97	1, 87	0.05	4.26	1, 48	0.04	—	—	n.s.
10.5	11	3.7[a]	5	10.9	11	4.7[a]	9	15.12	1, 87	0.0002	3.48	1, 87	0.07	6.47	1, 48	0.01	—	—	n.s.
135	38	106[a]	47	133	32	97[a]	39	3.71	1, 78	0.06	3.71	1, 78	0.06	4.15	1, 44	0.05	—	—	n.s.
40.9	20	27.8[a]	21	42.7	17	25.6[a]	18	8.09	1, 78	0.005	6.30	1, 78	0.01	6.97	1, 44	0.01	—	—	n.s.
14.5	8	8.2[a]	9	13.4	9	7.3[a]	8	—	—	n.s.	4.36	1, 79	0.04	—	—	n.s.	—	—	n.s.
36.8	35	6.1[a]	14	30.1	24	7.7[a]	14	11.86	1, 64	0.001	—	—	n.s.	—	—	n.s.	5.50	1, 35	0.03
45.4	38	8.9[a]	13	42.4	45	12.3[a]	23	22.79	1, 64	0.0001	—	—	n.s.	4.41	1, 36	0.04	5.32	1, 35	0.03
9.55	2.2	8.45	2.7	9.00	2.5	7.32[a]	3.2	—	—	n.s.	3.13	1, 62	0.08	—	—	n.s.	7.53	1, 33	0.01
3.99	1.3	2.80	1.4	3.73	1.3	2.46[a]	1.4	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
3.37	1.4	2.44	1.4	3.50	1.3	2.18[a]	1.4	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
3.59	1.4	2.15[a]	1.5	3.24	1.3	1.71[a]	1.5	3.82	1, 64	0.06	—	—	n.s.	—	—	n.s.	—	—	n.s.
3.18	0.6	1.49	1.0	3.19	0.6	1.72[a]	1.2	3.27	1, 64	0.08	—	—	n.s.	—	—	n.s.	—	—	n.s.
2.58	1.2	1.17[a]	0.8	2.44	1.3	1.10[a]	1.2	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
3.34	0.8	2.01[a]	0.9	3.21	0.8	1.83[a]	1.1	3.17	1, 64	0.08	—	—	n.s.	—	—	n.s.	—	—	n.s.
12.6	4.7	13.3	4.3	13.0	4.0	12.5	4.4	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
13.2	2.6	9.7[a]	4.9	13.1	2.2	9.3[a]	4.6	—	—	n.s.	3.27	1, 76	0.07	—	—	n.s.	—	—	n.s.
8.61	3.5	6.30[a]	4.2	8.45	3.4	6.19[a]	3.8	—	—	n.s.	2.88	1, 76	0.09	—	—	n.s.	—	—	n.s.
1.73	0.4	1.41[a]	0.4	1.75	0.5	1.46[a]	0.4	—	—	n.s.	3.27	1, 74	0.07	—	—	n.s.	—	—	n.s.
2.25	0.7	1.73[a]	0.8	2.17	0.7	1.70[a]	0.7	—	—	n.s.	4.08	1, 74	0.05	—	—	n.s.	—	—	n.s.
1.38	0.4	1.23	0.3	1.47	0.5	1.29[a]	0.4	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
1.76	0.6	1.55	0.5	1.83	0.7	1.55[a]	0.5	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
2.17	0.7	1.59[a]	0.6	2.09	0.8	1.69[a]	0.7	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
1.55	0.5	1.29[a]	0.4	1.63	0.6	1.35[a]	0.5	—	—	n.s.	3.46	1, 74	0.07	—	—	n.s.	—	—	n.s.
1.54	0.6	1.29[a]	0.4	1.61	0.7	1.37[a]	0.5	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
1.21	0.3	1.06	0.1	1.26	0.3	1.17	0.3	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
1.59	0.6	1.28[a]	0.5	1.65	0.7	1.43[a]	0.6	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
1.55	0.4	1.24[a]	0.3	1.56	0.5	1.28[a]	0.4	—	—	n.s.	—	—	n.s.	—	—	n.s.	—	—	n.s.
131	17	128[a]	16	130	15	130	15	4.77	1, 81	0.03	7.72	1, 81	0.007	5.86	1, 48	0.02	—	—	n.s.
22.3	2.1	21.7[a]	2.3	21.9	2.2	21.8	2.3	5.34	1, 81	0.02	8.36	1, 81	0.005	6.67	1, 48	0.01	—	—	n.s.

Patients were asked to rate the degree to which their treatment assignment was logical and relevant to their problems. There was a significant difference across the three therapy assignments (cognitive-behavioral therapy, supportive psychotherapy, and medication only) in ratings after the first session (logical: $F=4.28$, df=2, 94, $p=0.02$; relevant: $F=4.68$, df=2, 94, $p=0.01$). Patients assigned to medication only rated their treatment as less logical than did patients assigned to cognitive-behavioral therapy or supportive psychotherapy and less relevant than did those assigned to supportive psychotherapy ($p<0.05$ by Tukey's honestly significant difference). There were no significant differences between ratings of cognitive-behavioral therapy and supportive psychotherapy. At the end of treatment, there were no significant differences in ratings across therapy assignment.

A total of 227 audiotaped therapy sessions were assessed by an independent rater. There was a difference between treatments in the degree of understanding conveyed and in interpersonal effectiveness. On both measures, cognitive-behavioral therapy and supportive psychotherapy were similar to each other but superior to medication alone (understanding: $F=51.1$, df=2, 224, $p=0.0001$, $p<0.05$ by Tukey's honestly significant difference; interpersonal effectiveness: $F=9.01$, df=2, 223, $p=0.0002$, $p<0.05$ by Tukey's honestly significant difference).

The proportion of patients terminating treatment prematurely was 34% overall and did not differ significantly across groups ($\chi^2=1.91$, df=4, $p>0.70$); the rate of premature termination was highest in the medication only group (43%), but this was not significantly greater than the rate of premature termination among patients receiving psychological treatment (32%) ($\chi^2=1.2$, df=1, $p>0.20$).

One hundred of the 120 patients remained in treatment long enough to have the opportunity to have their medication changed from desipramine (or desipramine placebo) to fluoxetine (or fluoxetine placebo). Overall, this change was made with 74% of the eligible patients. The frequency of changing medication was lower among patients receiving cognitive-behavioral therapy than among those receiving supportive psychotherapy (57% versus 84%) ($\chi^2=6.7$, df=1, $p<0.01$). This difference appears to reflect the greater improvement in binge eating attained by those receiving cognitive-behavioral

TABLE 4. Frequency of Remission of Binge Eating and Vomiting for Patients With Bulimia Nervosa and Comparisons of Treatments

	Cognitive-Behavioral Therapy				Supportive Psychotherapy							
	+ Medication		+ Placebo		+ Medication		+ Placebo		Medication Only		Combined	
Behavior	N	%	N	%	N	%	N	%	N	%	N	%
Based on diary	N=23		N=25		N=22		N=22		N=28		N=120	
Binge eating	12	52	6	24	4	18	4	18	8	29	34	28
Vomiting	11	48	6	24	3	14	5	23	7	25	32	27
Binge eating and vomiting	11	48	5	20	2	9	3	14	6	21	27	23
Based on Eating Disorder Examination	N=18		N=16		N=17		N=17		N=20		N=88	
Binge eating	12	67	6	38	5	29	5	29	7	35	35	40
Vomiting	9	50	5	31	3	18	2	12	5	25	24	27
Binge eating and vomiting	9	50	3	19	3	18	2	12	5	25	22	25

*p=0.09. **p=0.07. ***p=0.06. †p=0.05. ††p=0.04. †††p=0.03. ‡p=0.02. ‡‡p=0.01.

therapy (see later discussion). Among patients receiving psychological treatment, there was no difference in the frequency of changing medication between those assigned to placebo and those assigned to medication (64% versus 76%) (χ^2=1.5, df=1, p>0.20).

Among patients receiving medication, the average maximum dose of desipramine was 188 mg/day (SD=89), and the average maximum dose of fluoxetine was 55 mg/day (SD=15). The maximum desipramine dose differed across therapy conditions: for cognitive-behavioral therapy, 143 mg/day (SD=92); for supportive psychotherapy, 220 mg/day (SD=80); and for medication only, 198 mg/day (SD=83) (p<0.01; supportive psychotherapy and cognitive-behavioral therapy differed by Tukey's honestly significant difference). The fluoxetine dose did not differ significantly across therapy conditions.

Response to Treatment

At baseline, the five treatment groups did not differ on any outcome measure. In all treatment groups, the end-of-treatment frequencies of binge eating and vomiting and most measures of psychopathology were statistically significantly lower than the frequencies before treatment (table 3). Thus, there was significant clinical improvement in all groups.

Comparison of Patients Receiving Psychological Treatment With Medication or Placebo. The comparison of cognitive-behavioral therapy with supportive psychotherapy and of the combination of psychological treatment and antidepressant medication versus psychological treatment and placebo was conducted by using a 2×2 factorial design; data from the medication-only group were not used in these comparisons. There were no statistically significant interactions between type of psychological treatment (cognitive-behavioral therapy versus supportive psychotherapy) and medication (active versus placebo) on any outcome measure.

Cognitive-Behavioral Therapy Versus Supportive Psychotherapy. The frequencies of binge eating and of vomiting per week were calculated from the last 2 weeks of patient diaries and from the Eating Disorders Examination interview, which focused on the preceding month. Data from both sources indicated that cognitive-behavioral therapy had a much greater impact than supportive psychotherapy in reducing binge eating and vomiting (table 3). Examination of the rates of cessation of binge eating and vomiting also favored cognitive-behavioral therapy over supportive psychotherapy (table 4).

There were few other indications of significant differences in outcome between cognitive-behavioral therapy and supportive psychotherapy. Cognitive-behavioral therapy was associated with a greater reduction in the score of the Eating Attitudes Test, a self-rating instrument that assesses both behavioral and attitudinal symptoms of eating disorders (table 3). However, there were no differences between cognitive-behavioral therapy and supportive psychotherapy in improvement in mood, assessed by both the Beck inventory and the SCL-90.

There was a significant difference between cognitive-behavioral therapy and supportive psychotherapy in change in weight during treatment; cognitive-behavioral therapy was associated with a weight gain of 1.13 lb., compared with a weight loss of 1.29 lb. for supportive psychotherapy.

Medication Versus Placebo. On several measures, there was evidence that patients receiving medication in combination with psychological treatment experienced greater improvement than did patients receiving placebo with psychological treatment. On the basis of patient diaries, medication affected binge eating more than placebo did. Reductions in Eating Attitudes Test scores were significantly greater in the patients receiving medication, as was improvement in scores on the Beck inventory and the depression subscale of the SCL-90 (table 3).

Patients receiving medication and psychological treat-

Cognitive-Behavioral Therapy Versus Supportive Psychotherapy		Medication Versus Placebo		Cognitive-Behavioral Therapy + Medication Versus Medication Only	
Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
3.0†††	1.1–8.0	2.3*	0.9–6.0	—	—
2.6†	1.0–6.9	—	—	—	—
4.3‡‡	1.4–13.3	—	—	3.7††	1.1–12.5
2.7†	1.0–7.5	—	—	—	—
4.1‡	1.3–13.4	—	—	—	—
3.3***	1.0–10.9	2.7**	1.0–7.5	—	—

ment lost an average of 1.54 lb., compared to a weight gain of 1.49 lb. with placebo and psychological treatment. This difference was statistically significant.

Comparison of Patients Receiving Medication Alone With Patients Receiving Psychological Treatment With Medication. We also assessed the benefits of combining medication and psychological treatment by comparing the outcome of patients treated exclusively with medication to the outcome of patients treated with either medication and cognitive-behavioral therapy or with medication and supportive psychotherapy. Because data from the medication-only cell were used in both comparisons, a Bonferroni correction was applied, and only comparisons with a p value of 0.025 or less were accepted as significant.

Cognitive-Behavioral Therapy Plus Medication Versus Medication Alone. The combination of cognitive-behavioral therapy and medication was superior to medication alone in reducing vomiting frequency, as assessed by patient diary, and the total Eating Attitudes Test score (table 3). Patients receiving medication alone lost significantly more weight than did patients receiving cognitive-behavioral therapy and medication (–3.50 lb., SD=5.9, versus –0.01 lb., SD=3.7).

Supportive Psychotherapy Plus Medication Versus Medication Alone. The only indications of statistically significant differences between the group receiving supportive psychotherapy with medication and that receiving medication alone were found on the basis of the Eating Disorders Examination. Surprisingly, the combination of supportive psychotherapy and medication was significantly inferior to medication alone in reducing frequency of binge eating (table 3). It should be noted that Eating Disorders Examination data on binge eating and vomiting were available from only 37 of the 50 patients relevant to this analysis. On the basis of patient diary information, which was available for all 50 patients, there were no statistically significant differences between patients receiving supportive psychotherapy plus medication and patients receiving medication alone. Supportive psychotherapy significantly added to medication alone in reducing the importance of shape and weight as assessed by the Eating Disorders Examination.

Results From Patients Who Completed Treatment. Additional analyses were conducted to examine behavioral changes (binge eating and vomiting as recorded in patient diaries) among the 79 patients who completed an entire course of treatment. The results were consistent with the intent-to-treat analyses, with two minor exceptions. First, there was a significant difference in reduction in binge eating, but not vomiting, between supportive psychotherapy plus medication and medication alone ($F=5.54$, $df=1, 30$, $p=0.03$). This finding is similar to the results of the intent-to-treat analysis of the Eating Disorders Examination data described in the preceding paragraph. Second, in the 2×2 analyses, there were trends toward an interaction between type of psychological treatment and type of medication, suggesting that the difference between medication and placebo was smaller among patients receiving supportive psychotherapy (binge eating: $F=3.85$, $df=1, 59$, $p=0.06$; vomiting: $F=2.92$, $df=1, 59$, $p=0.09$).

DISCUSSION

Cognitive-behavioral therapy is widely viewed as the preferred treatment for bulimia nervosa (21). Our findings are consistent with previous studies in showing that cognitive-behavioral therapy is significantly more effective than supportive psychotherapy (22, 23). Both psychological treatments were associated with clinically important improvement. Cognitive-behavioral therapy, however, was clearly superior in reducing the frequencies of binge eating and vomiting and in producing improvement on the Eating Attitudes Test, a self-report measure of behavioral and attitudinal features of eating disorders. There was also a trend favoring cognitive-behavioral therapy in reducing some measures of dietary restraint and of abnormal concerns with shape and weight. Additional evidence of the efficacy of cognitive-behavioral therapy was found in the comparisons showing that combining cognitive-behavioral therapy with antidepressant medication was superior to medication alone, while combining supportive psychotherapy with medication was not.

Supportive psychotherapy was designed to provide a credible comparison treatment resembling that employed by practitioners and equating for nonspecific factors such as patient expectations and the therapist-patient relationship. This was accomplished. Patients' ratings of the treatment's logic and relevance were similar for cognitive-behavioral therapy and supportive psychotherapy, and, as judged by an independent rater, there were no significant differences between the treatments in the therapists' ability to convey understanding and engage the patient. Therefore, the superiority of cognitive-behavioral therapy over supportive psychotherapy can be

attributed to specific therapeutic elements of cognitive-behavioral therapy. Comparative studies of cognitive-behavioral therapy and other psychotherapies have yielded less clear-cut findings. Cognitive-behavioral therapy was generally more effective than a brief psychodynamic psychotherapy (7) and, in the short-term, than interpersonal psychotherapy (24). However, after 1 year, the outcomes of cognitive-behavioral therapy and interpersonal psychotherapy were similar. Hence, while cognitive-behavioral therapy is currently the best established treatment for bulimia nervosa, additional research on the effects of other forms of psychological treatment is of theoretical and clinical interest.

In the current study, the use of antidepressant medication, when combined with psychological treatment, was modestly but significantly superior to placebo in reducing the frequency of binge eating and in improving mood. There were also trends favoring medication over placebo in the reduction of vomiting frequency and on several additional measures of psychopathology. Few other studies have examined advantages of combining medication and psychological treatment for outpatients with bulimia nervosa. In the only other placebo-controlled trial of which we are aware, Mitchell et al. (9) found that imipramine, when combined with an intensive form of group psychotherapy, was associated with greater reductions in depression and anxiety than was placebo. However, there was no evidence that antidepressant treatment added to the impressive reduction in binge eating and vomiting produced by group psychotherapy and placebo.

Although they did not employ a placebo condition, Agras et al. (11) compared individual cognitive-behavioral therapy alone to the combination of cognitive-behavioral therapy and a modest dose of desipramine for either 16 or 24 weeks. The improvement in binge eating and vomiting of patients receiving both medication and cognitive-behavioral therapy was not significantly greater than that of patients receiving cognitive-behavioral therapy alone. The combination of cognitive-behavioral therapy and 24 weeks of desipramine was superior to cognitive-behavioral therapy alone on only a single measure of dietary restraint.

The current study extends these results in finding that on several behavioral and psychological measures, the combination of antidepressant medication and psychological treatment was significantly superior to that of placebo and psychological treatment. It is possible that the benefit of medication was detectable in part because the effect of psychological treatment was somewhat less impressive than that observed in other studies (9, 11), thereby allowing more opportunity for the effect of medication to be observed. It is also likely that the two-stage intervention we employed enhanced the benefit. Two-thirds of the patients who were assigned to medication eventually received fluoxetine, either because desipramine caused intolerable side effects or because of inadequate improvement. Thus, the second stage of the medication intervention was used by a majority of patients. In a previous placebo-controlled study conducted in the same center with a similar patient population, we examined the effect of a single course of desipramine without psychological treatment (10). The average reduction in binge frequency was 47% among the patients receiving desipramine, and 13% had ceased binge eating at the end of treatment. In the present study, the average reduction in binge frequency among patients receiving medication only was 69%, and 29% ceased binge eating. These results suggest that the two-stage medication intervention was substantially more effective than a single course of a tricyclic antidepressant, the intervention employed in previous studies of medication and psychological treatment for bulimia nervosa.

At the time this study was conceived, two other groups had reported that psychological treatment of bulimia nervosa was superior to medication alone (9, 11). The current study was therefore not designed to address this issue and did not include a group that received psychological treatment alone (25). The post hoc finding that the benefit of medication alone was indistinguishable from that of cognitive-behavioral therapy plus placebo was surprising and suggests that the use of a two-stage medication intervention or of fluoxetine or both may improve the efficacy of medication alone treatment relative to that of cognitive-behavioral therapy.

The effects of cognitive-behavioral therapy and of medication on weight are of note. Compared with supportive psychotherapy, cognitive-behavioral therapy was associated with a small but statistically significant weight gain, while, compared to placebo, medication was associated with a small weight loss. Similar findings have been reported in previous studies. Cognitive-behavioral therapy has been associated with a small amount of weight gain (4, 26). Weight loss associated with fluoxetine is well documented (27, 28), and treatment of bulimia nervosa with tricyclic antidepressants has also been found to produce slight weight loss (9, 10, 29). These data suggest that the mechanisms by which cognitive-behavioral therapy and antidepressant medication affect eating behavior in patients with bulimia nervosa are different. One specific aim of cognitive-behavioral therapy is to encourage patients to avoid dieting and to consume foods that have been viewed as forbidden. The mechanisms by which antidepressant medications lead to a reduction in binge frequency remain unclear but may include a subtle reduction in appetite. Agras et al. (30) previously presented information suggesting that antidepressant medication led to an increase in dietary restraint among patients with bulimia nervosa. In the current study, there was no indication of a medication effect on restraint, while cognitive-behavioral therapy tended to reduce restraint as measured by the Eating Disorders Examination.

In closing, we note several limitations of the current study. First, our design did not include a psychotherapy-only group. Therefore, the conclusion that medication adds to psychological treatment rests on the assumption, which has been questioned (25), that psychotherapy plus placebo is equivalent to psychotherapy alone. Second, while medication was provided in double-blind fashion for four of the five treatment

groups, the presence of side effects may sometimes have compromised this methodological precaution. Similarly, neither clinician nor patient was blind to the type of psychological treatment administered. Third, while a two-stage medication intervention more fully reflects the range of possible pharmacological interventions than does a trial using only a single agent, additional medications and more complex strategies are available and might be even more effective. Fourth, the current report is based only on data available at the end of treatment; data on outcome during the succeeding year have not yet been analyzed.

Despite these limitations, we believe that the current study has implications for clinical practice. Although studies of other forms of psychotherapy, such as interpersonal psychotherapy, are warranted, our results support the view that at present, cognitive-behavioral therapy is the psychological treatment of choice for bulimia nervosa. Our data also suggest that a two-stage medication intervention using fluoxetine adds significantly to the benefits of psychological treatment. However, the modest gains of adding medication to psychotherapy must be weighed against the risk of side effects and the costs of medication and monitoring. Conversely, the modest gains of adding psychological treatment to medication must be examined in the context of the cost and limited availability of cognitive-behavioral therapy for eating disorders. Such decisions would be greatly aided by knowledge of factors that would allow the clinician to identify those patients most likely to benefit from medication, psychological treatment, or their combination and by information on the most advantageous way of sequencing treatments.

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