HHS Public Access

Author manuscript

Eat Weight Disord. Author manuscript; available in PMC 2023 August 01.

Published in final edited form as:

Eat Weight Disord. 2022 August ; 27(6): 1971–1990. doi:10.1007/s40519-022-01367-w.

A scoping review of non-specific predictors, moderators, and mediators of family-based treatment for adolescent anorexia and bulimia nervosa: A summary of the current research findings

Sasha Gorrell, PhD[1], **Catherine E. Byrne, PhD**[2], **Paige J. Trojanowski, MA**[2], **Sarah Fischer, PhD**[2], **Daniel Le Grange, PhD**[1,3]

[1]Department of Psychiatry and Behavioral Sciences, University of California, San Francisco, San Francisco, CA

[2]Department of Psychology, George Mason University, Fairfax, VA

[3]Department of Psychiatry and Behavioral Neurosciences, The University of Chicago, IL (Emeritus)

Abstract

Purpose: This scoping review presents an up-to-date synthesis of the current evidence base for non-specific predictors, moderators, and mediators of family-based treatment (FBT) for adolescent anorexia and bulimia nervosa.

Methods: We identify ways in which end-of-treatment outcomes have been shown to differ based upon baseline clinical features and person-specific factors and explore psychological mechanisms that may explain differences in treatment response. We draw from this evidence base to outline recommendations for clinical practice, as well as directions for future clinical eating disorder research.

Results: Noted findings from review include that early response in weight gain and parental criticism may be particularly influential in treatment for anorexia nervosa. Further, for adolescents with either anorexia or bulimia nervosa, eating-related obsessionality may be a key intervention target to improve outcomes.

Conclusions: In addition to highlighting a need for attention to specific patient- and caregiver-level factors that impact treatment response, recommendations for research and clinical practice

Article Correspondence: Sasha Gorrell, Department of Psychiatry, University of California, San Francisco, 401 Parnassus Avenue, San Francisco, CA 94143. sasha.gorrell@ucsf.edu.

Authors' contributions: The motivation for the review was inspired by CB with the guidance of DL and SF; CB and SG performed the literature search; SG and CB drafted the manuscript and all authors critically revised the work.

Conflicts of interest/Competing interests: Dr. Le Grange receives royalties from Guilford Press and Routledge and is co-director of the Training Institute for Child and Adolescent Eating Disorders, LLC. All authors report no other biomedical financial interests or potential conflicts of interest.

Code availability Not applicable

Ethics approval: Not applicable

Consent to participate: Not applicable

Consent for publication Not applicable

Level of Evidence: Level I: Evidence obtained from: at least one properly designed randomized controlled trials; experimental studies

include testing whether certain targeted treatments (e.g., exposure-based approaches) may be suitable within the context of FBT for eating disorders.

Keywords

Family-based treatment; adolescent eating disorders; mediators; moderators; non-specific predictors

Eating disorders (EDs) are severe psychiatric disorders with high rates of mortality [1], suicide [2], and considerable global disease burden [3]. The clinical syndromes of anorexia nervosa (AN) and bulimia nervosa (BN) have been recognized in the diagnostic classification of psychiatric disorders for decades; given their complexity, high rates of comorbid psychopathology [4], and associated medical complications [5], early and effective intervention is critical [6].

Restrictive EDs, particularly AN, are notoriously difficult to treat [7], [8]. Family-based treatment (FBT) is the current first-line approach for treating adolescent AN and a recommended approach for adolescent BN [9]. Although treatment of AN in youth has better recovery rates than for adults, outcomes are not optimal [10], [11]. Understanding for whom and under what conditions a certain intervention approach works best is necessary to develop the most effective treatments, as well as to identify those for whom it is less successful [12], [13]. To that end, this review highlights research on non-specific predictors, moderators, and mediators that inform change processes in FBT.

Given that the strongest evidence base to date within the broader ED field lies in FBT for AN and BN, we focus on this treatment for these EDs. Recent reviews that have addressed factors that impact treatment for adolescent EDs have been limited either by their systematic nature that did not allow for inclusion of a broader range of studies [14], or by their more narrative nature that did not specifically home in on mapping gaps in knowledge within the current literature base [15]–[17]. In contrast, this scoping review includes studies that present a specific focus on non-specific predictors, moderators and mediators of FBT and based on our summary of the evidence, we identify areas where knowledge remains lacking, and raise questions for future research.

We focused our review on evidence from studies that have (i) examined the use of FBT for AN or BN in an adolescent population (ages 12 −19); (ii) used an RCT design to examine treatment effects (with exceptions to include case studies and pilot work, as warranted and noted in text); and (iii) identified at least one non-specific predictor, mediator, or moderator of change in the FBT therapeutic process. We did not include studies with therapy approaches that did not include FBT; studies that did not identify variables that could be explored as factors impacting treatment; and studies that focused on multi-family approaches to FBT (as this work is related to, but not FBT perse, and introduces family-systems-level factors that are beyond the scope of this review). Searches of electronic databases (PubMed, PsychInfo, Google Scholar) were conducted using specific keywords (family-based treatment, adolescent, eating disorders, moderators, mechanisms of change). Reference lists from other recent and comprehensive reviews were also consulted, e.g., [15]. The initial search using the aforementioned key words and other sources identified 63

studies that were read in full; in total, 36 met eligibility including 11 RCTs (Table 1), with the main findings summarized below.

Defining non-specific predictors, moderators and mediators

Non-specific predictors, moderators, and mediators of ED outcome have been of increasing interest, with several recently published reviews [18], [19], but none has comprehensively examined these associations specifically in FBT. Mechanisms of action are processes that occur within treatment that lead to therapeutic change and include treatment mediators [20]. Not all mechanisms of action are mediators, but all mediators are mechanisms of action [13]; therefore, studying mediators may narrow down the search for causal mechanisms when the objective is to enhance features of treatment that lead to improved outcomes or remove those that do not. Mediators do not precede treatment, but instead change as a result of treatment, and it is this change in the mediator which is associated with changes in the outcome [13]. In contrast, baseline variables in randomized controlled trials (RCTs) that impact outcomes are considered non-specific predictors or moderators [13]. Baseline variables that *interact with treatment type* to affect outcome are referred to as moderators, whereas variables that affect outcome, *irrespective of treatment type*, are considered non-specific predictors. In RCTs, posttreatment factors (not a moderator) that are uncorrelated with treatment type (not a mediator) that have a main effect on outcome may also be referred to as non-specific predictors.

Therapeutic change in FBT for AN and BN

Non-specific predictors—Non-specific predictors are fixed or variable factors that are not related to the treatment received and precede and have a main effect on that outcome (i.e., the predictor has the same effect on the outcome regardless of the treatment type). While commonly defined as baseline characteristics (e.g., sex; treatment site), non-specific predictors may also comprise posttreatment measures such as early weight gain if they demonstrate a main effect but do not interact or correlate with treatment type [13]. Although non-specific predictors may apply within other treatment modalities (e.g., cognitive-behavioral therapy (CBT)), in the interest of providing readers with information most applicable to the study of FBT, we focus in the following summary only on the impact that non-specific predictors had within studies of the FBT modality.

Findings for studies examining AN

Baseline factors.—Several studies identified factors related to severity of illness specifically at baseline (i.e., not only as an outcome). For example, Eisler et al. (2000) explored the comparative impact of two forms of outpatient family interventions (conjoint family therapy vs. separated family therapy) on both nutritional and psychological outcomes, determined by the Morgan and Russell Scales [21]. Regardless of treatment type, baseline non-specific predictors of better outcomes relative to the Morgan and Russell Scales included less previous ED treatment, shorter duration of illness, and higher percent estimated body weight (%EBW) at the beginning of treatment [21]. In an RCT comparing FBT with adolescent-focused therapy (AFT) for AN [22], remission was defined *a priori* as achieving a weight that is ≥ 95%EBW and a global Eating Disorder Examination

(EDE) score within one *SD* of norms. Based on this definition, individuals who had prior hospitalization, were older, or had a longer illness duration were less likely to achieve remission status by end-of-treatment (EOT) [23].

Weight response.—Five studies have investigated whether early response in terms of weight gain impacted remission status and other symptoms at EOT and at follow-up. In secondary analyses of the RCT comparing FBT v. AFT mentioned above ([22], Accurso et al. (2014) explored the impact of timing of weight gain on psychological symptoms [24]. Weight gain significantly predicted improved psychological outcomes, including EDE scores [24]. However, the impact of weight restoration on ED symptoms diminished over the 2-year treatment and follow-up time period, suggesting that earlier weight restoration had the greatest impact on ED symptom improvement. In contrast, depressive symptoms but not ED symptoms tended to ease over time even in the absence of weight gain [24].

In this same sample, Le Grange et al. (2014) assessed the association of early weight gain and remission from AN (defined as above) [25]. Results indicated that the earliest predictor of EOT remission was gaining > 5.8 lbs by session 3. Madden et al. (2015) also studied whether early weight change in FBT predicted remission at EOT and 12-month follow-up in an RCT comparing brief hospitalization for medical stabilization and hospitalization for weight restoration, followed by 20 sessions of FBT [26]. Analysis of the combined group found that gaining 3.97 lbs by session 4 of FBT predicted higher %EBW and EOT remission. In a study where response to treatment was defined as having achieved ≥ 95% EBW following 20 sessions of manulized FBT, analyses showed that a gain of at least 2.88% in EBW by session 4 best predicted remission at EOT [27]. Finally, using data from an RCT comparing conjoint FBT v. parent-focused therapy (PFT, a separated FBT format) [28], colleagues investigated the timing and amount of weight gain that predicted remission [29]. Early responders for those receiving conjoint FBT had gained > 6.17 lbs by session 5, while early responders for PFT had gained > 5.02 lbs by session 5. Weight gain of these amounts were the best predictors of remission at EOT in these respective treatments. Taken together, these studies suggest early weight gain as an early marker of treatment response in FBT for adolescent AN and the potential to identify those who may need more intensive intervention to increase the likelihood of achieving remission, regardless of treatment type.

Weight response in subclinical presentations.—While not directly tested in the context of the study, some factors impacting treatment outcome related to weight have been suggested by case studies that address EDs in ‘subclinical’ presentations. For example, in a case report of an individual who began FBT with low weight but denial of fear of weight gain (i.e., ‘subclinical AN’), weight gain itself became an important focus of progress in treatment, and an ultimate indicator of the success of the intervention as a whole. In this study, the patient was an identical twin; twin status is a non-specific predictor that was not empirically assessed in this case study, but was noted for its impact on the patient specifically in the effect of having a constantly visible image of oneself at a normal weight [30]. An FBT-based approach was also used in a case series ($n = 7$) describing an intervention for individuals with ‘mild’ ED presentations characterized by low weight [31]. In this 5-session, FBT-informed intervention, factors contributing to positive outcome in

both weight status and cognitive symptom remission were noted as parents taking control of meals and making nutrition "mandatory," with consistent praise and support.

Parental expressed emotion.—Several studies have investigated the impact of expressed emotion (EE; measure of caregiver attitudes towards a relative with a mental or physical illness, [32]) on outcomes. EE is characterized by five components: critical comments, hostility, emotional overinvolvement, positive remarks, and warmth. On the whole, EE has been shown to be relatively low in samples with EDs (e.g., [33], [34]). However, in one early study of adolescents who received family therapy for AN, results suggested that *change* (i.e., a decrease) in EE over the course of treatment was related to better outcomes according to the Morgan and Russell Scales [34]. Of note, although the association between levels of critical comments at baseline and treatment outcome was not replicated in later work [33], evidence of both maternal and paternal warmth was related to good outcome.

Findings from studies of EE and treatment outcomes continue to remain more consistent with its negative impact. For example, in addition to the non-specific baseline predictors described above, and counter to the null findings of Le Grange and colleagues (2011) [33], Eisler and colleagues (2000) found a significant main effect of maternal criticism, with greater criticism associated with worse outcomes [21]. In the follow-up to this study, only two factors remained as significant non-specific predictors: those with a history of inpatient treatment or maternal criticism were less likely to do well five years following EOT, regardless of treatment type [35]. Moreover, in the sample from the RCT comparing FBT v. AFT described above [22], Rienecke et al. (2016) explored the role of EE and family functioning on treatment outcomes [36]. Study results showed that paternal criticism predicted less improvement in ED psychopathology, and maternal hostility (a second EE subscale) predicted less improvement in general family functioning and family communication at EOT, regardless of treatment modality [36].

Building on the earlier work of Le Grange et al. (1992) [34], a study by Allan and colleagues (2018) also assessed *changes* in EE from baseline to EOT in the RCT comparing conjoint FBT v. PFT mentioned above [28]. There was a main effect of treatment type on EE at EOT such that compared to FBT, PFT was associated with a decrease in maternal criticism. Additionally, adolescents of mothers who demonstrated an increase in EE, or remained high in EE, were less likely to remit compared with adolescents for whom parental EE decreased or remained low. While this study cannot confirm why a decrease in maternal criticism was more likely to be observed in PFT than conjoint FBT, it is possible that because the adolescent is not present in PFT sessions, parents may have more of an opportunity to discuss and resolve any criticism toward their child. This explanation remains quite speculative, though.

Parental behavior.—Three studies have examined parental behavior more broadly, outside of EE. Rhodes et al. (2008) evaluated the use of parent-to-parent consultations as a potential augmentation to FBT, randomizing one group to standard treatment and the other group to recieve an additional parent-to-parent consultation between weeks three and five [37]. Findings showed that parent-to-parent consultation led to small increases in

the rate of early weight restoration [37]. Darcy et al. (2013) explored whether identified parental and patient behaviors observed in the first four sessions of FBT for AN predicted early response to treatment (defined by gaining at least 1.8kg by session 4; [27]). Video recordings of FBT sessions for this study centered only on those who received FBT within a broader comparative treatment RCT [22]. Behavioral analyses showed that adolescents who were less resistant in the first two sessions and whose parents made fewer critical comments yielded the highest rates of early response (i.e., weight gain of 1.8kg by session 4 [38]). In a third study of parental behavior, Ellison et al. (2012) examined whether key components of manualized FBT for AN predicted weight gain (i.e., parental control over eating disorder behavior; externalization of the illness; parental unity; parental consistency; or sibling support) [39]. Results indicated that parents taking control of eating disorder behavior, not criticizing the patient, and externalizing the illness predicted greater weight gain by EOT. The authors concluded that their findings demonstrated that the degree to which parents assume control over the eating disorder behavior is the central predictor of change in FBT [39].

Findings for studies examining BN

Compared to the studies on FBT for adolescent AN, considerably less work has examined FBT for BN [16]. In the first RCT testing the relative efficacy of FBT for BN v. individual supportive psychotherapy (SPT) [40], remission was defined as the absence of binge eating and compensatory behaviors in the previous four weeks, and partial remission was defined as no longer meeting diagnostic inclusion criteria. While there were several significant univariate non-specific predictors of treatment outcome, in multi-variate analyses, only higher eating concerns and higher depression scores at baseline were associated with decreased odds of meeting criteria for remission and partial remission at EOT, respectively [41]. At 6-month follow-up, higher EDE eating concerns remained associated with decreased odds of remission, and higher binge-eating/purging frequency was associated with decreased odds of partial remission [41]. With an eye to the potential importance of early symptom change, across both the FBT and SPT treatment arms, a reduction of binge eating and purging frequency by 85% or more by session 6 (6 weeks) was predictive of remission (defined as the absence of binge eating and purge symptoms in the previous 28 days) at EOT [42]. Within this same sample, Ciao and colleagues (2015) explored factors that contributed to psychological change at EOT [43]. The authors found that individuals taking psychotropic medications prior to treatment had faster reductions in EDE eating concerns and lower overall EDE eating concerns at EOT [43]. Age did not predict changes in ED symptoms, but it did significantly predict change in self-esteem such that older adolescents had faster change in self-esteem than younger adolescents and older adolescents had better overall self-esteem at EOT.

A few studies have investigated non-specific predictors of outcome in the most recent BN RCT comparing FBT v. CBT [44]. In the main outcome report, those with male gender, or lower scores on a measure of eating-related obsessionality, the Yale-Brown-Cornell Eating Disorder Scale (YBC-EDS), or higher scores on certain subscales of the Family Environment Scale (FES; *Cohesion; Intellectual–cultural orientation; Active-recreational orientation; Organization*) at baseline all showed higher abstinence rates at EOT [44].

In a follow-up investigation of this RCT sample, Gorrell et al. (2019) examined motivation for change around eating-related obsessionality as measured by the *Motivation for Change* subscale of the YBC-EDS [45]. Results indicated a direct effect of lower motivation for change in obsessionality at baseline on higher EDE global scores at EOT, with no interaction between motivation and treatment type [45]. Of note, this study supported an association between motivation and decrease in ED *cognitions* but did not find that motivation contributed to the likelihood of binge eating/purging abstinence (i.e., behavior change) at EOT, across treatment types.

Finally, the latest secondary analyses of this RCT data examined the timing of response in treatment and its impact on remission status [46]. In line with earlier work by Le Grange and colleagues (2008) that highlighted the importance of early symptom change in adolescents with BN [42], results indicated that reduction in purging at session two and binge eating at session four were independently related to abstinence at EOT, regardless of treatment type (i.e., FBT, CBT, or SPT). An interaction effect was not tested in this study, however slight differences emerged based on treatment group, such that reductions in symptoms most predictive of abstinence at EOT occurred slightly sooner for FBT.

Summary.—Drawing conclusions about non-specific predictors across studies, factors that might positively impact outcomes regardless of the type of treatment for AN include younger age and shorter duration of illness, less prior ED treatment (specifically, inpatient), higher weight, less parental criticism, and greater parental warmth. In addition, there is strong support for the association between early response in weight gain and positive outcome for AN at EOT and at follow-up. For BN, better outcome in reducing binge-eating and purging behavior appears to be uniquely related to less baseline EDE eating concern, compulsivity, and depression; an improved family environment; psychotropic medication use; higher motivation to change compulsive ED symptoms, and early symptom reduction in the course of treatment.

Mediators and moderators

As a reminder, mediators are variables that act after treatment has begun and indicate the mechanisms through which a treatment might achieve its objectives [13]. In contrast, moderators are factors that modify the effect of treatment on outcome (i.e., interaction effect) and can identify for whom treatments may work. To date, only three studies have examined mediation effects in AN, and one study in BN, detailed just below.

Mediators

Although a study detailed above [37] found that the use of parent-to-parent consultations led to small increases in body weight, the effect of this intervention on the rate of weight restoration was not mediated by parental efficacy. In another study investigating a mediation effect of self-efficacy, Byrne and colleagues (2015) explored data from a comparative treatment RCT [22], hypothesizing that increases in parental (FBT) vs. adolescent (AFT) self-efficacy would mediate change in these respective treatments [47]. Findings revealed that increases in parental self-efficacy resulted in significantly greater weight gain for

adolescents who received FBT, but increases in adolescent self-efficacy did not impact weight gain in those who received AFT [47]. Of note, in an earlier examination of potential mechanisms of change in this same study sample, early changes (from baseline to week four) on measures of depression, self-esteem, self-efficacy, parental self-efficacy, and BMI percentile were examined as potential mediators of remission at EOT, defined as ≥ 95% EBW plus within one *SD* of EDE norms. Of those tested, no treatment mediators of remission were identified [23]. Finally, findings from Sadeh-Sharvit and colleagues (2018) mirrored the effects from prior work [47], such that change in maternal self-efficacy from baseline to session 8 mediated weight gain by session 10. Only parents receiving FBT reported significantly greater self-efficacy [48].

For BN, one study investigating potential mediators of treatment effect did not find any significant treatment-by mediator effects. However, as a main effect, this study found that change in ED cognitions mid-treatment, specifically a subscale corresponding to weight concern, led to improved likelihood of abstinence from binge-eating and purging behavior at EOT and 6-month follow-up [49]. These results suggest that it is possible that FBT-BN exerts its effects by changing disordered thinking, a possibility that should be explored more thoroughly as an *a priori* hypothesis in future work.

Moderators

Findings for studies examining AN

Treatment alliance.—Forsberg and colleagues (2013) [50] examined the possible differential impact of treatment alliance on remission status (i.e., remission was defined as achieving ≥ 95%mBMI and EDE global scores within 1*SD* of community norms, with partial remission defined as > 85th %mBMI) within data from a prior RCT that compared FBT with AFT [22]. Results did not reveal a main effect or interaction effect for alliance on full remission; although a main effect was found for partial remission, there was no alliance by treatment moderation effect.

Parental expressed emotion.—Based on earlier work that provided foundational hypotheses for the importance of EE in family therapy for EDs [34], [50], three studies have identified potential moderating effects related to EE. Eisler et al. (2000) found that youth with high EE families were more likely to achieve good clinical outcomes (per the Morgan and Russell Scales) in a separated rather than conjoint format of FBT, whereas outcomes did not differ according to treatment type among those with low EE families. At five-year follow-up, patients from families with high levels of maternal criticism had done less well at EOT if they received conjoint as opposed to separated family therapy [35]. Examining data from an RCT described above [22], Rienecke et al. (2016) found a significant interaction between maternal hostility and treatment outcome, indicating that adolescents whose mothers displayed hostility had greater increases in %EBW in an individual treatment (AFT) as opposed to FBT [36].

Eating related obsessionality.—In addition to these parental factors, there may also be a unique effect of certain patient-level features on outcomes, depending on the format of FBT. Specifically, in an optimal FBT dose study, Lock et al. (2005) compared short-term

FBT (10 sessions over 6 months) to long-term FBT (20 sessions over 12 months [51]. While treatment dose was not a non-specific predictor of outcome, subgroups with more severe eating-related obsessive-compulsive thinking (i.e., YBC-EDS scores) were more successful with the higher dose of FBT [51]. Single-parent or divorced families also benefitted from the longer format.

Le Grange and colleagues (2012) aimed to identify treatment moderators and mediators of remission at EOT for adolescents with AN who received FBT v. AFT [23]. Of the 17 pre-randomization variables that were examined as potential moderators, only eating-related obsessionality (YBC-EDS) and ED-specific psychopathology (EDE Global scores) emerged as moderators at EOT. Participants with higher baseline scores on these measures benefited more from FBT than AFT. Perhaps a more tentative finding emerged for AN type at follow-up, such that those with binge-eating/purging type were more likely to have a change in their remission status having received FBT, rather than AFT. In secondary analysis of these data, a decrease in overall eating-relating obsessionality (YBC-EDS) was significantly associated with an increase in weight for individuals who received FBT [52]. However, there was no relation between change in obsessionality scores and change in weight in the AFT group. The findings of Agras et al. (2014) diverge slightly from favoring FBT in this moderation effect [53]. Specifically, in a study that randomized participants to two family therapies, FBT v. systemic family therapy, findings suggested that those with higher baseline YBC-EDS scores gained significantly more weight with systemic family therapy than with FBT [53]. In SFT, the focus is placed on the family system rather than on behavioral features of the ED as it would be in FBT (e.g., intervening on food rituals). Therefore, although this explanation is speculative in nature, it is possible that the exploration of family patterns of beliefs and behaviors in SFT facilitates less anxiety and exacerbation of eating-related obsessionality than the more symptom-focused approach of FBT. However, in secondary analyses of this same study data, it seems as if an interaction effect occurred between comorbid symptoms and treatment type, such that those who had higher depression and obsessionality scores *and* received FBT were less likely to require early hospitalization [54].

Finally, a non-randomized pilot study of FBT for a sample of youth with AN, BN, and Eating Disorder Not Otherwise Specified bears mention in that the authors compared their clinical sample to a non-clinical sample at baseline in an effort to determine the meaning of any changes post-intervention and at extended follow-up [55]. In this study, patients who enrolled in the treatment study were more rigid towards themselves and had a higher impulse control and a higher drive toward perfectionism (for themselves) than the non-clinical comparison group at baseline. Further, while other aspects of general psychopathology and ED symptoms remitted 36 months after the start of FBT, perfectionism scores remained high. While no predictors of treatment effects were directly tested in this study, findings suggest that an important potential variable of interest in impacting treatment response may be trait level rigidity and/or self-oriented perfectionism.

Findings for studies examining BN

Le Grange and colleagues (2008) did not find any moderators of remission or partial remission at EOT when comparing outcomes for treatment with FBT v. SPT [41]. However,

at 6-month follow-up, baseline EDE global scores moderated the effects of treatment on partial remission (defined as above) such that individuals with *less* severe baseline global EDE scores had greater partial remission when treated with FBT relative to SPT [41].

In contrast, using these same data and growth model analyses, Ciao et al., (2015) found that participants with *greater* baseline purging had faster change in eating concerns when receiving FBT v. SPT, whereas when baseline purging was low, participants did comparably well in both treatments [43]. Age was also a significant moderator such that younger adolescents receiving FBT v. SPT demonstrated greater change in eating concerns, whereas older adolescents showed an equal rate of change in both treatments; age did not moderate any other outcomes [43].

In another RCT for adolescents with BN, Le Grange et al. (2015) explored moderators of treatment outcomes when comparing FBT to CBT [44]. Results of this study showed that family conflict emerged as a significant moderator such that participants with lower FES Conflict subscale scores responded better to FBT than CBT, but there was no differentiation between the treatments in families with higher FES Conflict scores [44]. Similar to earlier findings in studies of AN [21], these results suggest that FBT may not be the treatment of choice for high-conflict families.

Summary.—Study of moderators of therapeutic change in treatment for AN suggest that individual therapy or a separated format of FBT may be advantageous in the context of EE defined maternal hostility. Further, for those with elevated eating-related obsessionality, a longer course of treatment might be indicated, and patients with more severe ED psychopathology or eating-related obsessionality may have better weight and cognitive symptom outcomes in a behaviorally focused approach (FBT) rather than an individual approach (AFT). Of note, some work also suggests that systemic family therapy, rather than FBT, may provide superior weight gain for those with high obsessionality.

For BN, FBT encourages parental control and management of ED behaviors, while CBT or SPT for BN are principally individual therapy approaches. While the literature base on adolescent BN is limited, available findings suggest that FBT might be more suited to address certain symptoms in adolescents who are younger or with lower family conflict, relative to an individual therapy. The finding that those with baseline *higher* behavioral symptoms (purging) and *lower* cognitive symptoms (EDE global scores) fared better in FBT relative to weight gain and cognitive symptom improvement rather than in SPT is interesting, and warrants further investigation.

Discussion

Although it is clear that FBT for youth with AN and BN produces positive outcomes in a majority of cases, the process by which this treatment works, and for which subsets of the patient population this treatment should be the first choice, are far from clear. Given that a majority of our findings were specific to AN, much of this discussion addresses conclusions and implications for this subgroup. The lack of RCTs for adolescent BN limits our understanding of the workings of FBT for this patient population—a dilemma that we

address below. Throughout, we discuss potential treatment implications based on the results of our review.

Several non-specific predictors were replicated across AN studies, particularly related to the severity of the illness when beginning treatment. Those starting treatment who were older or with longer duration of illness, more weight suppressed, or with more prior hospitalization or ED treatment, fared poorly in treatment regardless of receiving AFT or FBT and regardless of receiving a separated or conjoint FBT format [21], [23]. Although these findings are intuitive in nature, their relative robustness underscores the need for continued improvement in early intervention efforts whether an individual or family therapy approach is used [6]. Within FBT, PFT, or AFT, another particularly consistent finding for AN is the importance of early response in weight gain. It appears that weight gain of ~2kgs by the end of four weeks of treatment is most predictive of improved psychological outcomes (i.e., ED cognitive symptoms and depression [24]) and weight remission [24]–[26], [29] at EOT. Given the medical acuity of AN, providing patients and parents with appropriate recommendations for early weight goals should be a priority across both individual and family therapy treatments. Although comparatively limited, studies that have examined patient- and parent-level factors that predict clinical outcomes in BN suggest that, similarly to AN, early change in treatment is important [42], [46], and better prognosis in weight gain and cognitive symptom improvement may be related to lower eating concern [41] and obsessionality [44], [45]. The finding that baseline depression scores [41] and psychotropic medication use [43] impacted BN outcomes warrants future investigation.

A majority of studies focused on patient-level response, but there were additional parent-level factors that showed evidence of a direct effect on patient status at EOT for those with AN. In particular, several studies demonstrated that high EE, and in particular, parental criticism, was a non-specific predictor that negatively impacted progress in treatment [21], [33], [34], [36], [56]. When studying parental behavior outside of EE, two other studies found associations between fewer critical comments and improved weight gain [38], [39]. Criticism also demonstrated a moderating effect, leading to poorer outcomes for those who received conjoint v. separated FBT [21], [35] and FBT v. AFT [36], suggesting that for high EE families, individual therapy or a separated format of FBT (i.e., PFT) may be the better option for those with AN. Similarly, studies of BN suggest that higher family conflict (assessed with the FES) may indicate that better outcomes in behavioral symptom remission may result within in an individual, rather than family-based approach to treatment [44].

In addition to choosing a certain treatment format based on the presence of high EE or family conflict, another potentially helpful treatment tool may be psychoeducation at the start of treatment. Psychoeducation may be particularly helpful in guiding parents to align their behavior and communication with the best chance of good outcomes. For example, families and the treatment team may give the illness a name in an effort to separate the healthy part of the child from the ED, also called externalization [36]. By viewing the ED as an illness separate from the young person, parents may decrease criticism toward their child, and in turn, increase the likelihood of positive treatment outcomes. Clinicians may also provide psychoeducation around praise and positive reinforcement as a means of behavior change, as opposed to a critical response. Although it may be a challenge for some parents

to remain compassionate towards the young person during difficult periods of resistance from the ED, providing guidance around how to minimize criticism and increase parental warmth may be useful in creating an environment that optimizes treatment progress.

In addition to helping parents communicate effectively with their child while managing the ED (e.g., with less hostility and greater warmth), preliminary evidence suggests that finding ways to increase parental self-efficacy in the context of treatment may support better outcomes in weight gain, particularly in FBT compared to AFT [47]. However, earlier work that tested associations between parental efficacy and either the rate of weight restoration [37], or full remission status (i.e., weight ≥ 95%EBE plus EDE scores within 1 *SD* of norms) [23] did *not* find significant mediation effects. A pilot attempt to boost parental efficacy with intensive parental coaching early in treatment demonstrated the acceptability and preliminary utility of this approach in increasing the likelihood of improved weight gain by EOT [57]. Even despite some mixed findings in facilitating faster weight gain or cognitive change (i.e., remission), the premise that increasing parental self-efficacy in supporting the young person specifically in bringing about improved weight gain warrants further investigation.

Finally, a robust finding that spans both AN and BN is the negative impact of eating-related obsessionality. Among those with AN, adolescents with greater obsessionality required a longer course of treatment [51]. Of note, Le Grange and colleagues (2012) [23] showed that participants with higher levels of eating-related obsessionality had better outcomes in FBT than in individual treatment whereas Agras and colleagues (2014) showed that participants with higher levels of eating-related obsessionality did better in systemic family therapy than FBT [53]. In the Agras et al. (2014) study, both therapies (systemic family therapy and FBT) involved members of the family in treatment in addition to the individual with AN, which suggests that family involvement overall is more efficacious than individual treatment for individuals with high levels of eating-related obsessionality. Among those with BN, there was a direct effect of lower scores on eating-related obsessionality and improved abstinence of binge eating and purging [44], as well as a direct effect of motivation to change this behavior on improved EDE scores at EOT [45]. To date, no work has tested whether certain targeted treatments (e.g., exposure-based approaches) to address eating-related obsessionality may be suitable within the context of FBT for EDs but findings suggest that this may be a promising avenue for future research.

Summary and Conclusions

Simply comparing two treatments can yield a certain amount of information, but an investment in identifying mediators and moderators in clinical trial research can tell us *how* treatment works and *for whom* treatment works [58]. The delineation of non-specific predictors can also guide clinical decision-making, particularly if a known factor that impacts outcomes across treatment type can be readily manipulated (either enhanced or prevented). Caring for someone with an ED is invariably challenging, and family members often experience high levels of burden and distress [59]. Given that results from this review emphasize the important role parental behavior can play in facilitating good treatment outcome, it would be advantageous to explore clinical modifactions (e.g., increased attention

to parental self-efficacy) that can improve early response to FBT for AN and BN. Boosting parental empowerment to elicit early change may be particularly key, as multiple studies have identified early response (either in weight or in bulimic symptom reduction) as an important indicator of remission. Finally, across AN and BN, a promising avenue for future research will be testing methods (e.g., exposure-based approaches) to directly target eating-related obsessionality in the context of FBT. Recent work describing successes and challenges in using a family-based approach to interoceptive exposure among adolescents with low-weight EDs suggests that disgust may be an additional variable of interest in future exposure-based adaptations to FBT [60]. The preponderance of study in AN evidenced in this review demonstrates the need for increased examination of factors that directly impact and moderate FBT for BN. We also acknowledge that we focus our summary of non-specific predictors solely on those that were evidenced within studies of FBT. A more developed discussion of how these factors may impact adolescents in different treatment modalities is of interest, and could be considered as a topic of future review. Further, few studies in the extant literature are able to provide specific information on individuals who discontinued treatment, and are thus lost to follow-up. An important avenue for future work will be to ensure that as a field, we attend to learning the causes of attrition, and for whom and why a treatment led to discontinuation. Finally, many of these studies include secondary analyses of RCT data, limiting the overall number of individuals that these findings represent, as well as the potential replicability of this work in novel, non-RCT settings. Despite these limitations, results of this review underscore that focusing future research on exploring moderators and mediators of FBT outcomes will improve the overall efficacy of treatment of adolescents with restrictive EDs.

Funding:

This research received no specific grant from any funding agency, commercial or not-for-profit sectors. Dr. Gorrell is supported by the National Institute of Mental Health (K23MH126201).

Availability of data and material

Not applicable

References

[1]. van Hoeken D and Hoek HW, “Review of the burden of eating disorders: mortality, disability, costs, quality of life, and family burden,” Curr. Opin. Psychiatry, vol. 33, no. 6, pp. 521–527, Nov. 2020, doi: 10.1097/YCO.0000000000000641. [PubMed: 32796186]

[2]. Pisetsky EM, Thornton LM, Lichtenstein P, Pedersen NL, and Bulik CM, “Suicide attempts in women with eating disorders.,” J. Abnorm. Psychol, vol. 122, no. 4, pp. 1042–1056, 2013, doi: 10.1037/a0034902. [PubMed: 24364606]

[3]. Erskine HE, Whiteford HA, and Pike KM, “The global burden of eating disorders:,” Curr. Opin. Psychiatry, vol. 29, no. 6, pp. 346–353, Nov. 2016, doi: 10.1097/YCO.0000000000000276. [PubMed: 27532942]

[4]. Bühren K et al. , “Comorbid Psychiatric Disorders in Female Adolescents with First-Onset Anorexia Nervosa: Comorbidity in Adolescent Anorexia Nervosa,” Eur. Eat. Disord. Rev, vol. 22, no. 1, pp. 39–44, Jan. 2014, doi: 10.1002/erv.2254. [PubMed: 24027221]

[5]. Gaudiani JL, Sick Enough: A Guide to the Medical Complications of Eating Disorders, 1st ed. New York, NY : Routledge, 2019.: Routledge, 2018. doi: 10.4324/9781351184731.

[6]. Treasure J and Russell G, “The case for early intervention in anorexia nervosa: theoretical exploration of maintaining factors,” Br. J. Psychiatry, vol. 199, no. 1, pp. 5–7, Jul. 2011, doi: 10.1192/bjp.bp.110.087585. [PubMed: 21719874]

[7]. Anderson LK et al. , “Treating Eating Disorders at Higher Levels of Care: Overview and Challenges,” Curr. Psychiatry Rep, vol. 19, no. 8, p. 48, Aug. 2017, doi: 10.1007/s11920-017-0796-4. [PubMed: 28653117]

[8]. Walsh BT, “The Enigmatic Persistence of Anorexia Nervosa,” Am. J. Psychiatry, vol. 170, no. 5, pp. 477–484, May 2013, doi: 10.1176/appi.ajp.2012.12081074. [PubMed: 23429750]

[9]. Couturier J et al. , “Canadian practice guidelines for the treatment of children and adolescents with eating disorders,” J. Eat. Disord, vol. 8, no. 1, p. 4, Dec. 2020, doi: 10.1186/s40337-020-0277-8. [PubMed: 32021688]

[10]. Lock J and Le Grange D, “Family-based treatment: Where are we and where should we be going to improve recovery in child and adolescent eating disorders,” Int. J. Eat. Disord, vol. 52, no. 4, pp. 481–487, Apr. 2019, doi: 10.1002/eat.22980. [PubMed: 30520532]

[11]. Murray SB, Quintana DS, Loeb KL, Griffiths S, and Le Grange D, “Treatment outcomes for anorexia nervosa: a systematic review and meta-analysis of randomized controlled trials,” Psychol. Med, vol. 49, no. 4, pp. 535–544, Mar. 2019, doi: 10.1017/S0033291718002088. [PubMed: 30101734]

[12]. Carper MM, Makover HB, and Kendall PC, “Future Directions for the Examination of Mediators of Treatment Outcomes in Youth,” J. Clin. Child Adolesc. Psychol, vol. 47, no. 2, pp. 345–356, Mar. 2018, doi: 10.1080/15374416.2017.1359786. [PubMed: 28841335]

[13]. Kraemer HC, Wilson GT, Fairburn CG, and Agras WS, “Mediators and Moderators of Treatment Effects in Randomized Clinical Trials,” Arch. Gen. Psychiatry, vol. 59, no. 10, p. 877, Oct. 2002, doi: 10.1001/archpsyc.59.10.877. [PubMed: 12365874]

[14]. Hamadi L and Holliday J, “Moderators and mediators of outcome in treatments for anorexia nervosa and bulimia nervosa in adolescents: A systematic review of randomized controlled trials,” Int. J. Eat. Disord, vol. 53, no. 1, pp. 3–19, Jan. 2020, doi: 10.1002/eat.23159. [PubMed: 31506978]

[15]. Rienecke RD, “Family-based treatment of eating disorders in adolescents: current insights,” Adolesc. Health Med. Ther, vol. 8, pp. 69–79, 2017, doi: 10.2147/AHMT.S115775. [PubMed: 28615982]

[16]. Gorrell S, Loeb KL, and Le Grange D, “Family-based Treatment of Eating Disorders,” Psychiatr. Clin. North Am, vol. 42, no. 2, pp. 193–204, Jun. 2019, doi: 10.1016/j.psc.2019.01.004. [PubMed: 31046922]

[17]. Forsberg S and Lock J, “Family-based Treatment of Child and Adolescent Eating Disorders,” Child Adolesc. Psychiatr. Clin. N. Am, vol. 24, no. 3, pp. 617–629, Jul. 2015, doi: 10.1016/j.chc.2015.02.012. [PubMed: 26092743]

[18]. Linardon J, de la Piedad Garcia X, and Brennan L, “Predictors, Moderators, and Mediators of Treatment Outcome Following Manualised Cognitive-Behavioural Therapy for Eating Disorders: A Systematic Review: Predictors, Moderators, and Mediators of Outcome for Eating Disorders,” Eur. Eat. Disord. Rev, vol. 25, no. 1, pp. 3–12, Jan. 2017, doi: 10.1002/erv.2492. [PubMed: 27862611]

[19]. Vall E and Wade TD, “Predictors of treatment outcome in individuals with eating disorders: A systematic review and meta-analysis: PREDICTORS OF TREATMENT OUTCOME IN INDIVIDUALS WITH EATING DISORDERS,” Int. J. Eat. Disord, vol. 48, no. 7, pp. 946–971, Nov. 2015, doi: 10.1002/eat.22411. [PubMed: 26171853]

[20]. Kazdin AE, “Mediators and Mechanisms of Change in Psychotherapy Research,” Annu. Rev. Clin. Psychol, vol. 3, no. 1, pp. 1–27, Apr. 2007, doi: 10.1146/annurev.clinpsy.3.022806.091432. [PubMed: 17716046]

[21]. Eisler I, Dare C, Hodes M, Russell G, Dodge E, and Le Grange D, “Family Therapy for Adolescent Anorexia Nervosa: The Results of a Controlled Comparison of Two Family Interventions,” J. Child Psychol. Psychiatry, vol. 41, no. 6, pp. 727–736, Sep. 2000, doi: 10.1111/1469-7610.00660. [PubMed: 11039685]

[22]. Lock J, Le Grange D, Agras WS, Moye A, Bryson SW, and Jo B, "Randomized Clinical Trial Comparing Family-Based Treatment With Adolescent-Focused Individual Therapy for Adolescents With Anorexia Nervosa," Arch. Gen. Psychiatry, vol. 67, no. 10, p. 1025, Oct. 2010, doi: 10.1001/archgenpsychiatry.2010.128. [PubMed: 20921118]

[23]. Le Grange D et al. , "Moderators and mediators of remission in family-based treatment and adolescent focused therapy for anorexia nervosa," Behav. Res. Ther, vol. 50, no. 2, pp. 85–92, Feb. 2012, doi: 10.1016/j.brat.2011.11.003. [PubMed: 22172564]

[24]. Accurso EC, Ciao AC, Fitzsimmons-Craft EE, Lock JD, and Le Grange D, "Is weight gain really a catalyst for broader recovery?: The impact of weight gain on psychological symptoms in the treatment of adolescent anorexia nervosa," Behav. Res. Ther, vol. 56, pp. 1–6, May 2014, doi: 10.1016/j.brat.2014.02.006. [PubMed: 24632109]

[25]. Le Grange D, Accurso EC, Lock J, Agras S, and Bryson SW, "Early weight gain predicts outcome in two treatments for adolescent anorexia nervosa: Early Weight Gain for Adolescent Anorexia Nervosa," Int. J. Eat. Disord, vol. 47, no. 2, pp. 124–129, Mar. 2014, doi: 10.1002/eat.22221. [PubMed: 24190844]

[26]. Madden S, Miskovic-Wheatley J, Wallis A, Kohn M, Hay P, and Touyz S, "Early weight gain in family-based treatment predicts greater weight gain and remission at the end of treatment and remission at 12-month follow-up in adolescent anorexia nervosa: Early weight gain in adolescent anorexia nervosa," Int. J. Eat. Disord, vol. 48, no. 7, pp. 919–922, Nov. 2015, doi: 10.1002/eat.22414. [PubMed: 26488111]

[27]. Doyle PM, Le Grange D, Loeb K, Doyle AC, and Crosby RD, "Early response to family-based treatment for adolescent anorexia nervosa," Int. J. Eat. Disord, vol. 43, no. 7, pp. 659–662, Nov. 2010, doi: 10.1002/eat.20764. [PubMed: 19816862]

[28]. Le Grange D, Hughes EK, Court A, Yeo M, Crosby RD, and Sawyer SM, "Randomized Clinical Trial of Parent-Focused Treatment and Family-Based Treatment for Adolescent Anorexia Nervosa," J. Am. Acad. Child Adolesc. Psychiatry, vol. 55, no. 8, pp. 683–692, Aug. 2016, doi: 10.1016/j.jaac.2016.05.007. [PubMed: 27453082]

[29]. Hughes EK, Sawyer SM, Accurso EC, Singh S, and Le Grange D, "Predictors of early response in conjoint and separated models of family-based treatment for adolescent anorexia nervosa," Eur. Eat. Disord. Rev, vol. 27, no. 3, pp. 283–294, May 2019, doi: 10.1002/erv.2668. [PubMed: 30761665]

[30]. Loeb KL, Hirsch AM, Greif R, and Hildebrandt TB, "Family-Based Treatment of a 17-Year-Old Twin Presenting with Emerging Anorexia Nervosa: A Case Study Using the 'Maudsley Method,'" J. Clin. Child Adolesc. Psychol, vol. 38, no. 1, pp. 176–183, Jan. 2009, doi: 10.1080/15374410802575404. [PubMed: 19130366]

[31]. Spettigue W et al. , "A Brief Modified Family-Based Treatment Intervention for Youth With Mild Eating Disorders: A Case Series," Front. Psychiatry, vol. 11, p. 105, Mar. 2020, doi: 10.3389/fpsyt.2020.00105. [PubMed: 32210848]

[32]. Brown GW, Birley JLT, and Wing JK, "Influence of Family Life on the Course of Schizophrenic Disorders: A Replication," Br. J. Psychiatry, vol. 121, no. 562, pp. 241–258, Sep. 1972, doi: 10.1192/bjp.121.3.241. [PubMed: 5073778]

[33]. Le Grange D, Hoste RR, Lock J, and Bryson SW, "Parental expressed emotion of adolescents with anorexia nervosa: Outcome in family-based treatment," Int. J. Eat. Disord, vol. 44, no. 8, pp. 731–734, Dec. 2011, doi: 10.1002/eat.20877. [PubMed: 22072411]

[34]. le Grange D, Eisler I, Dare C, and Hodes M, "Family criticism and self-starvation: a study of expressed emotion," J. Fam. Ther, vol. 14, no. 2, pp. 177–192, 1992, doi: 10.1046/j.1992.00451.x.

[35]. Eisler I, Simic M, Russell GFM, and Dare C, "A randomised controlled treatment trial of two forms of family therapy in adolescent anorexia nervosa: a five-year follow-up," J. Child Psychol. Psychiatry, vol. 48, no. 6, pp. 552–560, Jun. 2007, doi: 10.1111/j.1469-7610.2007.01726.x. [PubMed: 17537071]

[36]. Rienecke RD, Accurso EC, Lock J, and Le Grange D, "Expressed Emotion, Family Functioning, and Treatment Outcome for Adolescents with Anorexia Nervosa: Expressed Emotion and Treatment Outcome," Eur. Eat. Disord. Rev, vol. 24, no. 1, pp. 43–51, Jan. 2016, doi: 10.1002/erv.2389. [PubMed: 26201083]

[37]. Rhodes P, Baillee A, Brown J, and Madden S, “Can parent-to-parent consultation improve the effectiveness of the Maudsley model of family-based treatment for anorexia nervosa? A randomized control trial: Parent-to-parent consultation for anorexia,” J. Fam. Ther, vol. 30, no. 1, pp. 96–108, Jan. 2008, doi: 10.1111/j.1467-6427.2008.00418.x.

[38]. Darcy AM, Bryson SW, Agras WS, Fitzpatrick KK, Le Grange D, and Lock J, “Do in-vivo behaviors predict early response in family-based treatment for anorexia nervosa?,” Behav. Res. Ther, vol. 51, no. 11, pp. 762–766, Nov. 2013, doi: 10.1016/j.brat.2013.09.003. [PubMed: 24091274]

[39]. Ellison R et al. , “Do the components of manualized family-based treatment for anorexia nervosa predict weight gain?,” Int. J. Eat. Disord, vol. 45, no. 4, pp. 609–614, May 2012, doi: 10.1002/eat.22000. [PubMed: 22270977]

[40]. le Grange D, Crosby RD, Rathouz PJ, and Leventhal BL, “A Randomized Controlled Comparison of Family-Based Treatment and Supportive Psychotherapy for Adolescent Bulimia Nervosa,” Arch. Gen. Psychiatry, vol. 64, no. 9, p. 1049, Sep. 2007, doi: 10.1001/archpsyc.64.9.1049. [PubMed: 17768270]

[41]. Le GRANGE D, Crosby RD, and Lock J, “Predictors and Moderators of Outcome in Family-Based Treatment for Adolescent Bulimia Nervosa,” J. Am. Acad. Child Adolesc. Psychiatry, vol. 47, no. 4, pp. 464–470, Apr. 2008, doi: 10.1097/CHI.0b013e3181640816. [PubMed: 18388765]

[42]. le Grange D, Doyle P, Crosby RD, and Chen E, “Early response to treatment in adolescent bulimia nervosa,” Int. J. Eat. Disord, vol. 41, no. 8, pp. 755–757, Dec. 2008, doi: 10.1002/eat.20566. [PubMed: 18570193]

[43]. Ciao AC, Accurso EC, Fitzsimmons-Craft EE, and Le Grange D, “Predictors and moderators of psychological changes during the treatment of adolescent bulimia nervosa,” Behav. Res. Ther, vol. 69, pp. 48–53, Jun. 2015, doi: 10.1016/j.brat.2015.04.002. [PubMed: 25874955]

[44]. Le Grange D, Lock J, Agras WS, Bryson SW, and Jo B, “Randomized Clinical Trial of Family-Based Treatment and Cognitive-Behavioral Therapy for Adolescent Bulimia Nervosa,” J. Am. Acad. Child Adolesc. Psychiatry, vol. 54, no. 11, pp. 886–894.e2, Nov. 2015, doi: 10.1016/j.jaac.2015.08.008. [PubMed: 26506579]

[45]. Gorrell S et al. , “Rituals and preoccupations associated with bulimia nervosa in adolescents: Does motivation to change matter?,” Eur. Eat. Disord. Rev, vol. 27, no. 3, pp. 323–328, May 2019, doi: 10.1002/erv.2664. [PubMed: 30734406]

[46]. Matheson BE, Gorrell S, Bohon C, Agras WS, Le Grange D, and Lock J, “Investigating Early Response to Treatment in a Multi-Site Study for Adolescent Bulimia Nervosa,” Front. Psychiatry, vol. 11, p. 92, Feb. 2020, doi: 10.3389/fpsyt.2020.00092. [PubMed: 32184746]

[47]. Byrne CE, Accurso EC, Arnow KD, Lock J, and Le Grange D, “An exploratory examination of patient and parental self-efficacy as predictors of weight gain in adolescents with anorexia nervosa: EXPLORATORY EXAMINATION,” Int. J. Eat. Disord, vol. 48, no. 7, pp. 883–888, Nov. 2015, doi: 10.1002/eat.22376. [PubMed: 25808269]

[48]. Sadeh-Sharvit S et al. , “Are parental self-efficacy and family flexibility mediators of treatment for anorexia nervosa?,” Int. J. Eat. Disord, vol. 51, no. 3, pp. 275–280, Mar. 2018, doi: 10.1002/eat.22826. [PubMed: 29314160]

[49]. Lock J, le Grange D, and Crosby R, “Exploring possible mechanisms of change in family-based treatment for adolescent bulimia nervosa,” J. Fam. Ther, vol. 30, no. 3, pp. 260–271, Aug. 2008, doi: 10.1111/j.1467-6427.2008.00430.x.

[50]. Forsberg S, LoTempio E, Bryson S, Fitzpatrick KK, Le Grange D, and Lock J, “Therapeutic alliance in two treatments for adolescent anorexia nervosa,” Int. J. Eat. Disord, vol. 46, no. 1, pp. 34–38, Jan. 2013, doi: 10.1002/eat.22047. [PubMed: 22836506]

[51]. Szmukler GI, Berkowitz R, Eisler I, Leff J, and Dare C, “Expressed Emotion in Individual and Family Settings: a Comparative Study,” Br. J. Psychiatry, vol. 151, no. 2, pp. 174–178, Aug. 1987, doi: 10.1192/bjp.151.2.174. [PubMed: 3690106]

[52]. Lock J, Agras WS, Bryson S, and Kraemer HC, “A Comparison of Short- and Long-Term Family Therapy for Adolescent Anorexia Nervosa,” J. Am. Acad. Child Adolesc. Psychiatry, vol. 44, no. 7, pp. 632–639, Jul. 2005, doi: 10.1097/01.chi.0000161647.82775.0a. [PubMed: 15968231]

[53]. Byrne CE, Wonderlich JA, Curby T, Fischer S, Lock J, and Le Grange D, "Using bivariate latent basis growth curve analysis to better understand treatment outcome in youth with anorexia nervosa," Eur. Eat. Disord. Rev, vol. 26, no. 5, pp. 483–488, Sep. 2018, doi: 10.1002/erv.2596. [PubMed: 29691947]

[54]. Agras WS et al. , "Comparison of 2 Family Therapies for Adolescent Anorexia Nervosa: A Randomized Parallel Trial," JAMA Psychiatry, vol. 71, no. 11, p. 1279, Nov. 2014, doi: 10.1001/jamapsychiatry.2014.1025. [PubMed: 25250660]

[55]. Lock J et al. , "Does family-based treatment reduce the need for hospitalization in adolescent anorexia nervosa?: Hospitalization in Adolescent Anorexia Nervosa," Int. J. Eat. Disord, vol. 49, no. 9, pp. 891–894, Sep. 2016, doi: 10.1002/eat.22536. [PubMed: 27062400]

[56]. Paulson-Karlsson G, Engström I, and Nevonen L, "A Pilot Study of a Family-Based Treatment for Adolescent Anorexia Nervosa: 18- and 36-Month Follow-ups," Eat. Disord, vol. 17, no. 1, pp. 72–88, Dec. 2008, doi: 10.1080/10640260802570130.

[57]. Allan E, Le Grange D, Sawyer SM, McLean LA, and Hughes EK, "Parental Expressed Emotion During Two Forms of Family-Based Treatment for Adolescent Anorexia Nervosa: Expressed Emotion and Family-based Treatment," Eur. Eat. Disord. Rev, vol. 26, no. 1, pp. 46–52, Jan. 2018, doi: 10.1002/erv.2564. [PubMed: 29105211]

[58]. Lock J et al. , "Can adaptive treatment improve outcomes in family-based therapy for adolescents with anorexia nervosa? Feasibility and treatment effects of a multi-site treatment study," Behav. Res. Ther, vol. 73, pp. 90–95, Oct. 2015, doi: 10.1016/j.brat.2015.07.015. [PubMed: 26276704]

[59]. Kraemer HC, "Messages for Clinicians: Moderators and Mediators of Treatment Outcome in Randomized Clinical Trials," Am. J. Psychiatry, vol. 173, no. 7, pp. 672–679, Jul. 2016, doi: 10.1176/appi.ajp.2016.15101333. [PubMed: 26988629]

[60]. Anderson LM, Smith KE, Nuñez MC, and Farrell NR, "Family accommodation in eating disorders: a preliminary examination of correlates with familial burden and cognitive-behavioral treatment outcome," Eat. Disord, pp. 1–17, Aug. 2019, doi: 10.1080/10640266.2019.1652473.

[61]. Hildebrandt T, Peyser D, and Sysko R, "Lessons learned developing and testing FAMILY-BASED interoceptive exposure for adolescents with l OW-WEIGHT eating disorders," Int. J. Eat. Disord, vol. 54, no. 11, pp. 2037–2045, Nov. 2021, doi: 10.1002/eat.23605. [PubMed: 34528269]

Strength and limits

A strength of this review is its focus on RCTs and rigorous evidence across the literature base. The review, while comprehensive in its inclusion of all available work, is limited by the lack of meta-analytic review, which is not indicated given the modest amount of literature that currently investigates FBT for BN.

What is already known on this subject?

To date, FBT is the first-line treatment for adolescents with AN and recommended for those with BN. Accordingly, it is known that for many adolescents, FBT may be an effective treatment approach, regardless of patient- or family-level factors.

What this study adds?

In synthesizing the evidence base for non-specific predictors, moderators, and mediators of FBT across AN and BN, this review delineates important factors that should be attended to in making treatment selections.

Table 1.

Study characteristics and key findings

Study and Location	Sample *N* (%female), mean age (*SD*)	Diagnosis	Treatment	Study design (original RCT)	Outcomes and timepoint	Brief summary of findings
Accurso et al., 2014 USA	121 (90.9%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. AFT	Secondary data analyses (Lock et al., 2010)	EDE global and subscale scores, BDI, RSES at EOT, 6- and 12m follow-up	Weight gain significantly predicted improved EDE scores at EOT; this effect diminished over follow-up. In contrast, depressive symptoms eased over time even in the absence of weight gain. Self-esteem did not evidence significant change over time.
Agras et al., 2014 USA and Canada	158 (89.2%) M_{age} (*SD*) = 15.3 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. SyFT	RCT	Remission, i.e., ≥ 95% EBW EOT, 6- and 12m follow-up	Compared to SyFT, FBT led to faster weight gain, fewer hospital days, and lower treatment costs. Those with higher CY-BOCS scores gained significantly more weight with SyFT at EOT compared with FBT; the reverse was true for low CY-BOCS scores.
Allan et al., 2018 AUS	107 (87.7%) M_{age} (*SD*) = 15.5 (1.5)	DSM-IV AN excluding amenorrhea	FBT v. PFT	Secondary data analyses (Le Grange et al., 2016)	Remission, i.e., ≥ 95%mBMI plus EDE global score within 1 *SD* of community norms EOT, 6- and 12m follow-up	Adolescents of mothers who demonstrated an increase, or remained high, in expressed emotion were less likely to remit than those for whom expressed emotion decreased or remained low; no noted effects for fathers. Compared to FBT, PFT led to decreased in maternal criticism, and an increase in maternal criticism was more likely to be observed in FBT than PFT.
Byrne et al., 2015 USA	121 (91%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. AFT	Secondary data analyses (Lock et al., 2010)	Weight gain per session and EOT	In FBT, increase in parental self-efficacy predicted subsequent weight gain compared to those who received FBT with lesser change in parental self-efficacy and those who received AFT. Adolescent self-efficacy did not predict weight gain.
Byrne et al., 2018 USA	121 (91%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. AFT	Secondary data analyses (Lock et al., 2010)	Weight gain and YBC-EDS scores per session	Decrease in YBC-EDs scores was significantly associated with an increase in weight for those receiving FBT. No relation between YBC-EDS scores and weight for those receiving AFT.
Ciao et al., 2015 USA	80 (97.5%) M_{age} (*SD*) = 16.1 (1.6)	DSM-IV BN or Partial BN	FBT-BN v. SPT	Secondary data analyses (Le Grange et al., 2007)	EDE, RSES, BDI EOT and 6m follow-up	All psychological outcomes improved through 6-month follow-up across both treatments. Younger adolescents and those with higher baseline purging had greater improvement with FBT compared to SPT.
Darcy et al., 2013 USA	*N* = 21; % female and full sample age not reported Original study: 121 (90.9%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT	Secondary data analyses (subsample from Lock et al., 2010)	Early response, i.e., weight gain > 1.8 kg by session 4	Adolescents who were less resistant in the first two sessions and whose parents made fewer critical comments yielded the highest rates of early response.

Study and Location	Sample *N* (%female), mean age (*SD*)	Diagnosis	Treatment	Study design (original RCT)	Outcomes and timepoint	Brief summary of findings
Doyle et al., 2010 USA	65 (89.2%) M_{age} (*SD*) =14.9 (2.1)	DSM-IV AN or Partial AN	FBT	Secondary data analyses (Le Grange et al., 2005; Loeb et al., 2007)	Remission, i.e., ≥ 95% EBW EOT	Gain of ≥ 2.88% in EBW by session 4 best predicted remission at EOT.
Eisler et al., 2000 UK	40 (97.5%) M_{age} (*SD*) = 15.5 (1.6)	DSM-IV AN or ICD 10	CFT v. SFT	RCT	Morgan and Russell Scales EOT	For families with high levels of maternal criticism, SFT was superior to CFT in achieving better Morgan and Russell Scale outcomes.
Eisler et al., 2007 UK	38; % female and age not reported Original study: 40 (97.5%) M_{age} (*SD*) = 15.5 (1.6)	DSM-IV AN or ICD 10	CFT v. SFT	Follow-up analyses (original study: Eisler et al., 2000)	Morgan and Russell Scales and BMI 5-year follow-up	At five-year follow-up (and similar to the original study), patients from families with high levels of maternal criticism had done less well at EOT if they received CFT compared to SFT.
Ellison et al., 2012 AUS	59 (94.02%) M_{age} (*SD*) = 14.57 (1.46)	DSM-IV AN	FBT	Secondary data analyses (subsample from Madden et al., 2015)	Weight gain per session and dropout from treatment	Parents taking control of ED behavior, not criticizing the patient, and externalizing the illness predicted greater weight gain by EOT.
Forsberg et al., 2013 USA	78 (90.9%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. AFT	Secondary data analyses (subsample from Lock et al., 2010)	Remission, i.e., ≥95%mBMI and EDE global score within 1*SD* of community norms and partial remission, i.e., > 85%mBMI EOT, 6- and 12m follow-up	No main effect or interaction effect for alliance on full remission; although a main effect was found for partial remission, there was no alliance-by-treatment moderation effect.
Gorrell et al., 2019 USA	109 (94%) M_{age} (*SD*) = 15.8 (1.5)	DSM-IV BN or Partial BN	FBT-BN vs. CBT-A	Secondary data analyses (Le Grange et al., 2015)	EDE global scores and abstinence from binge-eating and compensatory behavior at EOT	Across both treatments, adolescents who endorsed a higher level of motivation for change in ED-related preoccupations and rituals at baseline were more likely to have reduced attitudinal ED features at EOT. However, baseline YBC-EDS motivation scores had no effect on abstinence from binge eating and purging at EOT.
Hughes et al., 2019 AUS	106 (87.7%) M_{age} (*SD*) = 15.5 (1.5)	DSM-IV AN excluding amenorrhea	FBT v. PFT	Secondary data analyses (Le Grange et al., 2016)	%mBMI and remission defined by ≥95%mBMI plus EDE global score within 1 *SD* of community norms	Weight gain of ≥ 2.80 kg in FBT and 2.28 kg in PFT by session 5 were the best predictors of remission at EOT. Early response in FBT was predicted by greater paternal therapeutic alliance and lower paternal criticism. Early response in PFT was predicted by less severe ED symptoms and negative affect at baseline, lower maternal criticism, and greater adolescent therapeutic alliance.
Le Grange et al., 1992 UK	18 (88.9%) M_{age} (*SD*) = 15.33 (1.8)	DSM-III-R AN	CFT v. family counselling	Pilot RCT	Morgan Russell Scales and weight gain EOT	Both treatments gave rise to similar benefits in terms of weight gain and reduction in ED symptoms. In the full sample, levels of criticism at the start of therapy predicted progress at 6m: parental criticism was significantly higher in the families of patients

Eat Weight Disord. Author manuscript; available in PMC 2023 August 01.

Study and Location	Sample *N* (%female), mean age (*SD*)	Diagnosis	Treatment	Study design (original RCT)	Outcomes and timepoint	Brief summary of findings
						who did poorly, compared with those who fared better.
Le Grange et al., 2007 USA	80 (97.5%) M_{age} (*SD*) = 16.1 (1.6)	DSM-IV BN or Partial BN	FBT-BN v. SPT	RCT	Remission, i.e., abstinence from binge eating and purging over the past 28 days EOT and 6m follow-up	FBT led to a significantly greater number of adolescents who were abstinent at EOT and 6m, compared to SPT. Reduction in core bulimic symptoms was also more immediate for patients receiving FBT v. SPT.
Le Grange, Crosby et al., 2008 USA	80 (97.5%) M_{age} (*SD*) = 16.1 (1.6)	DSM-IV BN or Partial BN	FBT-BN v. SPT	Secondary data analysis (Le Grange et al., 2007)	Remission, i.e., abstinence from binge eating and purging over the past 28 days Partial remission defined as no longer meeting the partial DSM-IV criteria used in the study. EOT and 6m follow-up	Those with lower baseline depression were more likely to have partial remission at EOT and those with lower binge eating and purging at baseline were more likely to have partial remission at 6m. No moderators of effects of treatment were found at EOT. Using partial remission as an outcome: for those with low EDE scores, FBT-BN was superior at 6m.
Le Grange, Doyle et al., 2008 USA	80 (97.5%) M_{age} (*SD*) = 16.1 (1.6)	DSM-IV BN or Partial BN	FBT-BN v. SPT	Secondary data analyses (Le Grange et al., 2007)	Remission, i.e., abstinence from binge eating and purging over the past 28 days EOT and 6m follow-up	Reduction of bulimic symptoms early in treatment predicted remission in both groups.
Le Grange et al., 2011 USA	79 (89.9%) M_{age} (*SD*) = 15.2 (1.6)	DSM-IV AN	Long (12m) v. short (6m) FBT	Secondary data analyses (Lock et al., 2005)	Good outcome, i.e., achieving weight ≥ 95% EBW EOT	Maternal and paternal baseline warmth were associated with good outcome at EOT.
Le Grange et al., 2012 USA	121 (91%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. AFT	Secondary data analyses (Lock et al., 2010)	Remission, i.e., ≥95%mBMI and EDE global score within 1*SD* of community norms EOT, 6- and 12m follow-up	At EOT, those with higher YBC-EDS scores or higher baseline EDE global scores benefitted more from FBT; neither remained significant at follow-up. Those with AN binge/purge subtype did less well over follow-up. No mediators of treatment were identified.
Le Grange et al., 2014 USA	121 (91%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. AFT	Secondary data analyses (Lock et al., 2010)	Remission, i.e., ≥95%mBMI and EDE global score within 1*SD* of community norms EOT and 12m follow-up	Early weight gain facilitated remission by EOT for those receiving FBT or AFT. Weight gain was not significantly associated with remission at follow-up in either group.
Le Grange et al., 2015 USA	109 (94%) M_{age} (*SD*) = 15.8 (1.5)	DSM-IV BN or Partial BN	FBT-BN v. CBT-A	RCT	Remission, i.e., abstinence from binge eating and purging over the past 28 days EOT, 6m, and 12m follow-up	Those receiving FBT were more likely to achieve abstinence at EOT and 6m; statistical differences between the two treatments did not remain at 12m.
Le Grange et al., 2016 AUS	107 (87.7%) M_{age} (*SD*) = 15.5 (1.5)	DSM-IV AN excluding amenorrhea	FBT v. PFT	RCT	Remission, i.e., ≥95%mBMI and EDE global score within 1*SD* of community norms	No moderators were identified at EOT. At 6m, those with higher YBC-EDS scores did better in FBT; those with higher treatment expectancies did better

Study and Location	Sample *N* (%female), mean age (*SD*)	Diagnosis	Treatment	Study design (original RCT)	Outcomes and timepoint	Brief summary of findings
					EOT, 6m and 12m follow-up	in PFT. At 12m, patients with shorter duration of illness did better in FBT, compared to PFT.
Lock et al., 2005 USA	89 (89.5%) M_{age} (*SD*) = 15.2 (1.7)	DSM-IV AN	Long (12m) v. short (6m) FBT	RCT	EDE scores and BMI at 6- and 12m follow-up	For those with higher YBC-EDS scores, longer FBT was superior in promoting weight gain. Using global EDE score: For participants in nonintact families, longer FBT was superior.
Lock et al., 2008 USA	80 (97.5%) M_{age} (*SD*) = 16.1 (1.6)	DSM-IV BN or Partial BN	FBT-BN v. SPT	Secondary data analyses (Le Grange et al., 2007)	Remission, i.e., abstinence from binge eating and purging over the past 28 days EOT and 6m follow-up	No significant treatment-by-mediator effects. In main effects, change in ED cognitions mid-treatment, specifically a subscale corresponding to weight concern, led to improved likelihood of abstinence from binge-eating and purging behavior at EOT and 6-month follow-up.
Lock et al., 2010 USA	121 (90.9%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. AFT	RCT	Remission, i.e., ≥95%mBMI and EDE global score within 1*SD* of community norms EOT, 6- and 12m follow-up	Both treatments were similarly effective in producing full remission at EOT but FBT was more likely to lead to full remission at both follow-up timepoints.
Lock et al., 2015 USA	45 (93.3%) M_{age} (*SD*) = 14.6 (1.4)	DSM-IV AN excluding amenorrhea	FBT v. FBT with intensive parent coaching	Pilot RCT	Parental self-efficacy (Parents v. AN Scale). Weight per session and %EBW at EOT	Poor early responders (i.e., weight gain < 2.3 kg [4.8 lbs] by session 4) whose caretakers received intensive parent coaching achieved full weight restoration (>95%mBMI) by EOT at similar rates as those who had responded early.
Lock et al., 2016 USA and Canada	158 (89.2%) M_{age} (*SD*) = 15.3 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. SyFT	Secondary data analyses (Agras et al., 2014)	Remission, i.e., ≥ 95% EBW, hospitalization EOT, 6- and 12m follow-up	Those who had higher depression and obsessionality scores *and* received FBT were less likely to require early hospitalization.
Loeb et al., 2009	*N* = 1 female, aged 17	Subclinical AN (i.e., low weight but denial of fear of weight gain)	FBT	Case study	Weight and menstrual status	Despite initial denial of cognitive symptoms, weight gain became an important focus of progress in treatment, and an ultimate indicator of the success of the intervention as a whole.
Madden et al., 2015 AUS	82 (95.1%) M_{age} (*SD*) = 14.99 (146)	DSM-IV AN	Short v. longer hospitalization plus FBT	RCT	Hospital admission days and remission, i.e., ≥95%mBMI and EDE global score within 1*SD* of community norms	Gaining 3.97 pounds by session 4 of predicted higher %EBW and EOT remission. Cost savings would be greatest from combining shorter hospitalization with FBT.
Matheson et al., 2020 USA	71 (93%) M_{age} (*SD*) = 15.69 (1.55)	DSM-IV BN or Partial BN	FBT-BN vs. CBT-A	Secondary data analysis (Le Grange et al., 2015)	Abstinence of binge-eating and compensatory behaviors in the 28 days prior	Reduction in purging at session 2 and binge eating at session 4 were independently related to abstinence at EOT, regardless of treatment type.
Paulson-Karlsson et al., 2008 Sweden	32 (100%) M_{age} (*SD*) = 15.4 (1.4)	DSM-IV AN, BN, EDNOS	SFT and CFT	Pilot (non-randomized)	Remission, i.e., no longer meeting DSM-IV criteria EOT	72% at 18m follow-up and 78% at 36m follow-up had remitted. While general psychopathology and ED symptoms remitted 36 months after the start of FBT, perfectionism scores remained high.

Study and Location	Sample *N* (%female), mean age (*SD*)	Diagnosis	Treatment	Study design (original RCT)	Outcomes and timepoint	Brief summary of findings
Rienecke et al., 2016 USA	121 (91%) M_{age} (*SD*) = 14.4 (1.6)	DSM-IV AN excluding amenorrhea	FBT vs. AFT	Secondary data analysis (Lock et al., 2010)	%EBW, dropout rates, EDE global scores, family function EOT	Youth whose mothers expressed greater hostility had greater weight gain in AFT compared to FBT. Both general family functioning and family communication were better at EOT for families whose mothers expressed no hostility.
Rhodes et al., 2008 AUS	20 (100%) M_{age} (*SD*) = 14	DSM-IV-TR AN	FBT vs. FBT with consult	RCT	Morgan and Russell Scales and %EBW at each session and EOT	Parent-to-parent consultation led to small increases in the rate of early weight restoration but this effect was not mediated by parental self-efficacy.
Sadeh-Sharvit et al., 2018 USA and Canada	158 (89.2%) M_{age} (*SD*) = 15.3 (1.6)	DSM-IV AN excluding amenorrhea	FBT v. SyFT	Secondary data analyses (Agras et al., 2014)	Remission, i.e., ≥ 95% EBW, parental self-efficacy EOT, 6- and 12m follow-up	Change in maternal self-efficacy from baseline to session 8 mediated weight gain by session 10. Only parents receiving FBT reported significantly greater self-efficacy.
Spettigue et al., 2020 Canada	7 (85.7%) M_{age} = 15.0, range 13–17	'Mild' presentation of restrictive ED, characterized by low weight (89% EBW)	5-session FBT informed treatment (DREAMS)	Case series	Qualitative chart review: physician notes and family feedback	Factors contributing to positive outcome in weight status and cognitive symptom remission were parents taking control of meals and making nutrition "mandatory," with consistent praise and support.

Note (in order of appearance in table): DSM = Diagnostic and Statistical Manual of Mental Disorders; AN = anorexia nervosa; AFT = adolescent-focused therapy; EDE = Eating Disorder Examination; EOT = end of treatment; FBT= Family-based treatment; BDI = Beck Depression Inventory; RSES= Rosenberg Self-Esteem Scale; SyFT = Systemic Family Therapy; RCT = randomized controlled trial; EBW= Expected Body Weight; CY-BOCS = Children's Yale–Brown Obsessive Compulsive Scale; PFT, Parent-Focused Treatment; YBC-EDS, Yale-Brown-Cornell Eating Disorder Scale; BN = bulimia nervosa; Partial BN = meeting all DSM-IV criteria except binge-eating or purging frequency (lowered to 1×/week over 6m; SPT = Supportive Psychotherapy for Adolescent Bulimia Nervosa; Partial AN (per DSM-IV) = criterion A (weight 85% of expected) met in the recent past but recently achieved partial weight restoration through hospitalization prior to the initiation of outpatient treatment; or met DSM-IV criteria B-D and had engaged in significant dietary restriction, but was currently ≥85% of EBW; CFT = conjoint family therapy; SFT= separated family therapy; ED = eating disorder; CBT-A = Cognitive-Behavioral Therapy for Adolescent Bulimia Nervosa; %mBMI = percent median body mass index for age and gender; EDNOS = eating disorder not otherwise specified.