UC San Diego UC San Diego Previously Published Works

Title

Comparison of 2 Family Therapies for Adolescent Anorexia Nervosa: A Randomized Parallel Trial

Permalink https://escholarship.org/uc/item/9wg9p412

Journal JAMA Psychiatry, 71(11)

ISSN 2168-622X

Authors

Agras, W Stewart Lock, James Brandt, Harry <u>et al.</u>

Publication Date

2014-11-01

DOI

10.1001/jamapsychiatry.2014.1025

Peer reviewed



HHS Public Access

Author manuscript JAMA Psychiatry. Author manuscript; available in PMC 2018 October 03.

Published in final edited form as:

JAMA Psychiatry. 2014 November; 71(11): 1279–1286. doi:10.1001/jamapsychiatry.2014.1025.

Comparison of 2 Family Therapies for Adolescent Anorexia Nervosa:

A Randomized Parallel Trial

W. Stewart Agras, MD, James Lock, MD, PhD, Harry Brandt, MD, Susan W. Bryson, MA, MS, Elizabeth Dodge, MSc, Katherine A. Halmi, MD, Booil Jo, PhD, Craig Johnson, PhD, Walter Kaye, MD, Denise Wilfley, PhD, and Woodside Blake, MD

Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, California (Agras, Lock, Bryson, Jo); Sheppard Pratt Health System, Baltimore, Maryland (Brandt); Department of Psychological Medicine, University of Otago, Otago, New Zealand (Dodge); Department of Psychiatry, Weill Medical College, Cornell University, New York, New York (Halmi); Eating Recovery Center, Denver, Colorado (Johnson); Center for Eating Disorders, Department of Psychiatry, University of California, San Diego (Kaye); Department of Psychiatry, Washington University, St Louis, Missouri (Wilfley); Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada (Woodside).

Abstract

IMPORTANCE—Anorexia nervosa (AN) is a serious disorder with high rates of morbidity and mortality. Family-based treatment (FBT) is an evidence-based therapy for adolescent AN, but less than half of those who receive this approach recover. Hence, it is important to identify other approaches to prevent the development of the chronic form of AN for which there is no known evidence-based treatment.

OBJECTIVE—To compare FBT with systemic family therapy (SyFT) for the treatment of adolescent-onset AN.

DESIGN, SETTING, AND PARTICIPANTS—Research in Anorexia Nervosa (RIAN) is a 2group (FBT and SyFT) randomized trial conducted between September 2005 and April 2012. Interviewers were blinded to the treatment condition. A total of 564 adolescents receiving care at 6

- Acquisition, analysis, or interpretation of data: Agras, Brandt, Bryson, Halmi, Jo, Johnson, Kaye, Wilfley, Woodside.
- Drafting of the manuscript: Agras, Lock, Brandt, Jo, Johnson, Kaye, Wilfley, Woodside.

Corresponding Author: W. Stewart Agras, MD, Department of Psychiatry and Behavioral Sciences, Stanford University, Room 1322, 401 Quarry Rd, Stanford, CA 94305 (sagras@stanford.edu).

Author Contributions: Dr Agras had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Agras, Lock, Brandt, Dodge, Halmi, Johnson, Kaye, Woodside.

Critical revision of the manuscript for important intellectual content: Agras, Lock, Brandt, Dodge, Halmi, Jo, Johnson, Kaye, Wilfley, Woodside.

Statistical analysis: Bryson, Jo.

Obtained funding: Agras, Lock, Brandt, Halmi, Johnson, Kaye, Wilfley, Woodside.

Administrative, technical, or material support: Agras, Lock, Brandt, Halmi, Johnson, Kaye, Wilfley, Woodside.

Study supervision: Agras, Lock, Dodge, Halmi, Johnson, Kaye, Wilfley, Woodside.

Conflict of Interest Disclosures: Dr Agras receives royalties from Oxford University Press. Dr Lock receives royalties from Guildford Press and Oxford University Press and payments from the Training Institute for Child and Adolescent Eating Disorders. Dr Kaye is a consultant to the Eating Disorder Center of Denver. Dr Wilfley is on the Boards of the Wellspring Healthy Living Academy and the Childhood Obesity Initiative (United Health Group). No other disclosures were reported.

outpatient clinics experienced in the treatment of AN were screened. Of these, 262 adolescents did not meet the inclusion criteria and 138 declined to participate; hence, 164 adolescents (aged 12–18 years) of both sexes meeting the criteria for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* AN (except for amenorrhea) were enrolled. Three participants were withdrawn from FBT and 7 were withdrawn from SyFT after serious adverse events occurred.

INTERVENTIONS—Two manualized family therapies with 16 one-hour sessions during 9 months. Family-based therapy focuses on the facilitation of weight gain, whereas SyFT addresses general family processes.

MAIN OUTCOMES AND MEASURES—The primary outcomes were percentage of ideal body weight (IBW) and remission (95% of IBW). The a priori hypothesis was that FBT would result in faster weight gain early in treatment and at the end of treatment (EOT).

RESULTS—There were no statistically significant differences between treatment groups for the primary outcome, for eating disorder symptoms or comorbid psychiatric disorders at the EOT or follow-up. Remission rates included FBT, 33.1% at the EOT and 40.7% at follow-up and SyFT, 25.3% and 39.0%, respectively. Family-based therapy led to significantly faster weight gain early in treatment, significantly fewer days in the hospital, and lower treatment costs per patient in remission at the EOT (FBT, \$8963; SyFT, \$18 005). An exploratory moderator analysis found that SyFT led to greater weight gain than did FBT for participants with more severe obsessive-compulsive symptoms.

CONCLUSIONS AND RELEVANCE—The findings of this study suggest that FBT is the preferred treatment for adolescent AN because it is not significantly different from SyFT and leads to similar outcomes at a lower cost than SyFT. Adolescents with more severe obsessive-compulsive symptoms may receive more benefits with SyFT.

TRIAL REGISTRATION—clinicaltrials.gov Identifier NCT 00610753

Early identification of anorexia nervosa (AN) and the continued development of effective interventions are crucial because, as the illness progresses into adulthood, it becomes increasingly difficult and more expensive to treat.¹⁻³ Moreover, AN has one of the highest morbidity and mortality rates of all psychiatric disorders.⁴ Family therapy has been a mainstay of treatment for adolescent AN since the pioneering work of Minuchin et al.⁵ Most controlled trials^{5–7} to date have consisted of a family therapy that focuses on engaging the parents to manage the eating disorder; this approach is often referred to as family-based *therapy* (FBT). The first controlled trial⁸ using FBT found that this type of therapy was superior to individual psychotherapy for adolescents with a duration of AN of less than 3 years. This result was maintained at a 5-year follow-up evaluation.⁹ Two subsequent controlled trials^{10,11} found similar results confirming the superiority of FBT over individual psychotherapy. However, few studies have examined other family therapies for adolescent AN. One study¹² compared a version of FBT and family psycho-education for hospitalized adolescents with AN. The investigators identified no difference in outcome between the groups. A second study¹³ examined the addition of systemic family therapy (SyFT), an approach that does not focus on engaging the family to manage the eating disorder, to treatment as usual for adolescent AN. The combined approach was more effective, suggesting that SyFT may be useful in the treatment of AN. Hence, the present study

compared 2 family therapies differing in the focus on engaging the family to manage the disorder. We hypothesized that FBT, because of the early focus on refeeding, would be more rapidly effective, superior to SyFT for weight gain, and have a greater percentage of remission at the end of treatment.

Methods

Study Design

The Research in Anorexia Nervosa (RIAN) is a 2-group (FBT and SyFT) randomized trial. The study was approved by the institutional review board at each site. After the study was described to participating families, written informed consent was obtained from the parents and assent was obtained from the adolescents and their siblings. The participants did not receive financial compensation. A data and safety monitoring board appointed by the National Institute of Mental Health evaluated the participants' safety and trial progress. The design of the trial has previously been published.¹⁴ The study was conducted between September 1, 2005, and April 31, 2012, and involved a randomized parallel comparison of FBT and SyFT. The study was designed to detect a moderate effect size (Cohen d = 0.5) on differences in the percentage of ideal body weight (%IBW) between groups. With use of a 5% 2-tailed significance test, 160 participants were required for a power of 0.88. Participants were randomized within sites to one of the 2 family therapies using a computer-generated program.

The study originally involved a coordinating center and 6 clinical sites, and all were experienced in the treatment of AN (Table 1). One site was closed early in the trial because of an inability to recruit sufficient participants and was replaced by the Stanford site.

Sample Characteristics

One hundred sixty-four adolescents (aged 12–18 years) meeting diagnostic criteria for the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, definition of AN, except for the amenorrhea criterion, and with weight up to 87% of their IBW were entered into the study. Exclusion criteria included current psychotic illness, mental retardation that would prohibit the use of psychotherapy, bipolar disorder, pregnancy, dependence on drugs or alcohol, previous family therapy for AN, taking medications that may induce weight loss, and medical instability, including being at a weight at or below 75% of the IBW. Participants who were medically unstable were eligible for entry to the study when they became medically stable for outpatient treatment.

Participant Safety and Adverse Events

We followed the guidelines of the American Academy of Pediatrics¹⁵ and the Society for Adolescent Medicine¹⁶ for medical hospitalization of the adolescent with AN. If hospitalization was required, the participant was returned to the study arm as randomized after discharge. However, participants were withdrawn from treatment if they were hospitalized for longer than 28 days because too much treatment time would have been lost. Safety procedures also included within-site physician visits, monthly electrolyte determination, and the following tests at baseline, 8 weeks, 6 months, and 9 months:

Page 4

electrocardiography, liver function tests, serum electrolytes, blood urea nitrogen, creatine kinase, serum creatinine, and urinalysis. Data on adverse events were collected at all on-site medical visits and defined as an unfavorable change from the participant's condition at baseline. Serious adverse events were life-threatening events, death, hospitalizations for any cause, or other important medical or psychological events. All adverse events were reported to the data and safety monitoring board quarterly except for serious adverse events or unexpected hospitalizations; these were immediately reported.

Interventions

Both treatments were manualized and consisted of 16 one-hour sessions over a 9-month period. In a previous study,¹⁷ shorter treatment (10 sessions during 6 months) was as effective as longer treatment. We chose not to use the shorter treatment in the present study because patients with obsessive-compulsive features showed more improvement with the longer treatment and because this duration of treatment was believed to be more suitable for SyFT, thus ensuring an adequate comparison. Family-based therapy is a focused treatment that engages the family to facilitate weight restoration in their child.¹⁸ The therapist encourages the family to work out the best method to restore their child's normal eating behavior. When steady weight gain occurs, the therapist encourages the family to allow their child to begin independent age-appropriate eating. In the final sessions, issues concerning normal adolescent development are addressed. In SyFT, the focus is placed on the family system.^{19,20} Difficulties arise not in individuals themselves but in the relationships, interactions, and language that develop between individuals. The therapist adopts a neutral stance and, through exploration of family patterns of beliefs and behaviors, seeks ways to enable the family to draw on their existing strengths and generate new solutions to the problem that they have brought to therapy. There is no family meal or specific emphasis on normalization of eating or weight, although if the family raises this issue, the therapist will help them address it.

The 26 therapists were doctorate- or masters-level psychologists, psychiatrists, or social workers, with a mean of 6 years' experience in the treatment of adolescent AN. Treatment was delivered by different therapists for each family therapy to minimize cross-contamination. Therapists were not randomized to one or the other of the family therapies. Therapists were trained in separate workshops for each treatment and then completed treatment for 2 cases with supervision from experts in each type of family therapy (J.L. for FBT and E.D. for SyFT). Supervision of therapists continued at weekly intervals throughout the treatment phase and were provided centrally by the data and coordinating center and at the site level by a trained supervisor, with each treatment supervised separately. Elements of supervision included listening to therapy tapes, case discussions focusing on the process of treatment, behavioral rehearsal, and treatment planning.

Assessments

Assessments were conducted at baseline, the end of treatment (EOT) (36 weeks), the 6month follow-up, and the 1-year follow-up (88 weeks). Outcomes between treatments were compared at the EOT and 1-year follow-up. The 6-month assessment was used for statistical modeling. The primary outcome was percentage of IBW calculated using a computer

program based on the Centers for Disease Control and Prevention's²¹ growth charts with weight adjusted for age, sex, and height. *Remission* was defined as achieving a minimum of 95% of the IBW, which is supported by previous research^{22–24} demonstrating that this criterion was the best predictor of long-term recovery that included both weight and psychological components.

Assessors were blinded to treatment assignment. Weight was assessed on a balance beam scale with the participant in a hospital gown after voiding, and height was assessed using a stadiometer. The Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version, an interview used to detect psychiatric disorders in children and adolescents, was administered at baseline.²⁵ Parents and adolescents were interviewed to obtain summary ratings. Secondary outcome measures were administered at baseline and subsequent assessments except for treatment suitability, which was rated at the end of session 1. The Eating Disorder Examination is a standardized, investigator-based interview that measures the severity of the characteristic symptoms of eating disorders. It is exclusively concerned with the preceding 4 weeks.²⁶ Ouestionnaires completed at the same intervals included the Beck Depression Inventory,²⁷ the State-Trait Anxiety Inventory,²⁸ the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS),²⁹ the Rosenberg Selfesteem Scale,³⁰ the Yale-Brown-Cornell Eating Disorder Scale,³¹ and the Quality of Life Enjoyment and Satisfaction Questionnaire.³² Fidelity to each treatment was assessed at one of the sites by 6 raters with a graduate degree in psychology or social work and experience in treating eating disorders. Raters were trained in one of the 2 treatments by reading the manual and viewing tapes of the training workshop for clinicians and were also trained in the application of the appropriate fidelity instrument for which reliability was established. Each site provided 4 videotapes per family randomly sampled from each of the following blocks of sessions: 1 to 4, 5 to 8, 9 to 12, and 13 to 16.

Statistical Analysis

Baseline measures for the 2 treatments were compared using a 2-way analysis of variance for continuous baseline measures, with center, treatment, and the interaction as the independent measures. Categorical baseline measures were compared using logistic regression analysis. If the normality assumption was violated (eg, hospitalization), data were analyzed using nonparametric tests.

To assess the outcomes, we used standard linear mixed-effects modeling^{33,34} to model the change over time using all 4 repeated assessments (baseline, EOT, 6-month follow-up, and 12-month follow-up) for the primary and secondary variables with such data. Missing data points were treated as missing at random conditional on observed information using maximum likelihood estimation.³⁵ For IBW and Eating Disorder Examination outcomes, individuals' assessment weeks from base-line were log transformed to approximate linearity in the relationship between time and outcome. Based on the transformed data, growth modeling was conducted assuming a linear trend. After these analyses, estimated trajectories were transformed back to their original scale for easier interpretation. Mixed-effects modeling was performed by intent-to-treat analysis using all participants. The same analytic strategy was used for secondary outcomes. For remission, we conducted mixed-effects

growth modeling using 3 repeated measures (EOT, 6-month follow-up, and 12-month follow-up) because there is no variation in the data at baseline. We used a random intercept model with individually varying time scores (assessment weeks from baseline), treating remission status as a binary outcome. For the exploratory moderator analysis, we incorporated the MacArthur framework^{36,37} in the longitudinal modeling. Sixteen baseline variables were included: age, Beck Depression Inventory, binge eating, compensatory behavior, comorbidity, CY-BOCS, duration of AN, Global Eating Disorder Examination, intact family, sex, minority race/ ethnicity, perfectionism, self-esteem, Quality of Life Scale, the Yale-Brown-Cornell Eating Disorder Scale, and psychoactive medications. We used the Mplus program (version 7)³⁸ to conduct maximum likelihood estimation for all longitudinal mixed-effects analyses. Treatment costs were calculated using specific site costs for hospital per diem rates and for family therapy sessions. If hospital costs were not available (eg, a site might use several hospitals to admit medically unstable patients), the average per diem rate in that state or Canadian province was used. Total costs for each site were divided by either the number of patients enrolled in the study by treatment or the number who achieved remission.

Results

Participant Characteristics

As shown in Figure 1, a total of 564 adolescents were screened; 164 were eligible and entered the study, with 82 participants randomly allocated to each treatment arm. Three participants (the total from the closed site) were not included in the analysis because the site would have the same influence as other locations on the estimation of the main effects of treatment despite its smaller sample size. In addition, 3 participants who were hospitalized before receiving treatment and did not return to the study were excluded. Hence, there were 78 participants in FBT and 80 in SyFT, for a total of 158 individuals included in the analysis.

There were no significant differences between groups for any demographic or baseline variable. The mean (SD) age of participants was 15.3 (1.8) years, and 89.2% (n = 141) were female. Most participants were white (79.1%), with 10.1% Hispanic and 5.1% Asian. The mean duration of illness was 13.5(13.9) months. The most common comorbid condition was major depression, followed by obsessive-compulsive and anxiety disorders. The mean percentage of IBW at baseline was 81.9%, and 44.3% of the adolescents engaged in some form of compensatory behavior (Table 1 and Table 2).

Treatment Suitability

Adolescents' ratings of treatment suitability at the end of the first treatment session on a 0 to 10 scale did not differ significantly between the 2 treatments: 5.3 (3.3) for FBT and 5.6 (2.6) for SyFT. Parents' ratings were significantly different between treatments (fathers: 7.9 [2.3] for FBT and 7.0 [1.7] for SyFT; $F_{1,115} = 4.8$; P = .03; and mothers: 8.1 [2.0] for FBT and 7.4 [2.0] for SyFT; $F_{1,136} = 5.1$; P = .02).

Treatment Fidelity and Exposure to Treatment

A total of 421 therapy tapes were audited (210 FBT and 211 SyFT). The overall mean scores for fidelity were FBT 4.15 (0.94) and SyFT 4.38 (0.48) on a 0 to 6 scale. There were no statisti cally significant differences between the groups for the numbers or trajectories of treatment dropouts or for withdrawals from treatment. Twenty-six percent of the participants withdrew from FBT (n = 20) and 25% (n = 20) withdrew from SyFT. The major reasons for the dropouts were dissatisfaction with treatment and transportation difficulties. Three (4%) participants were withdrawn from FBT and 7 (9%) were withdrawn from SyFT for prolonged medical instability during the treatment period. The numbers of treatment sessions completed excluding dropouts and withdrawals were identical at 15.6 (1.0) for the 2 treatments.

Primary and Secondary Outcomes

Table 2 and Figure 2 summarize the results of the longitudinal analyses for the primary and secondary outcomes. There were no statistically significant differences between treatment groups for IBW at either EOT or follow-up. The percentage of IBWs for FBT at EOT and 12-month follow-up were 92.1% and 94.6%, respectively; the corresponding results for SyFT were 91.1% and 93.3%. However, we found that adolescents who received FBT gained weight significantly faster over the first phase (8 weeks) of treatment ($F_{1,146} = 8.8$; P = .003) in accord with our hypothesis. Remission rates for FBT were 33.1% at the EOT and 40.7% at the 12-month follow-up; the corresponding rates for SyFT were 25.3% and 39.0%. The only significant difference between the treatments in the secondary outcomes was the Rosenberg Self-esteem Scale favoring SyFT (Table 2).

Predictors and Moderators of Outcome

Two predictors of weight gain regardless of treatment were found: younger patients (P=.04) and those with a shorter duration of illness (P=.04) gained more weight. Intact families (P=.02) and AN without binge eating or purging (P=.04) had higher rates of remission regardless of the treatment used.

The CY-BOCS total score at baseline moderated the effect of treatment on the IBW (P= . 02). Individuals with a higher score denoting greater obsessive-compulsive psychopathology gained significantly more weight with SyFT by the end of treatment, whereas those with lower scores gained less weight (Figure 3). Conversely, individuals with high scores on the CY-BOCS gained less weight with FBT, whereas those with low scores gained more weight. Participants with a high score on the CY-BOCS also had higher scores on the global Eating Disorder Examination ($T_{156} = 3.7$; P < .001), the Beck Depression Inventory ($T_{156} = 4.2$; P < .001), the State-Trait Anxiety Inventory ($T_{153} = 5.1$; P < .001), and for compensatory behaviors such as purging, laxative use, and excessive exercise (75% vs 40%); $\chi^2_1 = 12.0$; P < .001). However, participants with a high score on the CY-BOCS did not differ significantly on weight at baseline from those with low scores.

Adverse Events

There were no deaths and no significant difference between treatment groups for serious adverse events, with 12 participants (15.4%) with an event in FBT and 20 (25.0%) in SyFT.

Twenty-seven events were for hospitalization due to medical instability, and the remainder were for suicidal ideation or suicide attempts.

Costs of Treatment

The median number of days per hospitalization was 8.3 for FBT and 21.0 for SyFT (U=51; P=.02; number needed to treat, 2). This outcome resulted in mean treatment costs per individual (family therapy plus hospitalizations until the EOT) of \$8963 for FBT and \$18 005 for SyFT. The mean costs per individual in remission were \$21 847 for FBT and \$46 465 for SyFT.

Treatment During Follow-up

Treatments during the follow-up period did not differ significantly between treatment groups (n = 114). For FBT, 35.1% (n = 19) received some form of psychotherapy during the 12-month period after the end of study treatment compared with 25.0% (n = 15) of the SyFT group. Medical management for AN was continued in 11.1% (n = 6) of the FBT group and 15.0% (n = 9) of the SyFT group. Hospitalization occurred in 5.6% (n = 2) of the FBT group and 1.7% (n = 1) of the SyFT group during the follow-up period.

Discussion

To our knowledge, the present study is the largest randomized clinical trial comparing forms of family therapy for the treatment of adolescent AN. We found no statistically significant differencesbetweenthe2familytherapiesforweightgainorweight remission to 95% or greater of the IBW at the EOT or 12-month follow-up. Hence, our hypothesis that FBT would be more effective than SyFT at the EOT or follow-up was not supported. One reason for this outcome may be procedural overlap between the treatments. In SyFT, families seek solutions that may involve parents focusing on a range of behaviors, including weight. There was, however, evidence for our second hypothesis that participants who received FBT would gain weight faster compared with those in SyFT in the early stage of treatment. The rapidity of weight gain with FBT early in treatment may have decreased medical instability. This in turn may have reduced the use of hospitalization significantly and lowered the treatment cost, with FBT costing approximately half as much as SyFT. These findings replicate a previous finding¹¹ that significantly fewer participants in FBT were hospitalized compared with those receiving individual psychotherapy for adolescent AN. Parents also rated FBT as significantly more suitable than SyFT after the first treatment session and may be more likely, therefore, to choose a family therapy focused on weight gain.

We also identified a moderator for change in weight for a subgroup of participants, with high scores on the CY-BOCS showing significantly greater improvement in SyFT compared with FBT. Obsessive-compulsive features have been found to moderate outcomes in previous family therapy studies^{17,39} of adolescent AN. These findings suggest that SyFT may be the preferred treatment for adolescents with AN and obsessive-compulsive symptoms.

The strengths of the present study include the successful recruitment of a sample with sufficient power to test the comparisons of interest, use of manualized treatments, training and supervisory processes across treatment sites, use of standardized interviews and

outcome measures, and use of assessors blinded to treatment allocation. One limitation of the study is that the results apply only to adolescents weighing more than 75% of their IBW because this group was deemed to meet the standard of care required for safe outpatient treatment. A further limitation is the loss of a site owing to a failure to recruit, requiring replacement of that site. Costs calculated are estimates of direct costs of care and do not take societal costs into account. In addition, we were not able to account for costs of treatment during the follow-up period.

Conclusions

From a clinical viewpoint, this study adds to the growing evidence supporting the usefulness of family therapy in the treatment of adolescent AN. For example, previous studies^{3–5} have found that FBT is superior to individual psychotherapy. The findings from the present study suggest that the type of family therapy matters. Each family therapy has specific advantages that are clinically important. Although both treatments are equally effective in terms of weight gain, FBT promotes early weight gain that may reduce the need for hospitalization, leading to lower costs at the EOT. However, SyFT may be more effective for adolescents with more severe obsessive-compulsive features. The findings from this study and from previous research are encouraging because families averse to one form of treatment have other effective treatments from which to choose.

Acknowledgments

Funding/Support: The study was supported in part by the following grants from the National Institute of Mental Health: 1UO1 MH076290 (Dr Agras), MH 076254 (Dr Brandt), MH 076251 (Dr Halmi), MH 076250 (Dr Johnson), MH 076255 (Dr Wilfley), and 076252 (Dr Woodside).

Role of the Funder/Sponsor: The sponsor had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

- Bulik CM, Berkman ND, Brownley KA, Sedway JA, Lohr KN. Anorexia nervosa treatment: a systematic review of randomized controlled trials. Int J Eat Disord. 2007;40(4):310–320. [PubMed: 17370290]
- 2. Watson HJ, Bulik CM. Update on the treatment of anorexia nervosa: review of clinical trials, practice guidelines and emerging interventions. Psychol Med 2013;43(12):2477–2500. [PubMed: 23217606]
- Striegel-Moore RH, DeBar L, Wilson GT, et al. Health services use in eating disorders. Psychol Med. 2008;38(10):1465–1474. [PubMed: 17976250]
- 4. Harris EC, Barraclough B. Excess mortality of mental disorders. Br J Psychiatry. 1988;173:11-53.
- Minuchin S, Baker L, Rosman BL, Liebman R, Milman L, Todd TC. A conceptual model of psychosomatic illness in children: family organization and family therapy. Arch Gen Psychiatry. 1975;32(8): 1031–1038. [PubMed: 808191]
- 6. Hay P A systematic review of evidence for psychological treatments in eating disorders: 2005–2012. Int J Eat Disord. 2013;46(5):462–469. [PubMed: 23658093]
- Couturier J, Kimber M, Szatmari P. Efficacy of family-based treatment for adolescents with eating disorders: a systematic review and meta-analysis. Int J Eat Disord. 2013;46(1):3–11. [PubMed: 22821753]

- Russell GF, Szmukler GI, Dare C, Eisler I. An evaluation of family therapy in anorexia nervosa and bulimia nervosa. Arch Gen Psychiatry. 1987;44 (12):1047–1056. [PubMed: 3318754]
- Eisler I, Dare C, Russell GF, Szmukler G, le Grange D, Dodge E. Family and individual therapy in anorexia nervosa: a 5-year follow-up. Arch Gen Psychiatry. 1997;54(11):1025–1030. [PubMed: 9366659]
- Robin AL, Siegel PT, Moye AW, Gilroy M, Dennis AB, Sikand A. A controlled comparison of family versus individual therapy for adolescents with anorexia nervosa. J Am Acad Child Adolesc Psychiatry. 1999;38(12):1482–1489. [PubMed: 10596247]
- Lock J, Le Grange D, Agras WS, Moye AW, Bryson SW, Jo B. Randomized clinical trial comparing family-based treatment with adolescent-focused individual therapy for adolescents with anorexia nervosa. Arch Gen Psychiatry. 2010;67(10):1025–1032. [PubMed: 20921118]
- Geist R, Heinmaa M, Stephens D, Davis R, Katzman DK. Comparison of family therapy and family group psychoeducation in adolescents with anorexia nervosa. Can J Psychiatry. 2000;45(2): 173–178. [PubMed: 10742877]
- Godart N, Berthoz S, Curt F, et al. A randomized controlled trial of adjunctive family therapy and treatment as usual following inpatient treatment for anorexia nervosa adolescents. PLoS One. 2012;7(1):e28249. doi:10.1371/journal.pone.0028249. [PubMed: 22238574]
- Lock J, Brandt H, Woodside B, et al. Challenges in conducting a multi-site randomized clinical trial comparing treatments for adolescent anorexia nervosa. Int J Eat Disord. 2012;45(2):202–213. [PubMed: 21495052]
- Rosen DS; American Academy of Pediatrics Committee on Adolescence. Identification and management of eating disorders in children and adolescents. Pediatrics. 2010;126(6):1240–1253. [PubMed: 21115584]
- Golden NH, Katzman DK, Kreipe RE, et al.; Society for Adolescent Medicine. Eating disorders in adolescents: position paper of the Society for Adolescent Medicine. J Adolesc Health. 2003;33(6): 496–503. [PubMed: 14642712]
- Lock J, Agras WS, Bryson S, Kraemer HC. A comparison of short- and long-term family therapy for adolescent anorexia nervosa. J Am Acad Child Adolesc Psychiatry. 2005;44(7):632–639. [PubMed: 15968231]
- Lock J, Le Grange D, Agras WS, Dare C. Treatment Manual for Anorexia Nervosa: A Family-Based Approach. New York, NY: Guildford Press; 2013.
- Pote H, Stratton P, Cottrell D, Boston P, Shapiro D. Systemic Family Therapy Manual. Leeds, England: University of Leeds, Family Therapy Research Center; 2001.
- 20. Pote H, Stratton P, Cottrell D, Shapiro D, Boston P. Systemic family therapy can be manualized: research process and findings. J Fam Ther. 2003;25(3):236–262.
- Grummer-Strawn LM, Reinold C, Krebs NF; Centers for Disease Control and Prevention (CDC). Use of World Health Organization and CDC growth charts for children aged 0–59 months in the United States. MMWR Recomm Rep 2010;59(RR-9):1–15.
- 22. Couturier J, Lock J. What constitutes remission in adolescent anorexia nervosa: a review of various conceptualizations and a quantitative analysis. Int J Eat Disord. 2006;39(3):175–183. [PubMed: 16485268]
- 23. Couturier J, Lock J. What is recovery in adolescent anorexia nervosa? Int J Eat Disord. 2006;39(7): 550–555. [PubMed: 16791851]
- 24. Lock J, Agras WS, Le Grange D, Couturier J, Safer D, Bryson SW. Do end of treatment assessments predict outcome at follow-up in eating disorders? Int J Eat Disord. 2013;46(8):771– 778. [PubMed: 23946139]
- Kaufman J, Birmaher B, Brent D, et al. Schedule for affective disorders and schizophrenia for school-age children—present and lifetime version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997;36(7):980–988. [PubMed: 9204677]
- 26. Fairburn CG, Beglin SJ. Assessment of eating disorders: interview or self-report questionnaire? Int J Eat Disord. 1994;16(4):363–370. [PubMed: 7866415]
- 27. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4(6):561–571. [PubMed: 13688369]

- 28. Spielberger CD, Gorusch RL, Lushene RE. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1970.
- Scahill L, Riddle MA, McSwiggin-Hardin M, et al. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. J Am Acad Child Adolesc Psychiatry. 1997;36(6):844–852. [PubMed: 9183141]
- 30. Rosenberg M Conceiving the Self. New York, NY: Basic Books; 1979.
- Mazure CM, Halmi KA, Sunday SR, Romano SJ, Einhorn AM. The Yale-Brown-Cornell Eating Disorder Scale: development, use, reliability and validity. J Psychiatr Res. 1994;28(5):425–445. [PubMed: 7897615]
- 32. Endicott J, Nee J, Harrison W, Blumenthal R. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. Psychopharmacol Bull 1993;29(2):321–326. [PubMed: 8290681]
- Raudenbush S, Bryk A. Hierarchical Linear Models: Applications and Data Analysis Methods. New York, NY: Sage; 2002.
- Singer JD, Willet JB. Applied Longitudinal Data Analysis: Modeling Change and Event Occurrence. Oxford, England: Oxford University Press; 2003.
- 35. Little RJA, Rubin DB. Statistical Analysis With Missing Data. New York, NY: Wiley; 2002.
- 36. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and moderators of treatment effects in randomized clinical trials. Arch Gen Psychiatry. 2002;59(10):877–883. [PubMed: 12365874]
- Kraemer HC, Kiernan M, Essex M, Kupfer DJ. How and why criteria defining moderators and mediators differ between the Baron & Kenny and MacArthur approaches. Health Psychol. 2008;27(2) (suppl):S101–S108. [PubMed: 18377151]
- 38. Muthen LK, Muthen BO. Mplus Users Guide. Los Angeles, CA: Muthen & Muthen; 1998–2012.
- Le Grange D, Lock J, Agras WS, et al. Moderators and mediators of remission in family-based treatment and adolescent focused therapy for anorexia nervosa. Behav Res Ther. 2012;50(2):85– 92. [PubMed: 22172564]

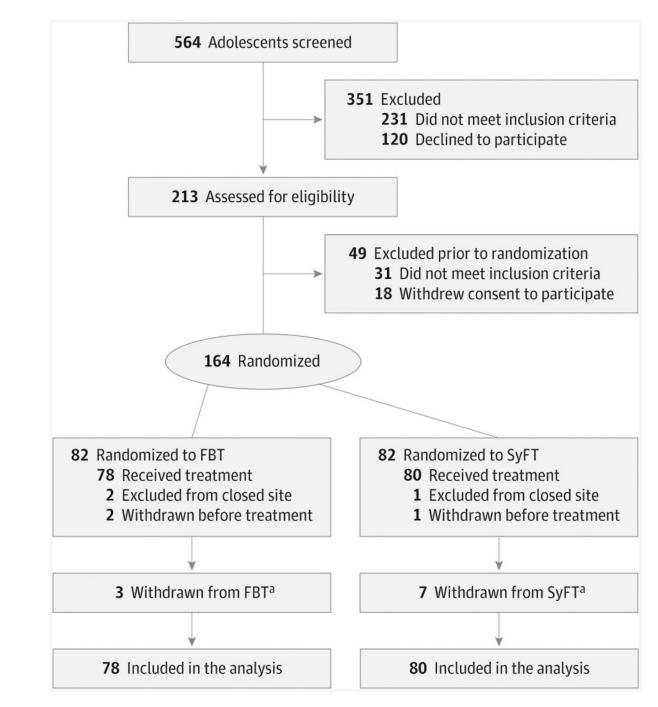


Figure 1. Participant Recruitment and Randomization in a Trial Comparing 2 Family Therapies for the Treatment of Adolescent Anorexia Nervosa

FBT indicates family-based therapy; SyFT, systemic family therapy.

^a Participants withdrawn during the treatment period were included in the analysis.

Agras et al.

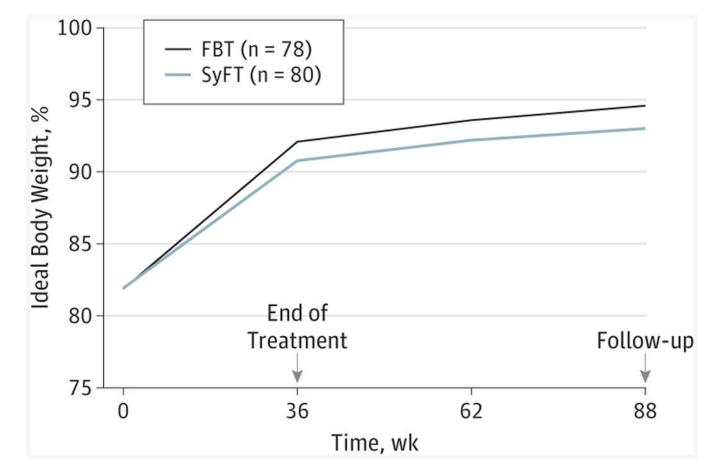


Figure 2. Change in the Primary Outcome

Change in the percentage of ideal body weight was measured from baseline to the 1-year follow-up. FBT indicates family-based therapy; SyFT, systemic family therapy.

Agras et al.

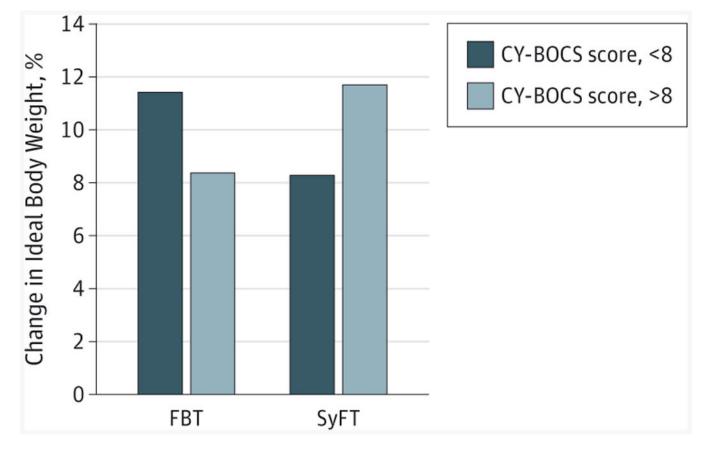


Figure 3. Moderator Effect Showing Weight Change From Baseline to End of Treatment High and low scores on the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) indicated. FBT indicates family-based therapy; SyFT, systemic family therapy.

Table 1.

Demographics of the Participants

	No. (%)			
Variable	FBT (n = 78)	SyFT (n = 80)	Total (N = 158)	
Study center, No. of participants				
Weill Medical College, Cornell University	14 (17.9)	16 (20.0)	30 (19.0)	
School of Medicine, University of California at San Diego	13 (16.7)	12 (15.0)	25 (15.8)	
School of Medicine, Washington University	14 (17.9)	13 (16.2)	27 (17.1)	
School of Medicine, University of Toronto	12 (15.4)	14 (17.5)	26 (16.4)	
School of Medicine, Stanford University	14 (17.9)	14 (17.5)	28 (17.2)	
Sheppard Pratt Health System	11 (14.1)	11 (13.8)	22 (13.9)	
Demographic characteristics				
Age, mean (SD), y	15.1 (1.7)	15.6 (1.8)	15.3 (1.8)	
Female sex	67 (85.9)	74 (92.5)	141 (89.2)	
Race/ethnicity				
White	59 (75.6)	66 (82.5)	125 (79.1)	
Asian	5 (6.4)	3 (3.8)	8 (5.1)	
Hispanic	7 (9.0)	9 (11.2)	16 (10.1)	
>1 Race/ethnicity	7 (9.0)	2(2.5)	9(5.7)	
Current comorbid psychopathologic disorder				
Depressive	20 (25.6)	20 (25.0)	40 (25.3)	
Anxiety	11 (14.1)	6(7.5)	17 (10.8)	
Obsessive-compulsive	8 (10.2)	10 (12.5)	18 (11.4)	
Other	7 (9.0)	9 (11.2)	16 (10.1)	
Duration of illness, mean (SD), mo	11.6 (9.8)	15.4 (16.9)	13.5 (13.9)	
Engages in compensatory behaviors	33 (42.3)	37 (46.2)	70 (44.3)	
Receiving psychoactive medications	14 (17.9)	16 (20.0)	30 (18.9)	

Abbreviations: FBT, family-based treatment; SyFT, systemic family therapy.

Table 2.

Differences for the Primary and Secondary Outcomes Based on Mixed-Effects Longitudinal Analysis

Variable	Mear	n (SD)	Group Difference	
	FBT	SyFT	Effect Size ^a	<i>P</i> Value
Ideal body weight, %				-
Baseline	82.2 (3.8)	81.7 (3.7)		
ЕОТ	92.1	91.1	<i>d</i> = 0.13	.31
12 mo	94.6	93.3	d = 0.14	.31
Remission, %				
ЕОТ	0.33	0.25	SRD = 0.08, NNT = 13	.22
12 mo	0.41	0.39	SRD = 0.02, NNT = 59	.84
Eating Disorder Examination				
Baseline	1.6 (1.3)	1.9 (1.5)		
EOT	1.2	1.2	d = -0.18	.10
12 mo	0.8	1.1	d = -0.20	.10
Beck Depression Inventory				
Baseline	13.9 (10.9)	15.6 (10.6)		
EOT	8.9	8.3	<i>d</i> = 0.075	.57
12 mo	7.6	6.7	<i>d</i> = 0.095	.57
Rosenberg Self-esteem Scale				
Baseline	22.7 (5.9)	24.0 (6.5)		
EOT	22.6	21.2	<i>d</i> = 0.22	.03
12 mo	22.4	20.6	d = 0.29	.03
Quality of Life and Enjoyment Scale (short form)				
Baseline	47.9 (9.5)	47.5 (9.2)		
EOT	51.9	53.1	<i>d</i> = -0.12	.35
12 mo	52.9	54.3	d = -0.15	.35
State-Trait Anxiety Inventory				
Baseline	45.5 (12.5)	45.3 (13.0)		
EOT	42.7	40.3	d = 0.21	.09
12 mo	42.1	39.1	d = 0.24	.09
Child Yale-Brown Obsessive Compulsive Scale				
Baseline	3.5 (7.1)	4.2 (7.7)		
EOT	3.7	4.4	d = -0.11	.44
12 mo	3.6	4.5	<i>d</i> = -0.13	.44
Yale-Brown-Cornell Eating Disorder Scale				
Baseline	10.7 (8.0)	12.1 (8.4)		
ЕОТ	6.5	7.5	d = -0.16	.26
12 mo	5.3	6.6	d = -0.18	.26

Abbreviations: EOT, end of treatment; FBT, family-based therapy; NNT, number needed to treat; SRD, standard rate difference; SyFT, systemic family therapy.

^aCohen *d* is the estimated group mean difference divided by estimated SD at the EOT or 12 months' follow-up.