Biomedical Science

Compliance and Outcome in Anorexia Nervosa

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Anorexia nervosa is notoriously difficult to treat, but little is known regarding the relationship of compliance to treatment outcome. We investigated in 41 adolescents who fulfilled DSM-III-R criteria for anorexia nervosa, the relationship between the completion of a standard psychosocial treatment program, subtypes of anorexia nervosa, and outcome as determined by standardized measurements. These adolescents were observed for an average of 32.4 months. Overall, 29 patients (70%) improved considerably, but 10 (24%) were symptomatic, and 2 (5%) remained in poor condition. There were no deaths. Of the 41 patients, 14 (34%) completed our entire treatment program, 15 (37%) received major treatment and failed in the outpatient follow-up phase only, 7 (17%) dropped out of inpatient treatment before its completion, and 5 (12%) refused treatment in our system altogether. Of all the dropouts, 10 received no further treatment. One patient was admitted to hospital elsewhere but again dropped out in the outpatient phase of that program. Seven patients (17%) received further outpatient treatment only, and 9 (22%) received inpatient and outpatient care and seemingly completed their treatment. Treatment completion significantly affected the measures of global clinical functioning and specific psychopathologic features, but only for those patients who completed the initial program. Bulimic patients did considerably worse on follow-up and were less likely to complete treatment. Patients with restricted anorexia nervosa were more likely to complete treatment than those with a bulimic subtype ($P = .03$). Differential compliance rates in the two subtypes confound the effects of treatment completion and need to be controlled for in future studies. Depression was not associated with noncompliance but, if present, was associated with poor outcome on follow-up and abated in only a third of those in whom it was initially present.

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Although the literature is replete with descriptions of the difficulties of working with patients with anorexia nervosa, especially of engaging them in treatment, few studies systematically address the role of compliance in the treatment outcome. Only one study to date has related compliance to outcome in the treatment of anorexia nervosa. Vandereycken and Pierloot retrospectively studied 133 female patients admitted to hospital because of anorexia nervosa and found a remarkably high dropout rate of 50% during the first year.[1] Educational and social statuses were significantly lower in the dropouts. Patients with exposure to behavior modification had a higher dropout rate than those who had their caloric intake prescribed by their physicians. On follow-up, there was no difference in mortality between groups. Body weight on follow-up was considerably lower in the dropout group. The authors detected only two patients who had improved without further treatment. No detailed information about the patients' psychopathology was available. Isager and co-workers, reporting on death and survival rates in 151 consecutive patients with anorexia nervosa, found that relapse rates were twice as high if patients were seen for less than a year, and patients in therapy for longer than that had a considerably smaller chance for relapse.[2] Russell and colleagues reported an evaluation of family therapy for eating disorders,[3] with the following distribution of treatment completion: 9% refused treatment altogether after treatment in the hospital; 10% dropped out within three months; 16% dropped out sometime after three months. Thus, 35% did not complete outpatient treatment. No information was given regarding the patients' inpatient program completion rate. There was a greater tendency for bulimic than anorexic patients to drop out. Dropping out affected outcome; dropouts were notably worse off at the one-year prospective follow-up on a variety of outcome measures. No information was available on whether dropouts received treatment elsewhere and how it might have affected their condition. Other studies addressed compliance,[4-8] but only a few were systematic[5] and only some provided unsystematic follow-up.[6-8]

The phenomenon of the treatment dropout is by no means unique to the treatment of anorexia nervosa.[9] Most studies of treatment outcome fail to include the entire inception cohort, thereby allowing for the overrepresentation of those with successful outcomes. According to Sackett and Haynes,

[T]he systematic loss to analysis of the most noncompliant patients (those who drop out entirely or who rarely attend appointments) invalidates the conclusions of a large number of compliance investigations and this failure cannot be overcome by statistical or pharmacologic maneuvers.[10(p22)]

In other psychiatric conditions, individual psychotherapy dropout rates are related to socioeconomic status, educational level,[9,11] and, possibly, sex, age, patient and therapist factors, and sociodemographic factors. Szmukler and associates found that bulimic symptoms, expressed emotion by parents, and the type of therapy offered all interacted to cause dropouts.[6]

Although the general quality of outcome studies of anorexia nervosa has improved substantially over the past five to ten years,[12-25] it is unclear how many studies report on the entire inception cohort. Patients dropping out of treat-

ment often are not included in the final analysis, thus artificially inflating treatment effect and obscuring differential effects of different treatments. In a recent review, Agras and Kraemer concluded that there is little evidence that different treatments have different outcomes.[24] A lack of accounting for differential compliance rates in different treatment conditions might well contribute to this finding.

Two other factors could be related to the lack of evidence for differential treatment effects: Several subcategories of anorexia nervosa influence the course of illness, such as the presence or absence of depression and the presence of bulimic symptoms.[12,17,23] The distribution of these subtypes should be controlled for to prevent uneven loading of various treatment methods. In addition, outcome is too narrowly defined in terms of weight and return of menses only—relatively convenient measures. More recently, sophisticated methods have become available to measure the more refined psychopathologic features of the syndrome. These permit an assessment of functional areas that might be influenced by treatment independent of weight and menstrual state.

We hypothesized that patients completing treatment would have more substantial reductions in specific eating disorders and behavior, along with larger reductions in depressive and bulimic symptoms. We also hypothesized that persistent bulimic symptoms and depression would be associated with a poor prognosis. At the Eating Disorders Program at Children's Hospital, Stanford (California) Medical Center, we were able to explore these factors in greater detail. Our first 50 patients were treated by psychosocial interventions only within a standard treatment program. Thus, we could test hypotheses regarding the effects of compliance on the outcome of anorexia nervosa.

Patients and Methods

Patients

We invited our first 50 patients to participate in the study; 41 (82%) gave informed consent. These 41 patients were evaluated by individual and family interviews. The follow-up sample, as well as the nine patients who refused to provide follow-up information, was not significantly different from our total population of eating disorder patients on various psychopathologic or demographic variables. Of the nine patients who refused to participate in the study, three had none or minor treatment, four had major treatment, and two completed treatment in our program. Reasons for not participating in the study were varied, but one of the most often cited was that the patient and the family did not want to be reminded of the illness. All subjects satisfied minimum criteria for inclusion in the study, which included a primary diagnosis of anorexia nervosa based on criteria of the *Diagnostic and Statistical Manual of Mental Disorders,* third edition, revised (DSM-III-R), by two of us (H.S. and I.F.L.), and at least a year had elapsed since the initial hospital treatment and discharge. In addition, both authors assigned patients to either "restrictive" or "bulimic" subgroups. Restrictive anorexia nervosa was diagnosed when patients achieved weight loss by dieting and

increased caloric expenditure alone. Patients were assigned to the bulimic subgroup when frequent (at least once a week for a month) overeating or purging was present. Accordingly, in the sample 30 (73%) patients had restrictive and 11 (27%) bulimic features. The mean age at diagnosis was 14.8 ± 2.4 years, and the mean age at the start of illness was 13.0 ± 2.0 years (± the standard deviation). The mean duration of illness before diagnosis was 9.8 ± 8.4 months, the mean age at follow-up was 17.6 ± 2.2 years, and the actual length of the follow-up period ranged between 12 and 72 months with a mean of 32.4 months. The male-to-female ratio was 1:6.

Follow-up Interviews

All follow-up interviews were carried out by one of us (C.M.), who was not present in the program when these patients were treated. All patients completed a follow-up diagnostic battery and a standardized interview modeled after a University of California, Los Angeles, follow-up study.[27] The DSM-III-R criteria for diagnosis were applied for the diagnosis of both anorexia nervosa and a secondary diagnosis of depression.

Measurements

The following measures were obtained from all subjects at baseline—that is, in the two-week diagnostic period preceding intervention—the Zung Self-Rating Depression Scale, which is a reliable and valid self-report inventory of depressive symptoms[28]; the Eating Attitude Test-26 (EAT), a 26-item, self-report questionnaire designed to measure objectively the presence of disturbed eating patterns and the symptoms of anorexia nervosa (the Eating Attitude Test has an α-reliability coefficient of 0.90)[29]; the Garfinkel global clinical score (GCS) for the assessment of anorexia nervosa.[22] The last measures body weight, menstrual state, eating habits, and social and vocational adjustment. Scores between 0 and 4 are considered asymptomatic and between 5 and 8 mildly, 9 and 13 moderately, and 13 and above severely symptomatic. The average score in our clinic population is 11.5 ± 4.5. These ratings were given by two independent raters between whom reliability was 0.82.

All these measures were repeated at follow-up. We also added the Eating Disorders Inventory (EDI),[30] which had then just become available. This is a 64-item, 8-factor, self-report questionnaire measuring specific features of eating disorders. The eight factors are a drive for thinness, bulimia, body dissatisfaction, ineffectiveness, interpersonal distrust, perfectionism, interoceptive awareness, and maturity fears.

Treatment Program

Our program has been described in detail elsewhere.[31] Briefly, it consists of an average treatment period of 16 months. Following a two-week diagnostic outpatient phase, a mean of six weeks is spent as an inpatient. Follow-up psychotherapy after the hospital stay extends for an average of 30 family sessions and 63 individual sessions. While in the hospital, patients receive behavior modification for weight gain, nutritional counseling, a medical evaluation, daily supportive group psychotherapy, and individual and family psychotherapy. Individual psychotherapy incorporates the principles stated by Bruch[32] and consists of three to five sessions per week as inpatients and weekly sessions as outpatients. Family therapy proceeds according to principles outlined by Minuchin and co-workers[33] and consists of biweekly inpatient or weekly or fewer outpatient sessions. All psychotherapeutic procedures were supervised by

one of us (H.S.). Three fourths of the family therapy was actually carried out by this author (H.S.), the rest by child psychiatry fellows under supervision. Group therapy occurred daily during the hospital stay and was supportive in nature. Behavior modification was offered on a fixed, internal, one-day reinforcement schedule during inpatient stays[23] for an average of about six weeks and produced a mean 5.2-kg weight gain. Daily nutritional counseling was available for inpatients and weekly counseling for outpatients. Vital signs and physiologic variables were monitored and feedback given daily during the hospital admission and weekly or biweekly on an outpatient basis by the staff of the Division of Adolescent Medicine (supervised by one of us [I.F.L.]). All treatment components were coordinated weekly in a therapeutic team meeting with patients' participation.

On the basis of the extent of their participation in the program at termination, patients were assigned therapy scores as follows:

0 = Treatment refusal: These patients were in our treatment program less than a week, permitting only diagnostic assessment;

1 = Partial treatment: These patients remained longer than a week but less than six weeks (mean duration of inpatient treatment in our program);

2 = Major treatment: These patients remained more than six weeks in our program, usually completing the inpatient portion of their treatment, but not completing their course of outpatient follow-up against the recommendations of the treatment team. Patients were medically and psychiatrically symptomatic when they decided to stop outpatient therapy;

3 = Complete treatment: These patients completed the diagnostic inpatient and outpatient phase and terminated with the consent of the treatment team. These patients were usually considered by the treatment team both medically and psychiatrically asymptomatic and stable.

Statistics

We applied a multivariate analysis of variance (MANOVA) with Roy's greatest root to test for differences on all outcome variables between groups, with a one-way median analysis as a follow-up procedure. Furthermore, Pearson's product moment correlation, Student's t test, and χ^2 with Yates's correction were employed as appropriate.

Results

Outcome in Total Sample

In general, the outcome was relatively good. Of the 41 patients, 15 (37%) were in the asymptomatic range (GCS 0 to 3), 14 (34%) in the symptomatic but improved range, 10 (24%) in the very symptomatic range (GCS 8 to 11), and 2 (5%) in the poor category (GCS 12 or worse). There were no deaths. The whole sample showed improvement from diagnosis on the global clinical score (12.3 ± 3.5 versus 5.3 ± 3.3, $t = 9.8$, $P < .001$), ideal body weight percentage ($80\% \pm 10\%$ versus $93\% \pm 12\%$, $t = 4.9$, $P < .001$), and Eating Attitude Test scores (53 ± 15 versus 24 ± 18, $t = 7.9$, $P < .001$), all by the two-tailed t test.

The total EAT and EDI scores and all EDI subscales except "maturity fears" and "perfectionism" showed a significant correlation with the global clinical score on follow-up, ranging from $+0.646$ to 0.378 ($P < .05$). These correlations indicate that those patients who appeared symptomatic to our rater also showed a persistent specific eating disorder by self-report, thus cross-validating our ratings.

At follow-up, of the 35 female patients, 16 (46%) had persistent amenorrhea, 7 (20%) had irregular menses, and 12 (34%) were menstruating monthly. Vomiting occurred in 9 of the 41 patients (22%) on diagnosis and at follow-up. Bingeing occurred in 14 (34%) at follow-up, a slight increase over the 10 (24%) at time of diagnosis. Laxatives were abused by 4 (10%) on follow-up, essentially unchanged from diagnosis (3 [7%]).

In terms of social adjustment, 10 (24%) patients were rated as not having any problems, 20 (49%) as having mild, 8 (20%) as having moderate, and 3 (7%) as having severe problems. Educational and vocational problems were absent in 26 (63%), mild in 9 (22%), moderate in 4 (10%), and severe in 2 (5%) patients.

The rate of readmission to a hospital was 29% (12 of 41 patients). Five patients were readmitted once, three were readmitted twice, and four were readmitted three times. In this category, there was a significant difference between patients with bulimic features and those with restrictive anorexia. Of 11 patients with bulimia, 7 (64%) had to be readmitted, but only 5 of 25 with restrictive anorexia (20%) were readmitted (χ^2 4.26, degree of freedom [df] 1, $P < .05$). The presence or absence of depression did not relate to the readmission rate.

Compliance With Treatment

Treatment score 0 (n = 5). Five patients (12%) refused any treatment. Of these, two did and three did not receive any further treatment outside our system. At follow-up, one was improved in that she had no further problems with weight or bingeing and purging and she had a return of her menses. The second patient was improved in terms of weight, but binged-purged uncontrollably. The third was highly symptomatic both in terms of weight and binge-purge pathology (GCS 13); this was unchanged from diagnosis. The other two refusing treatment had either inpatient (one patient) or only outpatient follow-up (one patient). On follow-up, both these patients had improved, but both were in the symptomatic range (GCS 5 to 8). Spontaneous recovery seems to have occurred in only one patient in this group; her initial global clinical score was 16.

Treatment score 1 (n = 7). Of the seven patients (17%) who had received only minimal intervention in our program—inpatient treatment dropouts—only one did not have any further treatment at all. He had improved substantially, although a three-week hospital stay in our program produced only a modest weight gain (2 kg). His global clinical score was 12 on diagnosis and 0 on follow-up. All other patients in this category had either inpatient and outpatient treatment (four) or outpatient-only treatment (two) in other systems.

Treatment score 2 (n = 15). Of these 15 patients, 6 (14%) had no further treatment, 5 were admitted to hospital and had outpatient treatment elsewhere, and 4 had only outpatient treatment in another program. Of the six with no further treatment in this group, four were in the symptomatic but improved category; one patient remained in the poor category. One patient was asymptomatic (GCS 3).

Treatment score 3 (n = 14). None of the 14 patients (34%) in the completed-treatment group required any additional treatment by the time of the 32-month follow-up. Nine were in the asymptomatic range, four had improved but were symptomatic, and only one was in the very symptomatic group because of the emergence of binge-purging in a patient with previous restrictive anorexia. Thirteen patients with restrictive anorexia and one with bulimic fea-

tures completed the program. Depression as a secondary diagnosis did not predict initial treatment completion.

Summary of Post-Dropout Treatment in Other Settings

Of the 27 patients who dropped out at any stage of treatment in our program, 17 received further treatment elsewhere. Of those 17 patients, 9 (22%) received both inpatient and outpatient care and seemed to complete their treatments, 1 was treated as an inpatient only, and 7 (17%) were treated as outpatients only. Patients who did not seek treatment after dropout were distinguished by the presence and degree of depression. Patients who continued in treatment were more likely to have a secondary diagnosis of major depression (7 of 10 versus 4 of 17; $\chi^2 = 3.87$, df 1, $P = .05$) and had higher Zung scores on diagnosis (51.5 ± 15 versus 41.5 ± 15, $t = 1.66$, $P = .05$ one-tailed). These groups did not differ on any other variable. Specifically, bulimic and restrictive features did not predict treatment status after the initial dropout.

Analysis of the Effects of Initial Treatment Completion

For the purposes of this analysis, we combined treatment refusers (score 0) and patients with only minimal treatment into one group ($n = 12$), contrasting this group with those patients who had received major (score 2, $n = 15$) and complete (score 3, $n = 14$) treatment. There were no significant differences among these groups at diagnosis on the basis of age, sex, socioeconomic status, duration of illness, global clinical score, Zung and EAT scores, previous treatment, or duration of follow-up, indicating that these groups were comparable in terms of important measures of chronicity and psychopathology. Table 1 summarizes the findings on follow-up.

TABLE 1.—Outcome in Treatment Groups of Anorexia Nervosa in 41 Adolescent Patients

Outcome Variable	Treatment Group*†			Significance
	Incomplete, $n=12$	Major, $n=15$	Complete, $n=14$	
GCS				
At diagnosis	11.8 ± 2.9	12.1 ± 2.8	11.4 ± 2.7	NS
At follow-up	6.7 ± 3.5	5.7 ± 3.4	3.6 ± 2.1	‡
Ideal body weight %				
At diagnosis	85 ± 14	78 ± 12	74 ± 2.7	NS
At follow-up	92 ± 8	89 ± 9.6	94 ± 9	NS
Menses, Reg/Irreg/None				
At diagnosis	0/2/7	1/0/12	1/0/13	NS
At follow-up	3/2/4	4/1/8	5/3/6	NS
GCS, social adjustment				
At diagnosis	3.6 ± 1.1	4.1 ± 1.5	3.6 ± 1.8	NS
At follow-up	2.7 ± 2.1	1.7 ± 1.4	0.9 ± 0.5	§
Zung				
At diagnosis	47 ± 16	44 ± 16	40 ± 13	NS
At follow-up	41 ± 8	39 ± 15	37 ± 8	NS
EAT				
At diagnosis	48 ± 15	46 ± 14	47 ± 18	NS
At follow-up	25 ± 16	28 ± 12	18.3 ± 18.1	¶
EDI				
At follow-up	45 ± 30	53 ± 31	28 ± 29	‖

Irreg = irregular, NS = not significant, Reg = regular

*Explanation of treatment groupings: Incomplete = treatment scores 0 and 1, Major = treatment score 2, Complete = treatment score 3. See text for a thorough discussion of treatment differences. Higher scores on the global clinical score (GCS), Eating Attitude Test (EAT), Eating Disorders Inventory (EDI), and the Zung Self-Rating Depression Scale indicate more severe disease.

†Except for Menses, scores are given as the mean ± standard deviation.

‡Median one-way analysis: $\chi^2 = 7.2$, $df = 2$, $P = .03$.

§Median one-way analysis: $\chi^2 = 10.0$, $df = 2$, $P = .006$.

¶Median one-way analysis: $\chi^2 = 4.66$, $df = 2$, $P = .09$.

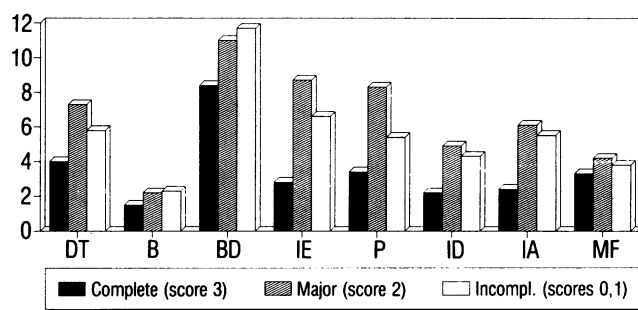‖Median one-way analysis: $\chi^2 = 6.53$, $df = 2$, $P = .04$.

Figure 1.—The graph shows the Eating Disorder Inventory results in anorexic patients at follow-up by subscale (multivariate ANOVA, Roy's greatest root = 0.661, F[8,32] = 2.64, $P = .02$). DT = drive for thinness, B = bulimia, BD = body dissatisfaction, IE = ineffectiveness, P = perfectionism, ID = interpersonal distrust, IA = interoceptive awareness, MF = maturity fears

By MANOVA, there were significant overall differences among treatment groups on the continuous outcome variables, GCS, EDI, EAT, Zung (Roy's greatest root = 0.338, F [4,36] = 3.04, $P = .03$). One-way median analyses at follow-up showed substantially lower GCS, EAT, and EDI scores in those completing treatment. The differences in GCS remained significant when the ratings of social adjustment are looked at alone, omitting eating habits, body weight, and menstrual status. Zung scores, however, did not differentiate the groups and neither did ideal body weight percentage and menstrual status.

When MANOVA was applied to the subscales of the EDI (Figure 1), significant differences were found (Roy's greatest root = 0.661, F[8,32] = 2.64, $P = .02$). Patients completing treatment scored notably lower on drive for thinness, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, and lack of interoceptive awareness.

Effects of Treatment in Other Settings

In the course of the follow-up interviews, we also obtained information regarding what kind of treatment the patients had received and grouped them as follows:

- none (10 patients);
- partial (8 patients). Patients received either inpatient or outpatient treatment, but, as best we could tell, they did not complete these programs either;
- major (9 patients). These patients usually received both inpatient and outpatient intervention and seemed to follow through to termination.

These groups did not differ at diagnosis with regard to restrictive or bulimic features, GCS or EAT scores, age, sex, or socieconomic status. They did differ in terms of the secondary diagnosis of depression; none of the ten patients who had gone on without further intervention had such a diagnosis, but four of the eight with partial treatment and six of those with major treatment did ($\chi^2 = 9.85$, df 2, $P = .007$).

The MANOVA on the outcome variables of these subgroups was significant (Roy's greatest root = 0.853, F (4,21) = 4.5, $P = .009$) (Table 2). One-way median analyses showed the significant differences on Zung scores and on the ratings of the social-vocational functioning of the GCS (Table 2). There were no significant differences on EDI, EAT, and GCS scores or weight or menses at follow-up.

When all three groups are compared with those who completed treatment in our program, patients completing treatment are found to consistently achieve the lowest scores of all groups on the GCS, the social-adjustment portion of the GCS, the EDI and EAT, and the second lowest

score (after those with no follow-up treatment at all) on the Zung (compare Table 1). Some of the differences were significant by one-way median analysis—GCS: $\chi^2 = 8.61$, df 3, $P = .01$; GCS, social-vocational adjustment: $\chi^2 = 8.25$, df 3, $P = .02$; EAT: $\chi^2 = 6.2$, df 3, $P = .05$; EDI: $\chi^2 = 8.04$, df 3, $P = .02$. Ideal body weight percentage, menses, and Zung scores were not significantly different.

Outcome of Patients With Anorexia With Bulimic Features

On admission, patients with anorexia with bulimic features did not differ from those with restrictive features in terms of sex, socioeconomic status, age, duration of illness, length of hospital stay, duration of follow-up, and previous interventions. They did differ on the global clinical severity score ($t = 4.69$, $P < .001$), reflecting the rating system's added severity points for binge-purge behavior. They also differed on admission weight ($t = 2.93$, $P < .01$), with anorexic patients with bulimia being closer to their ideal body weight ($87\% \pm 15\%$) than those with restrictive anorexia ($72\% \pm 13\%$). On follow-up, bulimic anorexic patients were considerably worse off on six of nine measures than were those with restrictive anorexia (Table 3). Depression scores and outcome for weight and menses were not

significantly different, but these patients had greater difficulty on follow-up with specific eating disorder psychopathology as measured by the Eating Disorders Inventory. These differences remained significant when bulimic behavior was corrected for by subtracting the bulimia subscale from the total.

Their elevated global clinical scores originate not only from binge-purge behavior but from their social adjustment in general. As previously indicated, fewer anorexic patients with bulimic features than with the restrictive type completed our treatment program, reflecting greater problems with compliance.

The Influence of Depression on Outcome

We reanalyzed our sample's outcome variables by dichotomizing the group by either the presence or absence of a secondary diagnosis of depression by DSM-III-R criteria or a critical value of the Zung of 40 points. Results were comparable, so we report only the analysis with the DSM-III-R diagnosis.

A secondary diagnosis of major depression by DSM-III-R diagnostic criteria was applied to 8 of 27 patients with restrictive anorexia and 8 of 14 with bulimic features (χ^2 0.25, not significant). This was reduced to 6 and 4 patients, respectively, on follow-up (χ^2 0.00, not significant). By a Zung score of 40, moderate to severe depression was diagnosed in 24 of 41 patients (58%). This number dropped to 15 (37%) on follow-up. It seems that by either method of measuring depression, only a third of our depressed patients responded to the psychosocial treatment package with improvement in their moods. It also seems that depressed patients with anorexia were significantly worse off on five of seven outcome variables (Table 4).

We then repeated our original MANOVA on all the outcome variables, this time with the Zung score as a covariant. Although there was evidence for overall Zung scale differences among the groups (Roy's greatest root = 1.61, F $(4,34) = 13.7$, $P = .0001$), there also was evidence for additional treatment and compliance effects. The findings for a treatment effect in the three treatment groups remained significant (Roy's greatest root = 0.367, F $(3,35) = 3.21$, $P = .02$). Patients completing treatment were significantly better on the GCS ($P = .01$), the social adjustment portion of the GCS ($P = .008$), and the EDI ($P = .005$) but not on the EAT or the ideal body weight percentage.

TABLE 2.—Outcome in Anorexic Groups Who Received Treatment Elsewhere*

| Outcome Variable | Treatment Elsewhere | | | Signifi-cance |
	None, n = 10	Partial, n = 8	Major, n = 9	
GCS†	5±3.6	6.3±2.3	7.3±3.9	NS
Ideal body weight %†	91.5±11	89±11.6	89±6.5	NS
Menses, Reg/Irreg/None	2/1/6	3/1/3	2/1/3	NS
GCS, Social Adjustment†	1.5±1.7	1.4±1.3	3.4±1.7	‡
Zung†	32.5±10.1	46±10	42±12	§
EAT†	22.3±15	25±13.5	33±20	NS
EDI†	35±20	62±35	56±31	NS

Irreg = irregular, NS = not significant, Reg = regular

*Higher scores on the global clinical score (GCS), the Eating Disorders Inventory (EDI), the Eating Attitude Test (EAT), and the Zung Self-Rating Depression Scale indicate more severe disease.
†Scores are given in the mean ± standard deviation.
‡Median one-way analysis: $\chi^2 = 5.9$, $df = 2$, $P = .02$.
§Median one-way analysis: $\chi^2 = 7.8$, $df = 2$, $P = .02$.

TABLE 3.—Comparison of Outcome of Anorexia With Restrictive and Bulimic Features*

| Outcome Variable | Anorexia Nervosa | | t | P |
	Restrictive, n = 27	Bulimic, n = 14		
GCS†	4.5±2.7	6.7±3.8	2.15	.04
Ideal body weight %†	88±10	93.4±6.5	1.9	NS
Menses, Reg/Irreg/None	7/4/14	5/2/4	2.9	NS‡
GCS, Social Adjustment†	1.1±1.4	2.7±1.5	3.3	.002
Zung†	37±10	43±10	1.94	.06
EAT†	24±17	24±17	0.07	NS
EDI†	36±28	56±34	2.1	.05
EDI minus bulimia subscale†	34±2	52±31	2.0	.05
Treatment categories, Inc/Major/Complete	6/8/13	6/7/1	7.0	.03‡
Major depression as secondary diagnosis	19/8	8/6	0.03	NS‡

Inc = incomplete, Irreg = irregular, NS = not significant, Reg = regular

*Higher scores on the global clinical score (GCS), the Eating Disorders Inventory (EDI), the Eating Attitude Test (EAT), and the Zung Self-Rating Depression Scale indicate more severe disease.
†Scores are given as the mean ± standard deviation.
‡Analysis by χ^2.

TABLE 4.—Comparison of Outcome in Anorexic Adolescents With and Without Secondary Diagnosis of Major Depression by DSM-III-R Criteria*†

Outcome Variable	With Depression, n = 14	Without Depression, n = 27	t	P
GCS	7.0±3.1	4.4±3.0	2.15	.01
Ideal body weight %	90±9	89±9	0.33	NS
Menses, Reg/Irreg/None	3/2/6	9/4/12	2.0	NS‡
GCS, Social Adjustment	2.3±1.9	1.4±1.4	1.8	.08
Zung†	48±9	34±8	4.8	.000
EAT†	36±20	18±12	3.6	.001
EDI†	68±32	28±20	4.8	.000
Treatment Categories, Inc/Major/Complete	5/5/4	7/10/10	0.5	NS‡

DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised,[26]
Inc = incomplete, Irreg = irregular, NS = not significant, Reg = regular

*Higher scores on the global clinical score (GCS), the Zung Self-Rating Depression Scale, the Eating Attitude Test (EAT), and the Eating Disorders Inventory (EDI) indicate more severe disease.
†Except for Menses, scores are given as the mean ± standard deviation.
‡Analysis by χ^2.

When we repeated this MANOVA with only the groups who had received treatment in other settings, there was a significant overall difference (Roy's greatest root = 0.852, F (4,21) = 6.5, P = .009). The group that had the most favorable outcome, however, was the one that had no further intervention. Furthermore, the only significant difference on specific outcome variables was on the social adjustment portion of the global clinical score (P = .008). All other differences—GCS, EDI, EAT and ideal body weight percentage—were not significant.

Outcome by Depression and Bulimic Features

Splitting the sample into groups based on the presence or absence of bulimia and depression, there were no significant differences on global clinical score, ideal body weight percentage, menses, and treatment completion, but the EDI, EAT, and the social adjustment ratings on the GCS were significantly different. Depression seems to most adversely influence psychopathology (EAT and EDI). Bulimia seems to influence mostly social adjustment and, possibly, treatment completion (Table 5).

Discussion

Our hypotheses were generally supported, but there were some important exceptions with respect to depression and bulimic behavior.

The outcome in the total sample is comparable to that reported in other treatment programs.[1-8,12-25] The fact that there were no deaths is probably due to our close medical supervision and the age of the sample. The difference in readmission to hospital rates between patients with bulimia and those with restrictive anorexia most likely reflects the former's problems with electrolytes and fluids that present as life-endangering emergencies. Spontaneous recovery seems to be rare (5%), having occurred in only one patient with a treatment score of 0 and another with a treatment score of 1. This rate is comparable to that reported by Vandereycken and Pierloot.[1] One of our patients had restrictive anorexia, the other a bulimic subtype; neither of them had a secondary diagnosis of depression.

Compliance with treatment was better than we expected and somewhat better than reported by Vandereycken and Pierloot.[1] Of the 27 patients who did not complete our program, 17 did go on to seek treatment elsewhere. In all, 9 seemed to complete their course of treatment, thus bringing the number of total compliance in 50 patients to 23 (46%). Only 3 of 41 patients (7%) refused any treatment altogether, either with us or elsewhere; 15 (37%) received at least some intervention, either with us or elsewhere. These percentages are not too different from findings in the treatment of other illnesses.[9,10] Patients suffering from anorexia seemingly are no worse a risk for noncompliance than other patients, at least in the adolescent age range. As the length of illness becomes more protracted and wearing, this favorable picture may change dramatically, an issue well worth further investigation. Also of interest was that patients with restrictive anorexia were more compliant with treatment, at least initially, while those with bulimic features had a much higher dropout rate. No other baseline variable predicted this. Because compliance rates for patients with bulimic and restrictive anorexia were comparable in subsequent treatment programs, it is possible that this phenomenon represents the bulimic anorexic patients' dissatisfaction with our program, which did not treat bulimic behavior in any specific way. We conceptualized bulimic symptoms as a by-product of starvation and reasoned that they would decline as weight rehabilitation proceeded. We subsequently revised this approach and now address bulimic symptoms in specific protocols. On the other hand, bulimic and restrictive anorexic patients' different patterns of engaging in treatment may have more general significance and relate to the patients' differing ways of forming treatment alliance or to more or less well-functioning families who see to it that treatment prescriptions get carried out.[3,4,6,12,15]

Although depression at diagnosis does not predict compliance initially, it does predict who will seek further treatment after the initial dropout. Depression, which is usually accompanied by more severe symptoms, does not seem to permit spontaneous recovery or recovery after minimal intervention but seems to lead patients to further treatment.

When the effects of completing the initial treatment program at Children's Hospital were examined, significant differences were noted between the groups on three of the four major outcome variables—GCS, EAT, EDI—but not in terms of depression. With some of the components of the GCS, the groups all fared equally well in terms of weight and menses. Differences manifest themselves on more subtle measures of general and specific features of eating disorders. This argues for the inclusion of such measures in future studies. Although the groups are almost identical in terms of weight and menstrual status, those who completed treatment could be less at risk for relapse in the years to come, most notably as they leave their families of origin. The exclusion of these measures might help explain the findings of Agras and Kraemer that there seem to be no specific treatment effects evident in anorexia nervosa.[24]

TABLE 5.—Outcome by Depression and Bulimic Features*†

	Type of Anorexia Nervosa					
Outcome Variable	Restrictive, Not Depressed, n = 19	Restrictive, Depressed, n = 8	Bulimic, Not Depressed, n = 8	Bulimic, Depressed, n = 6	χ^2	P
GCS‡	3.8 ± 2.5	6.1 ± 2.6	5.8 ± 3.8	8 ± 3.6	5.6	NS
Ideal body weight %‡	88 ± 10	88 ± 10	93 ± 7	94 ± 6.7	2.5	NS
Menses, Reg/Irreg/None	5/3/9	2/1/5	4/1/3	1/1/1	12.5	NS
GCS, Social Adjustment‡	1.1 ± 1.3	1.4 ± 1.7	2.1 ± 1.5	3.5 ± 1.4	11.4	.009
EAT‡	17 ± 12.5	39 ± 19	19 ± 13	31 ± 21	8.6	.04
EDI, minus bulimia subscale‡	25 ± 21	57 ± 24	35 ± 15	75 ± 34	15.5	.001
Treatment categories, Inc/Major/Complete	4/6/9	2/2/4	3/4/1	3/3/0	7.4	NS

Inc = incomplete, Irreg = irregular, NS = not significant, Reg = regular

*Higher scores on Garfinkel global clinical score (GCS), Eating Disorders Inventory (EDI), Eating Attitude Test (EAT), and Zung Self-Rating Depression Scale indicate more severe disease.
†Analyses by either χ^2 or median one-way analysis.
‡Scores are given as the mean ± standard deviation.

Our findings are also in line with those of Isager and associates that treatment beyond a year significantly reduced the risk for relapse.[2] Although the groups did not differ on several important variables at the outset, the distribution of restrictive and bulimic characteristics confounds our analysis, thus making it impossible to claim the specific effects of our treatment without examining those of treatment elsewhere.

These post hoc analyses suggest that either patients who complete the initial program have some favorable characteristics not measured in our assessment, or that our program is particularly effective with patients with restrictive anorexia. Subsequent treatment produced no significant differences on any of the major outcome variables (GCS, EDI, EAT), and those who received no further treatment at all had the most favorable outcome on all variables. Compared with the group who initially completed treatment, all three groups look less favorable; the one group closest to those completing treatment is the one with no further treatment. This suggests that patients who drop out initially are at a higher risk for a more protracted course, are less responsive to further treatment, and are probably at a higher risk for relapse. The presence of bulimic symptoms seems to confer greater morbidity, even when the added weight for bulimic symptoms is corrected for in the measurements. This finding is in line with several investigations[3,17,22,25] but not others.[12] The problems are not confined to specific eating problems but reflect general adjustment as well. In their study, Toner and colleagues found no differences among anorexic subgroups after seven years.[12] Our follow-up period is only half theirs, so it is possible that ultimately patients with bulimic features will become comparable to those with the restrictive subtype. Conversely, these features may be of different prognostic importance in adolescents.

Our findings of depression in a sizable portion of these patients replicates those from other studies in this adolescent population.[17,25,34] These mood problems do not resolve with the refeeding process, predict higher morbidity on follow-up, and are less responsive to treatment subsequent to initial treatment dropout. The use of antidepressants in patients with persistent mood disturbance after refeeding is recommended. When we repeated our initial between-treatment group analyses, using the Zung scores as a covariant, we still found a significant effect of treatment completion on outcome. Differences still favored those completing treatment. By contrast, when the same analysis of covariance between groups who had received treatment in other settings after dropout at Stanford was done, no such differences were detected. This suggests that our program may have specific effects that merit exploration in a controlled design.

When the possible differential effects of bulimic symptoms and depression are examined, our results suggest different influences. Depression seems to increase the self-report of an eating disorder, while bulimia worsens social adjustment, even when the weighing of bulimic symptoms is corrected. Depression seemingly increases "internalizing" symptoms (self-described suffering), but bulimia is more likely to be accompanied by "externalizing" symptoms (maladjustment readily observable by others).

The limitations of our study include a relatively small sample size, the relatively short duration of follow-up, and a lack of baseline data on one of the outcome measures.

Our results confirm the importance of reporting treatment compliance in outcome studies before judging the effectiveness of a treatment approach. It underlines the importance of a multimodal assessment beyond weight to achieve a complete picture of the effects of treatment. Presumably, weight gain accompanied by the correction of distorted attitudes is of better prognostic value than weight gained without such changes. Bulimic behavior needs special targeting beyond weight gain and psychotherapy.

Finally, depression does not seem to respond to psychosocial treatment alone and seems to contribute to a poor prognosis. Some of these patients might be better helped by psychopharmacologic intervention.

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