Transdiagnostic treatment for eating disorders

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Less is more

- Ludwig Mies van der Rohe

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Chapter 1

Introduction

General introduction

Mrs. M

Mrs. M is a 40-year-old married woman with a son of 18 years old. She has an eating disorder for more than 20 years and never received treatment before. In her childhood there were a lot of unmet emotional needs and a history of being bullied in primary school. She developed severe self-esteem problems, an intense anxiety of being judged and a dysfunctional level of perfectionism. From the age of 12 she became dissatisfied with her weight (which was in the normal range) and body shape and from the age of 16 she began to skip meals and lost weight. Her focus and attention on shape and weight intensified and her eating pattern became more and more restrictive. At the age of 19 she had a body mass index (BMI; weight/height^2) of 14. At the age of 20 she met her present husband and started to eat more regular and gained weight, however after a while she developed binges and because of a great fear of gaining more weight she began to compensate by vomiting and taking laxatives. In the past years, periods of restrictive eating had alternated with periods of binge eating and compensation behavior. Her preoccupation with shape and weight increased resulting in a diversity of eating disorder related behaviors (i.e. continuously checking her weight on the scale, checking her shape in mirrors, dietary rules and weighing her food). These behaviors took her several hours a day. As a result, she lost her job as a successful lawyer. When her son went to live on his own, she became more isolated. At the time of referral, a severe bulimia nervosa was diagnosed with comorbid a social anxiety disorder. Her weight was within the normal range. Mrs. M expressed the need to stop the binges and improve her self-esteem.

Eating disorders

Eating disorders are mental disorders in which people experience severe disturbances in their eating behaviors and related thoughts and emotions. People with eating disorders typically become pre-occupied with food and their body weight. Eating disorders are responsible for significant elevated mortality rates (Arcelus et al., 2011) and loss of quality of life (Jenkins et al., 2011).

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders DSM5 (American Psychiatric Association, 2013) three specific eating disorders are specified: anorexia nervosa, bulimia nervosa and binge eating disorder. A large percentage of people with eating disorders, in both clinical and community samples, do not meet the full DSM-5 diagnostic criteria for

these disorders and are diagnosed with 'otherwise specified feeding or eating disorder' (Keel et al., 2011; Machado, Goncalves, & Hoek, 2013; Smink, van Hoeken, & Hoek, 2013).

Onset of anorexia nervosa is often in early to mid-adolescence. In bulimia nervosa and binge eating disorder onset is more commonly in later adolescence and young adulthood (Stice, Marti, & Rohde, 2013). Among women the lifetime prevalence for anorexia nervosa is 1-4%, 1-2% for bulimia nervosa, 1-4% for binge eating disorder and 2-3% for sub-threshold eating disorders/otherwise specified feeding or eating disorder (Keski-Rahkonen & Mustelin, 2016; Smink et al., 2013). Most patients with anorexia nervosa and bulimia nervosa are female (Bulik et al., 2006; Hudson et al., 2007; Kessler et al., 2013). Among men 0.3-0.7% report eating disorders like anorexia nervosa and bulimia nervosa (Keski-Rahkonen & Mustelin, 2016). The lifetime prevalence for binge eating disorder among men is 2% (Hudson et al., 2007). Although most patients with eating disorders are young women, it is important to be aware that eating disorder psychopathology can arise at any age, and in both females and males (Hay et al., 2014).

Of all patients diagnosed with an eating disorder, 70% also meet the diagnostic criteria of another DSM disorder, e.g. anxiety disorders (>50%), mood disorders (>40%), self-harm (>20%), and substance use (>10%) are common (Keski-Rahkonen & Mustelin, 2016).

The aetiology of eating disorders is regarded as multifactorial and complex (Collier & Treasure, 2004). Risk factors include biological factors (e.g. genetic factors, serotonin function), socio-cultural factors (e.g. cultural attitudes to weight and shape) and psychological factors (e.g. personality traits like self-esteem and perfectionism).

The way in which eating disorders are classified in the DSM-5 supports the view that there are a number of distinct conditions clearly differentiated from each other, each requiring its own treatment protocol. However, patients with anorexia nervosa, bulimia nervosa, binge eating disorder and otherwise specified feeding or eating disorder have many features in common. Moreover, diagnoses are often unstable, with clinical features changing over time and switching for example from anorexia nervosa to bulimia nervosa, which is illustrated by the case description of Mrs. M. Accordingly, Fairburn et al. suggest that transdiagnostic mechanisms play a role in the persistence of eating disorders (Fairburn, Cooper, & Shafran, 2003). If this is the case,

treatments that are capable of addressing these mechanisms should be effective for all eating disorders. This transdiagnostic view is important in the outline of this thesis.

Psychological treatments for adults

The major guidelines for the treatment of eating disorders recommend, based on research, cognitive behavior therapy (among which cognitive behavior therapy enhanced; CBT-E) as the psychological treatment of first choice, especially for bulimia nervosa and binge eating disorder (Hay et al., 2014; Hilbert, Hoek, & Schmidt, 2017; National Institute for Health and Care Excellence (NICE), 2017; Netwerk Kwaliteitsontwikkeling GGz, 2017; Yager et al., 2014). There is also, albeit more limited, empirical evidence base for the effectiveness of interpersonal psychotherapy and dialectical behavior therapy in both bulimia nervosa and binge eating disorder.

For anorexia nervosa, the effectiveness of psychological treatments is less pronounced. Therapist-led manualized based psychological treatments, such as CBT-E, specialist supportive clinical management (SSCM) and the Maudsley model of anorexia nervosa treatment for adults (MANTRA) have the most promising effects, and as such should be the treatments of first choice. Most guidelines recommend outpatient or day patient treatments and only hospital admission when there are severe medical and/or psychological risks (Hay et al., 2014; Hilbert et al., 2017).

Especially for bulimia nervosa and binge eating disorder, there is clear evidence of the effectiveness of cognitive behavior therapy, however it is not being used as widely in clinical practice as guidelines recommend. Waller et al. reported poor adherence among CBT eating disorder clinicians with no single core CBT technique being routinely used by 50% of the sample (Waller, Stringer, & Meyer, 2012). Although in a replication study among Dutch therapists 83.2% of clinicians reported the use of a CBT treatment manual for eating disorders, the application of the specific CBT techniques was also below the level one would expect if following protocols (Mulkens et al., 2018). Different reasons for this non-adherence have been investigated. Particularly in CBT clinicians who were anxious, older, or more experienced in working with patients with eating disorders, delivery of CBT techniques was lower than protocols would suggest (Waller et al., 2012). Furthermore, while research showed that the therapeutic alliance does not drive change in behaviors in eating disorder therapies (Graves et al., 2017), non-delivery of CBT for eating disorders has been associated with clinicians' beliefs about the power and

importance of the therapeutic alliance in achieving good therapy outcome (Mulkens et al., 2018). Finally, clinicians often claim that existing evidence-based protocols do not apply to their patient group (Tobin et al., 2007). It could be hypothesized that, in the eating disorder field, this is partly due to the mismatch between the large percentage of patients with eating disorders who do not meet the full DSM-5 criteria for an eating disorder (subsequently classified as otherwise specified feeding or eating disorder) and the diagnosis specific protocols. Although it is clear that the regular eating disorder therapy in clinical practice varies and that therapists often do not adhere to evidence-based protocols, there are no empirical data about the exact content, effectiveness and efficiency of the regular eating disorder therapy.

CBT-E

CBT-E is a specific form of cognitive behavior therapy suitable for the full range of eating disorder diagnoses (Fairburn, 2008). It is based on a transdiagnostic theory of the maintenance of eating disorders, which assumes that most of the mechanisms involved in the persistence of eating disorders are common to all eating disorders, rather than being specific for each diagnostic group separately. According to this theory, a dysfunctional evaluation of self-worth, overly based on shape and weight, is the core psychopathology of all eating disorders (Fairburn et al., 2003). CBT-E focusses on strategies and procedures to modify this over-evaluation of shape and weight. This is known as the 'focused' version of CBT-E (CBT-Ef). The treatment protocol can be extended with interventions targeting additional maintaining mechanisms that are expected to obstruct change and improvement (low self-esteem, clinical perfectionism, and interpersonal problems). This extended protocol is known as the 'broad' version of CBT-E (CBT-Eb). For both versions of CBT-E, two variants of intensity have been developed involving either 20 sessions in 20 weeks for patients who are not significantly underweight (BMI >17.5), or 40 sessions in 40 weeks for patients who are significantly underweight (BMI ≤17.5). For otherwise specified feeding or eating disorders, CBT-E might have an advantage over other cognitive behavior therapy protocols because of its transdiagnostic reach.

The strategy underpinning CBT-E is to construct a transdiagnostic formulation of the processes that are maintaining the patient's psychopathology and to use this formulation to identify the features that need to be targeted in treatment. This formulation is constructed at the beginning of treatment, but will be revised, if needed, during therapy. In this way a tailor-made treatment is created.

Stage 1 (sessions 1–7) is an intensive initial stage, with appointments twice a week. The therapist and the patient together set up the formulation of the underlying maintaining factors, which will be used as a base for the remainder of the treatment. The aims of this stage are to engage the patient in treatment.

Stage 2 (sessions 8–9) are weekly appointments. This is a brief stage in which the therapist and patient take stock, review progress, identify any emerging barriers to change, modify the formulation and plan stage 3. This stage is important to identify problems with the therapy, to remove barriers and adjust treatment if needed. After stage 2 the treatment will become more personalized.

Stage 3 (sessions 10–17) is the main body of treatment. There are weekly appointments. The aim is to address the main mechanisms that are supposed to maintain the patient's eating disorder. How this is done precisely varies from patient to patient. The therapist can choose to pay attention to one or more defined maintaining factors. Often the over-evaluation of shape and weight is an important maintaining mechanism that will be addressed in this stage.

Stage 4 (sessions 18–20) is the final stage of treatment and the focus shifts to the future. The appointments are scheduled at two-week intervals. There are two aims: the first one is to ensure that the changes are maintained (over the subsequent 20 weeks until a review appointment is held), and the second one is to minimize the risk of relapse in the long term. A personalized maintenance plan is made.

After 20 weeks there is a review session. The most important aim in this session is to review what has been learned and achieved during treatment and what risk factors are to be taken into account when therapy has ended.

Mrs. M

The focused version of CBT-E (Fairburn, 2008) was indicated.

In the *first stage* of treatment engaging Mrs. M was an important goal. She was demoralized and had little hope that change was possible. Jointly creating the formulation (see Figure 1.1) at the start helped her to understand the processes that appeared to be maintaining her eating problem. The real time registrations, in session weighing and regular eating triggered anxiety and shame. However, the twice-weekly sessions, the growing realization of the interacting mechanisms of her eating disorder and her understanding about what needed to be changed to overcome her binges helped her to stay motivated. At the end of stage 1, as a result of the regular eating, the frequency of the binges and compensatory behavior decreased. This decline together with the experience that her weight did not increase, created hope that change was possible.

After stage 1 an evaluation took place (*stage 2*) during which the three most important factors that maintained her eating disorder and needed attention in *stage 3* were jointly determined;

1. The over-evaluation of shape and weight; that is, the judging of self-worth largely, or even exclusively, in terms of shape and weight and the ability to control them. In stage three she learned to decrease the shape checking behaviors (i.e. frequently mirror use, wearing tight clothes, comparing her shape with others, measuring her leg size) and increase the importance of other domains in her life for self-evaluation. She was encouraged to focus on enjoyable activities. She initiated social activities with her son and husband, contacted friends and started creative activities, dancing and reading.

2. The event-related changes in her eating pattern were addressed by learning problem solving strategies and more functional ways to regulate her emotions. Binge eating, for example, mainly took place in the evening when she felt lonely and bored. She learned to identify this problem, considering as many solutions as possible, thinking of the pros and cons of each solution, choose the best solution and act on it. As a result she initiated more social activities in the evening (a walk on the beach, going to the theatre or cinema and following dance classes).

3. Dietary restraint and dietary rules were identified in stage 1 (for example; not eating apple pie because of the fear of gaining weight) and tackled in stage 3 by breaking the rules in question (eat a piece of apple pie without compensating behaviors) in order to explore the consequences of doing so (weight remained stable). As a result, more functional cognitions were created ("I can eat a piece of apple pie without gaining weight").

At the end of stage 3 the binges and compensatory behavior were absent. However, although reduced, dietary rules and concerns about shape and weight were still present. In *stage 4* a maintenance plan was made. The most important goal of this plan was to identify with Mrs. M a limited number of activities that she should engage in the next 20 weeks. She was stimulated to behave in line with the ways identified during treatment to obtain the full benefits of treatment.

After 20 weeks a *review session* was planned. Mrs. M reported no binges and compensatory behavior, a regular eating pattern and a stable weight. She picked up her work as a lawyer again and her social network was increased. This progress had an enhancing effect on her self-confidence. Although she still was not satisfied with her shape and weight, it no longer determined most of her self-esteem.

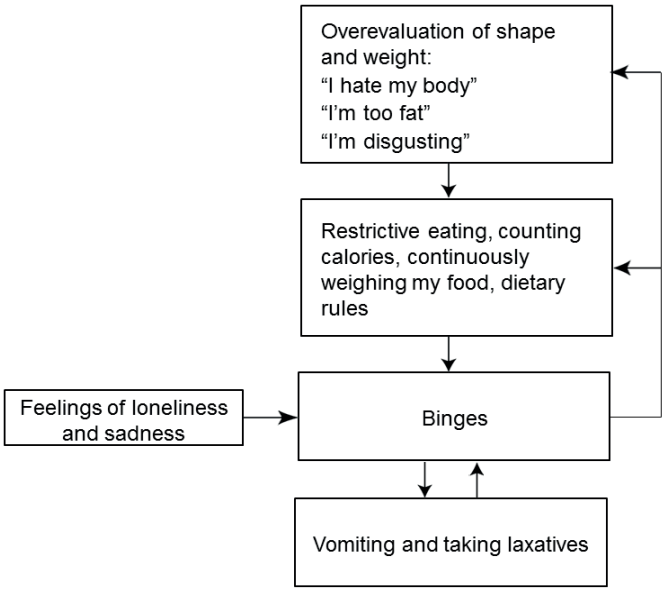

Figure 1.1. Transdiagnostic formulation Mrs. M according to the focused version of CBT-E

Reflection

Due to the severity of the eating disorder, negative self-esteem and the co-morbid social anxiety disorder, two questions were part of the therapist's consideration during the therapy process;

1. Was her negative self-esteem an important maintaining factor of the eating disorder (indication for the broad version of CBT-E)?

2. Would 20 sessions be enough to tackle this complex eating disorder psychopathology?

In the first stage of treatment detailed information was collected from the registrations to investigate if the proposed transdiagnostic model (Figure 1.1) accurately explained the ongoing processes of her eating disorder. CBT-E assumes that not all clinical features need to be addressed in treatment. The psychopathology of an eating disorder is compared to the analogy of a house of cards. If one wants to bring down the house, the key structural cards need to be identified and removed, and then the house will fall down. Furthermore, a principle that underpins CBT-E is that it is better to do a few things well rather than many things badly ("less is more"). Therapist and patient agreed that, not self-esteem but the over-evaluation of shape and weight was the most important maintaining factor and accordingly was the most important to address in therapy. According to the rationale of the broad version of CBT-E, participants with more self-esteem problems are expected to respond less on the focused version of CBT-E. Although severe self-esteem problems were present, the focused version of CBT-E was successful. No additional attention for self-esteem problems was needed.

When the treatment of Mrs. M approached stage 4, not all eating disorder psychopathology was absent. Mrs. M was anxious to end therapy and the therapist was in doubt whether or not to end the therapy. In supervision, the therapist discussed reasons to continue therapy. The assumption of CBT-E, that further improvement is to be expected after therapy has ended together with positive experiences of the supervisor in similar CBT-E treatment processes helped the therapist to end the therapy within the 20 sessions. This had an additional advantage that Mrs. M could experience further improvement after treatment had ended which had an enhancing effect on her self-esteem.

Self-esteem and eating disorders

Self-esteem can be broadly defined as an individual's overall sense of self-worth or personal value (Rosenberg, 1965). Low self-esteem is reported to be an important factor associated with the aetiology and persistence of eating disorders (Cervera et al., 2003; Fairburn et al., 2003; Jacobi et al., 2004; Lo Coco et al., 2011; Sassaroli, Gallucci, & Ruggiero, 2008). Self-esteem is considered to be dependent on one's perceived ability to achieve certain life goals (Emler, 2001; Noordenbos, Aliakbari, & Campbell, 2014; Zeigler-Hill et al., 2013). Whereas most people evaluate themselves on the basis of different domains in life (e.g., work, relationships, parenting, hobbies, appearance etc), people with eating disorders judge themselves mainly on the basis of shape, weight and/or eating habits and their ability to control them (Fairburn et al., 2003). As a result, the judging of self-worth becomes largely dependent on shape and weight and the ability to control them. As mentioned earlier, this over-evaluation of shape and weight is seen as the core psychopathology of most eating disorders (Fairburn, 2008). Moreover, low self-esteem is thought to maintain the overvaluation of weight and shape and is also believed to contribute to patients' feelings of hopelessness about their capacity to change, thereby impacting their compliance with treatment (Fairburn, 2008). Fairburn describes that enhancing self-esteem may lead to better therapeutic outcomes.

Self-esteem is a complicated construct with different operationalizations in the existing literature. Different, however interrelated, dimensions of self-esteem have been described, such as whether it is stable or unstable (Kernis et al., 1993; Kernis & Goldman, 2006; Kernis, Grannemann, & Barclay, 1989), externally or internally contingent (Crocker & Luhtanen, 2003; Crocker & Park, 2004; Vonk & Smit, 2012) and implicit or explicit (Borton et al., 2012; DeHart, Pena, & Tennen, 2013; Koole & Pelham, 2003). Most studies of self-esteem in relation to eating disorders focus only on explicit self-esteem. Little is known about the relation between other dimensions of self-esteem and eating disorder psychopathology.

Treatment for self-esteem problems

It is often thought that amelioration of psychopathology symptoms during psychotherapy is associated with the automatic enhancement of self-esteem (Fennell & Jenkins, 2004). The precise mechanisms underpinning these effects are not known (Linardon, Kothe, & Fuller-Tyszkiewicz, 2019). In the meta-analysis of Linardon et al. (2019) some support was found for the beneficial effects of psychotherapy for eating disorders on self-esteem, however these

effects were small. He describes that the examined treatment studies did not directly target low self-esteem, possibly resulting in these relatively small effects. This raises the question if integrating additional therapeutic interventions, designed to directly address low self-esteem, into existing treatment protocols would result in larger improvements in self-esteem.

In the broad version of CBT-E, interventions to address core low self-esteem are based on Fennell's approach (1998, 2016). This approach is characterized by the identification and Socratic challenging of dysfunctional negative automatic thoughts, assumptions, and core beliefs about one's own worth and importance, and it is accompanied by a range of specific behavioral experiments. Most of these experiments are concerned with the anticipated reactions of others to the personal values and capacities of the patient. In the meta-analysis studying the effect of Fennell's approach (Kolubinski et al., 2018) in a variety of populations small to medium (one-day workshop) and large summary effect sizes (weekly sessions) were found. The decision whether or not to use the broad version of CBT-E is made in stage two, a stage where barriers to change are becoming clear. For most patients the focused version of CBT-E is effective (Fairburn et al., 2009). Fairburn (2008) recommends only to use the broad version including the possibility to address core low self-esteem, when this is maintaining the eating disorder.

Another, somewhat different, approach to address low self-esteem is competitive memory training COMET (Korrelboom, 2011). COMET is aimed at making patients feel what they already know by enhancing the accessibility of positive self-representations from long-term memory. According to Brewin (2006), cognitive therapy does not modify the negative meaning of concepts directly, but rather influences the relative retrievability from long-term memory of the different meanings that are associated with these concepts. Strengthening the possibility of retrieving positive self-representations that are in retrieval competition with negative self-representations is considered to be the key element of COMET.

In several randomized controlled trials COMET showed to be effective in improving self-esteem in various populations (Korrelboom, Maarsingh, & Huijbrechts, 2012; Korrelboom, Marissen, & van Assendelft, 2011; Staring et al., 2016; van der Gaag et al., 2012). One study has been completed in a group of hospitalized and day-treatment patients with eating disorders and/or personality disorders (Korrelboom et al., 2009). In this study, self-esteem was enhanced, and depression was diminished.

Research aims

As described above, regular eating disorder therapy (treatment as usual) in clinical practice varies greatly. There are no empirical data about the exact content, effectiveness and efficiency of this treatment as usual. Although CBT-E is an evidence-based treatment for eating disorders, randomized controlled trials that studied the effectiveness of this protocol were mainly performed by the research group that developed the treatment protocol. This raises the question whether these results can be generalized to other treatment settings and populations. In addition, no former treatment studies compared the effectiveness of CBT-E with treatment as usual in terms of effectiveness and efficiency.

Therefore, the first aim of this thesis is to test the alleged superior effectiveness and efficiency of CBT-E compared to treatment as usual. In addition, to increase understanding of the content of treatment as usual, this treatment condition will be carefully monitored and differences in the duration and intensity between CBT-E and treatment as usual will be explored.

Furthermore, according to the rationale of the broad version of CBT-E, participants with more self-esteem problems, perfectionism and interpersonal problems are expected to respond less to the focused version of CBT-E. Identification of patient characteristics that could help to answer the question for whom CBT-E is more effective would enable treatment matching. Therefore, self-esteem, perfectionism and interpersonal problems, the supposed additional maintaining mechanisms for severe eating disorder psychopathology, will be examined as possible moderating variables.

Most studies of self-esteem in relation to eating disorder psychopathology focus only on explicit self-esteem. Little is known about the relation between other dimensions of self-esteem and eating disorders. The second aim of this thesis is to gain more insight into the relationship of explicit and implicit self-esteem as a multidimensional construct of self-esteem in an eating disorder sample.

Finally, notwithstanding its presumed critical role in maintaining eating disorders, only one study has specifically addressed the treatment of low self-esteem in this patient population. Competitive memory training (COMET) is described as a promising treatment intervention to enhance self-esteem, but its effectiveness has never been investigated in eating disorder patients

in a randomized controlled trial. The last aim of this thesis is to evaluate the cognitive behavioral intervention COMET for the treatment of low self-esteem in patients with eating disorders.

Outline of this thesis

Chapter 2 reports on the associations between the (severity of) eating disorders and explicit/implicit self-esteem.

Chapter 3 reports on the effectiveness of a cognitive behavioral intervention, competitive memory training (COMET), for the treatment of low self-esteem in patients with eating disorders.

Chapter 4 contains a systematic review of CBT-E effectiveness studies on bulimia nervosa, binge eating disorder and transdiagnostic samples.

Chapter 5 presents the study protocol and Chapter 6 reports the results of a randomized controlled trial investigating the effectiveness of CBT-E compared to treatment as usual for eating disorders.

Finally, Chapter 7 contains a summary and general discussion of the main findings. Furthermore, the strengths and limitations are considered, and implications and directions for future research as well as clinical practice are presented.

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Appendix

Diagnostic criteria for anorexia nervosa, bulimia nervosa, binge eating disorder and otherwise specified feeding or eating disorder according to the DSM-5 (American Psychiatric Association, 2013)

Anorexia nervosa

A. Restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. Significantly low weight is defined as a weight that is less than minimally normal or, for children and adolescents, less than minimally expected.
B. Intense fear of gaining weight or of becoming fat, or persistent behavior that interferes with weight gain, even though at a significantly low weight.
C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

Specify whether:

Restricting type: During the last three months, the individual has not engaged in recurrent episodes of binge eating or purging behavior (i.e. self-induced vomiting, or the misuse of laxatives, diuretics, or enemas). This subtype describes presentations in which weight loss is accomplished primarily through dieting, fasting and/or excessive exercise.

Binge-eating/purging type: During the last three months the individual has engaged in recurrent episodes of binge eating or purging behavior (i.e. self-induced vomiting, or the misuse of laxatives, diuretics, or enemas).

Specify current severity:

Mild: BMI more than 17
Moderate: BMI 16- 16.99
Severe: BMI 15-15.99
Extreme: BMI less than 15

Bulimia nervosa

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   1. Eating in a discrete period of time (e.g. within any 2 hour period), an amount of food that is definitely larger than what most individuals would eat in a similar period of time under similar circumstances;
   2. A sense of lack of control over eating during the episodes (e.g. a feeling that one cannot stop eating or control what or how much one is eating.
B. Recurrent inappropriate compensatory behaviors to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise.
C. The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for 3 months.
D. Self-evaluation is unduly influenced by body shape and weight.
E. The disturbance does not occur exclusively during episodes of anorexia nervosa.

Specify current severity:

Mild: An average of 1-3 episodes of inappropriate compensatory behaviors per week.
Moderate: An average of 4-7 episodes of inappropriate compensatory behaviors per week.
Severe: An average of 8-13 episodes of inappropriate compensatory behaviors per week.
Extreme: An average of 14 or more episodes of inappropriate compensatory behaviors per week.

Binge eating disorder

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both:
   1. Eating in a discrete period of time (e.g. within any 2 hour period), an amount of food that is definitely larger than what most individuals would eat in a similar period of time under similar circumstances;
   2. A sense of lack of control over eating during the episodes (e.g. a feeling that one cannot stop eating or control what or how much one is eating).

B. Binge eating episodes are associated with three or more of the following:
   1. Eating much more rapidly than normal;
   2. Eating until feeling uncomfortably full;
   3. Eating large amounts of food when not feeling physically hungry;
   4. Eating alone because of feeling embarrassed by how much one is eating;
   5. Feeling disgusted with oneself, depressed, or very guilty afterwards.

C. Marked distress regarding binge eating is present.

D. The binge eating occurs, on average, at least once a week for 3 months.

E. The binge eating is not associated with the recurrent use of inappropriate compensatory behavior as in bulimia nervosa and does not occur exclusively during the course of bulimia nervosa or anorexia nervosa.

Specify current severity:

Mild: 1-3 binge eating episodes per week.
Moderate: 4-7 binge eating episodes per week.
Severe: 8-13 binge eating episodes per week.
Extreme: 14 or more binge eating episodes per week.

Otherwise specified feeding or eating disorder

Symptoms characteristic of a feeing or eating disorder that cause clinical distress or impairment in social, occupational, or other important areas of functioning predominate.

- However DO NOT meet the full criteria for any of the disorders in the feeding and eating disorders diagnostic class.
- This category can also be used in situations to communicate the specific reason the presentation does not meet the criteria for a specific eating disorder.
- This is done by recording "other specified feeding or eating disorder" followed by the specific reason e.g. "bulimia nervosa-low frequency".

Examples:

1. **Atypical Anorexia Nervosa**: all of the criteria for anorexia nervosa are met, except that despite significant weight loss, the individual's weight is within or above the normal range.
2. **Bulimia Nervosa (of low frequency and/or limited duration)**: all of the criteria for bulimia nervosa are met, except that the binge eating and inappropriate compensatory behaviors occur, on average, less than once a week and/ or for less than 3 months.
3. **Binge-eating disorder (of low frequency and/or limited duration)**: all of the criteria for binge-eating disorder are met, except that the binge occurs, on average, less than once a week and/ or for less than 3 months.
4. **Purging disorder**: recurrent purging behavior to influence weight or shape (e.g. self-induced vomiting; misuse of laxatives, diuretics, or other medications) in the absence of binge eating.
5. **Night eating syndrome**: Recurrent episodes of night eating, as manifested by eating after awakening from sleep or by excessive food consumption after the evening meal. There is awareness of recall of the eating. The night eating is not better explained by external influences such as changes in the individual's sleepwake cycle or by local social norms. The night eating causes significant distress and/or impairment in functioning. The disordered pattern of eating is not better explained by binge-eating disorder and or another mental disorder, including substance use, and is not attributable to another medical disorder or to an effect of medication.

Chapter 2

Explicit, implicit and discrepant self-esteem in eating disorders

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~ submitted ~

Abstract

This study examined whether explicit self-esteem (ESE), implicit self-esteem (ISE) and the discrepancy between these two constructs – discrepant self-esteem (DSE) – are associated with (severity of) eating disorders (ED).

A between-group cross-sectional design with 36 patients with an ED and 37 participants without ED pathology was conducted. The Rosenberg Self-Esteem Scale, the self-esteem Implicit Association Test, the Eating Disorder Examination Questionnaire and the Mini International Neuropsychiatric Interview were administered to measure respectively ESE, ISE, ED psychopathology and ED diagnosis. Furthermore, five different operationalizations of DSE were examined.

Although both ESE and ISE were lower in patients with ED's than in the comparison group, there was no unique contribution of ISE in predicting ED status. Moreover, only ESE was a significant predictor for the severity of ED psychopathology. Outcomes for the role of DSE in ED were mixed. In conclusion, especially low ESE seems to be associated with (severity of) ED psychopathology.

Keywords

implicit self-esteem, explicit self-esteem, discrepant self-esteem, eating disorders, Implicit Association Test

Introduction

Low self-esteem is frequently reported to be a transdiagnostic factor associated with the etiology and persistence of psychopathology in general (Zeigler-Hill, 2011) including eating disorders (ED) (Cervera et al., 2003; Fairburn, Cooper & Shafran, 2003; Jacobi et al., 2004; Lo Coco et al., 2011; Sassaroli, Gallucci & Ruggiero, 2008). It is often referred to as one of the factors that can lead to strive to control eating, shape and weight in a way to gain some sense of self-worth resulting in a dysfunctional scheme of self-evaluation. As a result, the judging of self-worth becomes largely dependent of shape and weight and the ability to control them. This "overevaluation of shape and weight" is seen as the core psychopathology of most ED (Fairburn, 2008). Although, unlike anorexia nervosa (AN) and bulimia nervosa (BN), the overevaluation of shape and weight (and body dissatisfaction) is not a diagnostic criterion for BED, empirical evidence demonstrates that this is also markedly increased in individuals with BED (Ahrberg et al., 2011).

Most studies of self-esteem in relation to psychopathology used a self-report measure of self-esteem (Rosenberg, 1965) which taps participants' explicit personal reflection and evaluation of their positive and negative characteristics as a person, so-called explicit self-esteem (ESE). The last two decades, studies have started to differentiate ESE from implicit self-esteem (ISE). Research suggests that ESE and ISE stem from different sources and should be seen as different constructs (Rudman, 2004; Rudman, Phelan & Heppen, 2007). The differentiation between ESE and ISE stems from dual-process models (Gawronski & Bodenhausen, 2006; Zeigler-Hill, 2011) and is based on the assumption that there are two distinct processing modes: a rule-based, propositional processing mode and a relatively automatic, associative processing mode. Explicit attitudes reflect the outcome of the weighing of propositions and are based on knowledge about facts and values (Strack & Deutsch, 2004), whereas implicit attitudes are assumed to rely on associative, direct activation processes. The relevance of differentiating between ESE and ISE is further emphasized by the view that both facets of self-esteem are differentially involved in more controlled/strategic versus more automatic/spontaneous behaviors (Rudolph et al., 2010). ESE is considered to be relevant in the context of more deliberative behavior (in the context of eating disorders for example weighing oneself or dieting), while ISE is argued to be critically involved in more spontaneous behaviors (in the context of eating disorders for example checking or attentional avoidance of "ugly" body parts).

Cross-sectional studies investigating the relationship between ISE and symptoms in clinical disorders show mixed results. Most of these studies target depression (Franck, De Raedt & De Houwer, 2007; Franck, De Raedt, Dereu & Van den Abbeele, 2007; Lemmens et al., 2014; Risch et al., 2010; Rudolph et al., 2010) and/or (social) anxiety (Glashouwer, Vroling et al., 2013; Ritter et al., 2013; van Tuijl et al., 2016).

Research on ISE in individuals with ED is limited. VanderLinden et al. (2009) found a lower ISE in a group of patients with an ED (anorexia nervosa or bulimia nervosa) compared to a non-eating disorder control group. In this study no correlation was found between ESE and ISE, indicating that ESE and ISE could be different constructs of the self. Cockerham et al. (2009) compared patients with bulimia nervosa or binge eating disorder with a comparison group without an eating disorder. The ED group had lower ESE, but against the expectation, a more positive ISE than the comparison group. Hoffmeister et al. (2010) examined ISE and its link to body shape and weight concerns among restrained and unrestrained eaters, after increasing the participants' awareness of their body shape and weight. Whereas ISE increased for unrestrained eaters, it decreased for restrained eaters. They suggest that restrained eating status and/or initial level of body dissatisfaction might determine whether ISE decreases or increases as a result of an activation of the body schema. In a study including a BED sample, participants with BED were found to have lower ISE when compared to the comparison group (Brauhardt, Rudolph & Hilbert, 2014).

According to Zeigler-Hill (2011) a combination of high ESE and low ISE, or vice versa, points to discrepant self-esteem (DSE). Results from studies investigating the relationship between DSE and symptoms in clinical disorders among which depressive disorder (Creemers et al., 2012; Franck, De Raedt, Dereu & Van den Abbeele, 2007), social anxiety disorder (Schreiber et al., 2012; van Tuijl et al., 2014; van Tuijl et al., 2016) and narcissistic behavior (Jordan et al., 2003), are also mixed. Something to note is that in most of these studies different kinds of operationalizations of DSE were used (van Tuijl et al., 2016), complicating direct comparisons between studies and possibly explaining differences in outcome.

We only found two studies within the field of ED and DSE. Bos et al. (2010) found that DSE was not associated with eating problems in non-clinical adolescents. As mentioned before, in the study of Cockerham et al. (2009), participants with ED demonstrated a higher ISE than the healthy controls in combination with a lower ESE. The combination of a higher ISE and lower ESE in the ED group was interpreted as DSE.

In conclusion, although there is robust evidence for a relationship between low ESE and ED, research in the field of ED on ISE and DSE is still scarce. The purpose of this study was to gain more insight into the relationship of ESE, ISE and DSE in a transdiagnostic ED sample. More specifically, the purpose of the study was threefold: (a) to assess possible differences in ESE and ISE between ED patients as compared to a comparison group; (b) to assess the relation of ESE and ISE with the severity of ED; and (c) to assess possible differences in DSE between ED patients as compared to controls using different ways of operationalizing DSE.

Method

Participants

The clinical sample was recruited from a mental health center specialized in ED: PsyQ/ Parnassia Psychiatric Institute in the Netherlands. By spreading invitations via clinicians, patients were asked to participate after they had been diagnosed with an ED by certified clinicians. When clinicians thought participants had suicidal or psychotic symptoms, if there was intellectual disability or when the understanding of the Dutch language in reading and understanding was insufficient, patients were not approached. After signing informed consent, the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) was administered by three certified and trained psychologists to check whether participants still met diagnostic criteria at the time of testing. The MINI only classifies anorexia nervosa (AN) and bulimia nervosa (BN). A binge eating disorder (BED; which is not an official DSM-IV diagnosis) was classified when there were recurrent episodes (at least 2 days a week for 6 months) of binge eating in the absence of regular use of inappropriate compensatory behavior (e.g., purging, fasting, excessive exercise) typically seen in patients with BN. The total clinical sample comprised 36 participants with either AN (n=11), BN (n=7) or EDNOS (n=18 of which BED=15).

The comparison group of 37 participants was a convenience sample, personally recruited from an athletics club and via the social network of the researchers by an information letter. They were excluded when their knowledge of the Dutch language was insufficient to complete the questionnaires, had elevated levels of eating pathology on the SCOFF (Morgan, Reid & Lacey, 1999) or had received pharmacological or psychotherapeutic interventions for emotional problems in the past two years. Demographic and diagnostic characteristics of both groups are shown in Table 2.1.

The study protocol was approved by the Internal Review Board of Parnassia Psychiatric institute and written informed consent was obtained from all respondents.

Measures

Mini-International Neuropsychiatric Interview (MINI): ED and comorbid Axis I DSM-IV diagnosis were determined in the ED group using the MINI International Neuropsychiatric Interview 5.0.0 (Overbeek, Schruers & Griez, 1999; Sheehan et al., 1998). The MINI is a short, structured, diagnostic interview designed to verify the diagnostic criteria according to the DSM-IV. The MINI has a good correlation with the Structured Clinical Interview for DSM-IV-TR Axis I (SCID-I) (Pinninti et al., 2003).

Eating Disorder Examination Questionnaire (EDE-Q): The EDE-Q (Fairburn & Beglin, 1994; van Furth, 2000), is a 36-item self-report questionnaire providing an assessment of the specific psychopathology of ED behavior. This questionnaire was administered in both groups. Respondents rate the items on a 7-point scale, ranging between 0 (no days) and 6 (everyday) over the previous 28 days in which specific behaviors and attitudes occurred. It includes 22 items assessing the core attitudinal features of ED psychopathology. The 22 items together comprise four subscales, assessing restraint, shape concerns, weight concerns and eating concerns over the previous 28 days. The EDE-Q has good psychometric properties (Luce & Crowther, 1999; Mond et al., 2004). A validation study concerning the Dutch translation of the EDE-Q (Aardoom et al., 2012) did not support the theorized four subscales of the EDE-Q. In the current study the global EDE-Q score will be calculated by summing and averaging all individual items, so that all items possess equal weight. Higher scores are indicative of higher ED psychopathology.

SCOFF: The SCOFF (abbreviation is an acronym from the questions) (Morgan et al., 1999) is a widely used self-administered five question test to assess the possible presence of an ED. One point is assigned for every "yes"; a score ≥2 indicates a possible ED. The SCOFF is found to be capable to exclude ED (Morgan et al., 1999). The SCOFF was completed by the comparison group to exclude participants with a possible presence of an ED.

Self-report Symptom Checklist-90 (SCL-90): The SCL-90 (Arrindell & Ettema, 1986; Derogatis & Cleary, 1977) is a 90-item self-report checklist oriented to screen for a broad range of psychological problems and psychopathology

in the past seven days. It contains 90 items, scored on a 5-point severity scale, measuring eight primary symptom dimensions named 'anxiety', 'agoraphobia', 'depression', 'somatization', 'interpersonal sensitivity', 'cognitive-performance difficulty', 'hostility', and 'sleep disturbance'. Higher scores are indicative for more psychopathology. The Dutch version of the SCL-90 has been shown to have good psychometric properties (Arrindell & Ettema, 1986). The SCL-90 depression dimension was completed by both groups to describe their severity level of depressive symptoms.

Table 2.1. Gender and education level for the clinical (n=36) and the comparison group (N=37)

	ED	Percentage	CG	Percentage
Age (Mdn)	26		40	
Gender				
Male	2	5.4	1	2.7
Female	34	94.6	36	97.3
Education Level				
LO/LVO	2	5.6	0	0.0
LBO	1	2.8	1	2.7
MAVO	4	11.1	4	10.8
MBO	13	36.1	4	10.8
HAVO	5	13.9	2	5.4
HBO	8	22.0	10	27.0
VWO	0	0.0	6	16.2
WO	3	8.3	10	27.0
Diagnosis				
AN	11	30.6		
BN	7	19.4		
BED	15	41.7		
EDNOS	3	8.3		
Mean BMI (SD)	27.8 (10.2)			
MINI (SD)[a]	1.7 (1.4)			

ED = clinical group with an eating disorder, CG = comparison group;
LO/LVO = lower education, LBO = community college, MAVO = lower general secondary education,
MBO = intermediate vocational education, HAVO = higher general secondary education, HBO = higher professional education, VWO = pre-university education, WO = university;
AN = Anorexia Nervosa, BN = Bulimia Nervosa, BED = Binge Eating Disorder, EDNOS = Eating Disorder Not Otherwise Specified, BMI = Body Mass Index, MINI = Mini-International Neuropsychiatric Interview
[a] Mean amount of diagnosis on the MINI

Implicit Association Test (IAT): A self-esteem version of the IAT (Greenwald, McGhee & Schwartz, 1998) was used as a measure of ISE in both groups. The IAT is a computerized reaction time task originally designed to measure the relative strengths of automatic associations between two contrasted target concepts and two attribute concepts. Words from the two target concepts and the two attribute concepts appear in mixed order in the middle of a computer screen and participants are instructed to sort them with a left (Q) or right (P) response key. The assumption is that the categorization becomes easier when a target and attribute that share the same response key are strongly associated than when they are dimly associated. The target concept pair used in the self-esteem IAT was self-others (Dutch words for I, self, my, own and they, their, you, other, themselves). The attribute concept pair was positive - negative (Dutch words for successful, important, valuable, secure, meaningful, and unimportant, worthless, failure, useless, weak) (see Table 2.2 for an overview). When someone finds it easier (i.e. reaction time is faster) to sort words for the concept of self and positive with the same response key than of self and negative, it indicates a higher positive self-esteem. Higher IAT scores indicate higher implicit self-esteem. The IAT has been shown to have good psychometric properties (Bosson, Swann & Pennebaker, 2000). To calculate the IAT-effect we used the algorithm as proposed by Greenwald, Nosek & Banaji (2003) which has shown to perform best in the current measurement setting (Glashouwer, Smulders et al., 2013). Reaction times above 10,000 ms were excluded and error trials were replaced with the block mean plus an added penalty of 600 ms (Greenwald et al., 2003). Mean reaction times (RTs) of block 3 were subtracted from those of block 5 RTs, and RTs of block 7 were subtracted from RTs of block 9. The means of these two effects were divided by their inclusive standard deviation based on all responses in the relevant blocks (i.e., block 3, 5, 7 and 9), in order to control for individual variation (see Table 2.2 for overview of the blocks). The final score obtained is the IAT-D effect. In order to answer the research questions pertaining to DSE scores calculated according to methods d and e (see below), the raw scores of RSES and IAT were standardized.

Split-half reliability was used as a measure of internal consistency, using the Spearman-Brown prophecy formula (Brown, 1910; Spearman, 1910) in combination with the Pearson correlation between the D effect calculated from the two test blocks (no. 3 and 5) and the D effect calculated from the last two test blocks (no. 7 and 9).

Rosenberg Self-Esteem Scale (RSES): ESE was measured with the RSES (Franck et al., 2008; Rosenberg, 1965) in both groups: a 10-item self-report scale that measures personal evaluations of self-worth or self-acceptance with proven validity and reliability (Franck et al., 2008). Subjects are instructed to rate how much they strongly agree or disagree with each of the presented statements. The items are rated and scored on a 4-point Likert scale. Higher scores on the RSES (possible range 10-40) are indicative of more positive explicit self-esteem.

Table 2.2. Arrangement of the different IAT blocks

Block	Left label	Right label	No. of stimuli
1.	Negative	Positive	10
2.	Others	Me	10
3.	Others / Negative	Me / Positive	40
4.	Me	Others	10
5.	Me / Negative	Others / Positive	40
6.	Others	Me	10
7.	Others / Negative	Me / Positive	40
8.	Me	Others	10
9.	Me / Negative	Others / Positive	40

IAT = Implicit Association Test

Discrepant Self-Esteem (DSE): Former studies of DSE used different kinds of operationalizations of DSE (i.e., the extent that ISE and ESE differ). Overall, we found five different operationalizations of DSE in the literature and below we describe the way we used these in the present study:

a. Cockerham et al. (2009): DSE was not measured by creating a "discrepant variable". Instead, in this study lower ESE in combination with higher ISE (each compared to a healthy group; ESE clinical group<ESE healthy group and ISE clinical group>ISE healthy group) was interpreted as DSE (Zeigler-Hill, 2006). Group differences on ESE and ISE were analyzed using ANOVAs.
b. Brinol, Petty & Wheeler (2006): A centered index of the extent of discrepancy between ESE and ISE was formed, taking the absolute value of the difference between the standardized explicit and implicit measures, subtracted by its sample mean. A dummy variable was formed, indicating the direction of the discrepancy (0 when ESE > ISE and 1 when ISE > ESE). An interaction between the discrepancy index and the direction indicator

was used in a logistic regression analysis to assess whether the direction indicator influences the relationship between discrepancy index and the odds of the presence of an ED.

c. Van Tuijl et al. (2014): DSE was measured by the interaction score between mean centered RSES and IAT raw scores. A logistic regression analysis was used to assess whether the main effects and interaction effect were indicative for the presence of an ED.
d. Van Tuijl et al. (2016): The absolute difference between standardized scores of the IAT and RSES was computed for all participants. Two DSE variables were created: one for ISE>ESE; a 0 was assigned for participants where ESE was higher than ISE, and:one for ESE>ISE; a 0 was assigned for participants where the reverse was true.
   As such, an absolute difference score was derived on either ISE>ESE or ESE>ISE, which had a score of 0 on the other discrepant self-esteem variable. Using a two-step logistic regression analyses, ISE>ESE and ESE>ISE were added in the first step, followed by ESE in the second step to classify participants either as belonging to the clinical or comparison group.
e. Marissen et al. (2016): DSE was calculated by standardizing the scores (Z-scores) of RSES and IAT (De Raedt et al., 2006). Hereafter, distance between the standardized scores was computed by subtracting the standardized RSES scores from the standardized IAT scores. This calculation results in a score which indicates discrepancy between ESE and ISE. Lower scores of discrepancy indicate congruent scores between ISE and ESE, whereas higher scores imply a larger discrepancy between the two. ANOVA is used to assess the difference between the clinical and the comparison group.

Only method a. was used in a previous study on eating disorder psychopathology. The other described methods were used in a healthy population (method b), in a population of adolescents with symptoms of anxiety and depression (method c), in a clinical population with anxiety and depression (method d), and in a clinical population with narcissistic personality disorder (method e). Given this variety in operationalization of DSE in different fields of psychopathology, we choose not only to use the operationalization of Cockerham et al. (2009), but also other more recent operationalizations from other research fields than ED.

Procedure

First, participants completed a demographic information form. Subsequently, in another room, the IAT and the RSES were administered by using a laptop computer. After having received instruction for the IAT and the RSES, they were left alone by the researcher. After that, the comparison group filled in the SCL-90, the SCOFF and the EDE-Q. For the clinical group, the MINI was administered. Subsequently, the clinical group completed the SCL-90 and the EDE-Q. These self-report questionnaires were administered in the presence of the researcher and controlled for missing data at the end.

Statistical analysis

Following data screening, a Fisher Exact Test and two Mann-Whitney U tests were conducted to examine statistically significant differences between the clinical and the comparison group concerning gender, age and education level respectively. To assess the correlations between eating disorder pathology (EDE-Q), ESE and ISE, Spearman's rank correlation coefficients were calculated separately in both groups. Separate logistic regression analyses were used to examine whether the presence of an ED could be predicted by ESE and ISE scores. Moreover, separate linear regression analyses were performed to assess whether the severity of ED pathology could be predicted by ESE and ISE. When both ESE and ISE were significant independent predictors, ESE and ISE were investigated jointly.

In addition, logistic regression analyses were used to examine to what extent the five different operationalizations of DSE were predictive of the presence of an ED. There is no consistency between the five methods of DSE regarding the operationalization of the clinical features in the participants. Some studies used DSM diagnoses to indicate the clinical status of participants, while others made use of scores on questionnaires to measure disorder severity. To enhance comparability in DSE methods we chose to consistently use presence of diagnosis as outcome, i.e. the division of our participants into a clinical and comparison group.

The statistical analyses were performed using SPSS version 25.

Results

Group differences on demographic characteristics

Demographic characteristics of both groups are described in Table 2.1. With a Fisher Exact Test no statistically significant difference was found between the comparison group and the clinical group concerning gender (p=.62). A statistically significant difference was found between the comparison group (Mdn=40.00) and the clinical group (Mdn=26.00) concerning age (U=471.00, p=.03) and education level (Comparison: Mdn=7.00, experimental: Mdn=5.00, U=377.50, p=.001).

Correlations

Within the ED group ED psychopathology showed a strong and negative correlation with ESE (r=-.56, p<.001) and no significant correlation with ISE (r=-.07, p=.69). Furthermore, a strong and positive correlation was found between ESE and ISE (r=.57, p<.001). Within the comparison group ED psychopathology showed a comparable negative correlation with ESE (r=-.49, p<.05) and no significant correlation with ISE (r=.18, p=.30). But unlike the ED group, in the comparison group no significant correlation was found between ESE and ISE (r=.13, p=.44).

ESE and ISE

Means and standard deviations of all relevant variables are described in Table 2.3.

The Spearman-Brown split-half reliability of the IAT was adequate (r_{sb} = .76).

A logistic regression analysis showed that the presence of an ED diagnosis (MINI) was predicted by ESE (OR = .60, 95% CI [0.47, 0.76]) and ISE (OR = .19, 95% CI [0.05, 0.68]). When both ESE and ISE were investigated jointly, ESE remained significant (OR = .58, 95% CI [0.45, 0.76]), however the prediction by ISE became non-significant (OR = 2.56, 95% CI [0.25, 25.89]).

For the prediction of ED pathology (EDE-Q) with linear regression, ESE was found to be a statistically significant predictor (B = -4.66, p < .001). ISE was not found to be a significant predictor (B = -20.28, p = .08).

Table 2.3. Means and standard deviations

	ED		CG	
	M	**SD**	**M**	**SD**
EDE-Q	81.97	28.45	21.60	21.51
RSES	21.94	5.10	31.89	3.80
SCL-90 dep	42.61	15.78	20.49	4.27
IAT RT me+pos H1	845.72	222.91	948.91	233.81
IAT RT me+neg H1	1163.36	337.91	1215.52	477.39
IAT RT me+pos H2	804.75	157.41	916.28	245.19
IAT RT me+neg H2	964.70	233.68	1027.49	330.71
IAT D	0.37	0.45	0.62	0.33

ED = clinical group with an eating disorder; CG = comparison group;
EDE-Q: Eating Disorder Examination Questionnaire, RSES = Rosenberg Self-Esteem Scale, SCL-90 dep = Self-report Symptom Checklist-90 depression scale, IAT RT = Implicit Association Test reaction time (in milliseconds), IAT D = Implicit Association Test D effect

DSE

Analyses with five discrepant self-esteem methods were applied:

a. Cockerham et al. (2009): There was a statistically significant difference between the clinical and the non-clinical group on ESE, with higher scores (Table 2.3) for the non-clinical group ($F(1, 71) = 89.55$, $p < .001$, partial $\eta^2 = .56$). Groups also differed on ISE ($F(1, 71) = 7.60$, $p < .05$, partial $\eta^2 = .09$), with higher scores for the non-clinical group.
b. Brinol et al. (2016): A significant main effect of the direction of discrepancy was found ($OR = 6.46$, 95% CI [2.06, 20.31]), indicating that for ISE>ESE the odds for being in the clinical group is 6.46 times larger than for ESE>ISE. The absolute difference and its interaction with direction were not statistically significant.
c. Van Tuijl et al. (2014): No statistically significant effect for the discrepancy measure was found ($OR = 0.94$, 95% CI [0.54, 1.61]).
d. Van Tuijl et al. (2016): When ISE>ESE this was a significant predictor of being in the non-clinical group (OR = 0.15, 95% CI [0.03, 0.69]). ESE>ISE was not a significant predictor (OR = 1.54, 95% CI [0.52, 4.54]). After including ESE in the regression equation, ISE>ESE was no longer a significant predictor (OR = 0.33, 95% CI [0.03, 3.93]).

e. Marissen et al. (2016): Discrepancy scores showed a statistically significant difference between the clinical (M = 0.44, SD = 0.91) and the non-clinical group (M = -0.43, SD = 0.92), $F(1, 71) = 16.31$, $p < .001$, partial $\eta^2 = .19$) The clinical group reported higher ISE than ESE, where the non-clinical group reported higher ESE than ISE.

Discussion

The main findings of the present study were: (a) Both a lower ESE as well as lower ISE predicted an ED diagnosis. When ESE and ISE were investigated jointly only ESE remained a significant predictor; (b) Low ESE was found to be significantly associated with a higher level of ED psychopathology. No relationship was found between ISE and the severity of ED psychopathology; and (c) Different methods for determining DSE yielded mixed outcomes concerning the association of DSE with the presence of an ED.

Previous studies focused mainly on the role of ESE in ED diagnosis. In these studies low ESE in ED patients compared to non-clinical comparison groups is a robust and consistent finding (Cockerham et al., 2009; Sassaroli et al., 2008). This finding is confirmed in the present study. In addition, we also found that lower ESE is associated with more severe ED psychopathology.

The previous study (Cockerham et al., 2009) found a more positive ISE in the ED group compared to the comparison group. We found an outcome in the opposite direction; in the ED population ISE was significantly lower compared to our comparison group. This finding is in line with most recent studies of ISE in relation to psychopathology where, when an association is found, lower ISE is related to more psychopathology (Franck, De Raedt, Dereu & Van den Abbeele, 2007; Glashouwer, Vroling et al., 2013; Risch et al., 2010; Ritter et al., 2013).

An explanation for this difference in outcome could be related to some problematic methodological characteristics of the study of Cockerham et al. (2009). The sample size was very small and the clinical group was a self-selected sample and therefore vulnerable for self-selection. Another possible reason could be that the current study included all EDs because of the assumed transdiagnostic role of self-esteem in ED (Fairburn et al., 2003). The clinical sample of Cockerham et al. (2009) included only BN and BED. It might be that the diversity between these diagnostic groups has influenced the results of the

present study. Unfortunately, our sample size is too small to analyze the role of ISE in AN, BN and BED separately. Future research could focus on the question to what extent ESE and ISE as putative transdiagnostic factors are related to the presence of an ED per se, or whether their relationship with ED psychopathology differs across ED diagnoses.

The less robust association of ISE and ED (compared to the association of ESE) could be related to characteristics of the measures used. The association of the RSES with (severity of) ED pathology may be overinflated because of common-method variance (EDE-Q) or criterion contamination (as low self-esteem may express itself in e.g. a negative body image). Moreover, the RSES and measures of ED pathology emphasize more trait-like aspects, while the IAT is based on reaction time responses in a particular testing situation hampering the identification of significant relation with pathology. In particular, definitions and measures of implicit cognitive processes relative to explicit cognitive processes need further refinement and validation, both in their psychometric properties and in their specific applications to psychopathology (De Houwer et al., 2009; Fiedler, Messner & Bluemke, 2006).

There is only one previous study of DSE in ED (Cockerham et al., 2009). In this study DSE was not measured by creating a separate "discrepant variable" but lower ESE in combination with higher ISE was interpreted as DSE (Zeigler-Hill, 2006). Studies of DSE in other populations created a separate "discrepant variable" in different ways. Furthermore, the outcome variable differed between studies (presence of diagnosis vs severity of psychopathology) and some studies corrected for depression severity while others did not. Because of these differences in operationalization, outcome variables and covariates, direct comparisons of study results are complicated. Therefore, we used five different operationalizations of DSE and a single outcome variable (presence of ED) to facilitate direct comparisons in outcomes. We found equivocal results in how DSE relates to the presence of an ED. With one operationalization (Marissen et al., 2016) we found a significant association between DSE and ED diagnosis, while we found no significant association with the other four operationalizations. Apparently, the way DSE is related to ED critically depends of which method is used and therefore the outcomes of studies of DSE in relation to psychopathology must be interpreted with the greatest caution. More definitive conclusions can only be drawn when the concept of DSE will become better defined and operationalized accordingly. Present operationalizations seem mainly driven by statistical considerations and are only loosely connected to a clear conceptualization of DSE.

There are some limitations to consider in the present study. First of all, because of the sample size of this study only relatively large effect sizes could be reliably detected. It is conceivable that more subtle differences between groups have been missed. For the same reason, this study did not examine differences among the subgroups AN, BN and BED. Future studies should examine differences among those subgroups to ascertain whether findings in the area of self-esteem and eating pathology apply across different ED categories. Furthermore, as the present study was powered to detect large between group effects, our examination of the predictive value of different operationalizations of DSE without correction for multiple testing to reduce the chances of Type I error must be seen as exploratory awaiting more stringent testing in future studies. A last limitation is that there was no inclusion of a second clinical control group. Therefore, no conclusion can be drawn about the specificity of our outcomes for the group of ED patients.

To conclude, especially low ESE seems to be associated with (severity of) ED psychopathology. Future research should also include ISE measures to further examine the clinical relevance of this variable. Although our cross-sectional study showed no unique relationship of ISE with (severity of) ED psychopathology, only longitudinal (treatment) studies can help to determine the prognostic value of ESE and ISE for (differentially) predicting outcome and their sensitivity to change. Such studies could also help to answer the question whether specific interventions are needed to modify ISE as a distinct processing mode or whether consistently reducing ESE eventually also affects ISE (Greenwald et al., 2002).

Disclosure of potential conflicts of interests

The authors declared no potential conflicts of interest.

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Chapter 3

Competitive memory training (COMET) for treating low self-esteem in patients with eating disorders: a randomized clinical trial

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Abstract

This study evaluates a short stepwise cognitive-behavioral intervention for the treatment of low self-esteem in patients with eating disorders. Competitive memory training (COMET) for low self-esteem is based on insights and findings from experimental psychology. A total of 52 patients with eating disorders and low self-esteem were treated with COMET in a routine mental health center in addition to their regular treatment. These patients were randomized to receive eight weeks of COMET + treatment as usual (TAU), or to receive TAU only. Differential effects in favor of COMET +TAU were found for two indexes of self-esteem and for one index of depressive mood. Shortcomings of this study and possible clinical implications are discussed.

Keywords

self-esteem, memory retrieval, eating disorders, psychopathology, group treatment

Introduction

In addition to the over-evaluation of eating, body shape, weight and their control, low self-esteem is considered to be an important aspect of the clinical picture of the various eating disorders (Polivy & Herman, 2002). Self-esteem is the overall evaluation of one's personal worth or value as a person. In adult psychiatry no specific evidence-based treatment protocols for enhancing self-esteem are currently available. Usually, one implicitly expects that self-esteem will be automatically enhanced with the amelioration of the target symptoms of the disorder the patient is treated for; however, it is doubtful whether this is always the case. Several specific interventions to enhance self-esteem have been described (Fennell, 1997; Tarrier, 2001). Fennell's approach (1997) is characterized by the identification and Socratic challenging of dysfunctional negative automatic thoughts, assumptions and core beliefs about one's own worth and importance, and is accompanied by a range of specific behavioral experiments. Most of these experiments are concerned with the anticipated reactions of others to the personal value and capacities of the patient. The approach taken by Tarrier and colleagues (2001) seeks to focus the patient's attention on positive characteristics by discussing and monitoring concrete instances in which these positive characteristics were and are manifest; this method proved to be effective in two small studies in which patients with psychosis were investigated (Hall & Tarrier, 2003; Oestrich et al., 2007). We are not aware of any randomized study to test the efficacy of Fennell's approach.

In the present study, we applied a somewhat different approach to influence self-esteem. Patients regularly report that they do not feel worthwhile, although they (intellectually) know that they are. In problems in which dysfunctional expectations are the major issue, behavioral experiments are initiated to overcome this problem of knowing but not feeling. However, behavioral experiments might not be the most effective method to change the potency of implicit and self-referent opinions, which is the main issue in low self-esteem. To target such implicit and self-referent opinions, we developed a series of interventions, referred to as competitive memory training (COMET). Several of these COMET protocols have recently been tested. At the moment, two studies that used the COMET protocol for low self-esteem have been completed, one in a mixed group of outpatients and the other in a group of hospitalized and day-treatment patients with eating disorders and/or personality disorders (Korrelboom et al., 2009; Olij et al., 2006). In these

studies self-esteem was enhanced, and depression was diminished – both with large (within-group) effect sizes. However, these two studies were not randomized trials.

COMET for low self-esteem is aimed at making patients feel what they already know by making this (functional) knowledge more retrievable from long-term memory. According to Brewin (2006), cognitive therapy does not modify the negative meaning of concepts directly but rather influences the relative retrievability from long-term memory of the different meanings that are associated with these concepts. Strengthening the possibility of retrieving functional representations that are in retrieval competition with dysfunctional representations is considered to be the core activity of all psychological treatments. It is assumed that different processes and procedures influence this retrieval competition. COMET centers on three of these: emotional saliency, repetition, and association. Emotional saliency of functional self-concepts is stimulated in COMET by writing self-referent stories about scenes where positive characteristics are in action and by repeatedly verbalizing positive self-statements connected to these scenes (Lange et al., 1998). Deliberate manipulation of posture, facial expression (Camras, Holland, & Patterson, 1993) and imagery (Holmes et al., 2008) are also used to promote emotional saliency. Finally, positive mood is stimulated by listening to music that is specifically selected by the patients themselves (Krumhansl, 1997). By activating this already emotionally enhanced positive self-knowledge repeatedly, COMET further promotes an even higher and thus more competitive position of this knowledge in the retrieval hierarchy. Then, as a final step, this emotionally enhanced positive self-knowledge is associated with situations and cues that trigger dysfunctional negative self-concepts in daily life with a procedure that is considered to be a modern variant of counter-conditioning.

Having been developed independently of each other, COMET (Korrelboom, 2000) and Tarrier's (2001) procedure for treating low self-esteem share similarities as well as differences. In both treatments, patients are stimulated to retrieve and attend to positive autobiographical memories that are incompatible with low self-esteem. However, somewhat different from Tarrier;s method, COMET supports this emphasis on positive memories by explicitly making use of imagery, posture and facial expression, self-verbalizations, and music. On the other hand, Tarrier's method stimulates his patients to monitor and record behaviors in daily life that are indicative for positive self-esteem, whereas COMET relies on the counterconditioning

part of the intervention to firmly connect positive self-esteem with ongoing daily activities. In general, Tarrier's method seems to be more behaviorally oriented, whereas COMET has a more cognitive orientation.

In this brief report, we describe the first controlled test of the COMET protocol for low self-esteem in a routine outpatient treatment center for patients with eating disorders. The main hypothesis tested was that COMET + treatment as usual (TAU) would enhance self-esteem more than TAU alone.

Method

Overview

All patients in the study were recruited from the Department of Eating Disorders (DED) of PsyQ, one of the largest organizations for mental health in the Netherlands. Patients in this DED with such problems are treated with the usual evidence-based interventions. After a minimum of two months of this regular TAU, patients who still had eating problems and were low in self-esteem were asked by their (TAU) therapists to apply for the current study. After inclusion, patients were randomly assigned to one of the two conditions: eight weeks of COMET + (ongoing) TAU versus eight weeks of (ongoing) TAU (see Figure 3.1).

Patients

Inclusion criteria were actual diagnoses (at the time of recruitment) of bulimia nervosa (BN), anorexia nervosa (AN), or an eating disorder not otherwise specified (EDNOS). These diagnoses were based on an informal clinical interview by the researchers who were checking for (a) formal *Diagnostic and Statistical Manual of Mental Disorders,* 4th ed., text revision. (American Psychiatric Association, 2000) criteria in combination with (b) low self-esteem as reported by the patients and their referring therapists and confirmed in an informal clinical interview by the researchers. Patients were considered to have low self-esteem when they expressed feelings such as being inferior to others, being insecure, considering themselves as failures, and so forth. In addition, to be eligible for the study, patients had to be able to identify at least one positive personal characteristic, and they had to be in regular treatment (TAU) at the DED for at least two months. Finally, they had to give informed consent. Suicidal risk, comorbid major depression, and psychotic experiences - all assessed by the researchers in the clinical interview - were criteria for exclusion.

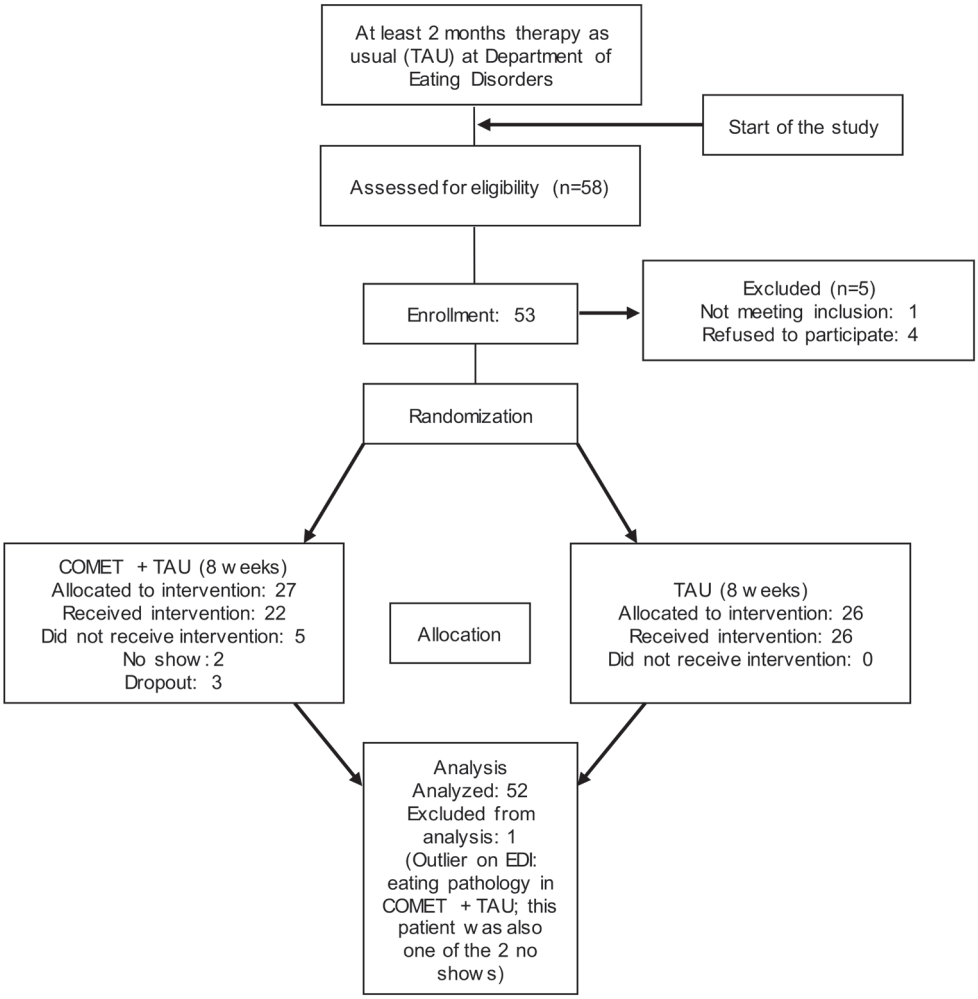

Figure 3.1. Overview of the study

COMET = competitive memory training; EDI = Eating Disorder Inventory-II

On the basis of findings in previous pilot studies on COMET for low self-esteem, large effect sizes were expected. In a baseline controlled study with hospitalized and day-treatment patients with personality disorders and eating disorders, pre- to post-treatment effect sizes varied between 0.9 and 1.3 on several measures of self-esteem (Korrelboom et al., 2009). In an uncontrolled pilot study with 75 outpatients with mixed primary disorders, the pre- to post-treatment effect size on the Rosenberg Self-Esteem Scale (RSES) (Rosenberg, 1965) was 1.2 (Olij et al., 2006). Therefore, with a power of 0.80 and two equal groups, a minimum of 52 patients was needed.

Enrollment was performed in five blocks, resulting in five COMET + TAU (experimental) groups and five waiting for COMET + TAU (control) groups. Between January 2006 and September 2007, 58 patients were referred for intake. Of these, 4 refused to participate in the randomization procedure, and 1 patient with binge eating disorder did not fulfill the diagnostic criteria for inclusion. Finally, a total of 53 patients were included in the study and randomized. Of these patients, 22 had their regular treatment on an outpatient basis; the remainder were treated on a day-treatment basis: 18 in low-intensity day treatment and 12 in high-intensity day treatment. All included patients were female, and all were Caucasian.

Instruments

All patients were assessed two times: at the start of the study, and again eight weeks later at the end of COMET + TAU or the waiting period + TAU. The measures listed below were assessed.

- *RSES* (Rosenberg, 1965). On a Dutch version of this 10-item scale, items had to be answered on a 4-point Likert scale ranging from 1 (strongly agree) to 4 (strongly disagree) . A high score means higher self-esteem. The RSES scale assesses global self-esteem and is sufficiently reliable and valid (Blascovich & Tomaka, 1991). While measuring a trait-like concept, such as self-esteem, the RSES has been shown to be sensitive to changes during therapy in several studies (Agras et al., 2000; Safer, Telch, & Agras, 2001). The RSES was considered the first primary outcome measure.
- *Beck Depression Inventory* (*BDI*) (Beck et al., 1961). A Dutch translation of this 21-item self-referent, 4-point Likert scale has proven to be reliable (Bouman et al., 1985) and to be valid (Bouman, 1989). High scores indicate more depression. The BDI was considered a secondary outcome measure.
- A valid and reliable Dutch translation of four subscales (Pursuit of Thinness, Bulimia, Body Dissatisfaction, and Ineffectiveness) of the *Eating Disorder Inventory-II (EDI-II)* (Garner & Olmstead, 1983; Schoemaker, van Strien, & van der Staak, 1994; van Strien, 2002) was administered. The first three subscales, covering the core symptoms of the eating disorders, were used to describe the study population. Body dissatisfaction was also used as a secondary outcome measure to control for the quality of TAU in improving eating pathology. The Ineffectiveness subscale is considered to be a measure for self-esteem and was the second primary outcome measure. Low scores on all four EDI-II subscales are favorable.

Therapists

All COMET sessions were conducted by two therapists - one a clinical psychologist (Martie de Jong) and the other an art therapist - acting as cotherapists. The senior therapist (Martie de Jong) had several years of experience in conducting cognitive-behavioral therapies and was specifically trained and supervised in COMET by Kees Korrelboom. The second therapist had no prior experience in cognitive-behavioral interventions.

Procedure

COMET was carried out in small groups as an additional treatment module to the ongoing regular treatment program. After informed consent, all 53 patients fulfilled the pretreatment measurements and were randomized to either eight weeks of COMET + (ongoing) TAU (experimental group) or to eight weeks of waiting + (ongoing) TAU (control group). Randomization was performed in five separate blocks (each consisting of 12-16 patients) by opening blinded envelopes in which both treatment conditions were concealed in advance. A total of 27 patients were randomized to the experimental group, and 26 to the control group.

After eight weeks, at the end of COMET, the post-treatment measurements were taken from both the experimental group and the control group. Whereas the length of the therapy period was the same for all patients in both conditions, the actual number of therapy contacts received in each condition could differ between patients.

Treatments

TAU – Regular treatment (TAU) in the DED is based on the Dutch multidisciplinary guidelines for eating disorders. Some patients are either treated individually or in groups on an outpatient basis, at a frequency of once a week or biweekly. Others are treated in a day-treatment setting of 1 (low intensity) or 3 (high intensity) days a week. All treatments have a mainly cognitive-behavioral orientation and consist of psycho-education, enhancing motivation, symptom-focused interventions, and social rehabilitation. In all these therapies the management of food and dieting is a central theme and concern.

COMET for low self-esteem – COMET for low self-esteem is a manualized, stepwise, cognitive-behavioral intervention (comprising eight sessions) and is practiced in small groups of 6-8 patients (in the present study, all women). Sessions are held once a week, each taking 1.5 hr. The COMET protocol encompasses four main steps.

1. *Identifying the negative self-image.* The patient describes in a few words what he/she thinks is negative about himself/herself.
2. *Identifying a credible positive self-image that is incompatible with the negative self-image.* The patient is asked whether he/she really believes that this negative image of himself/herself is totally true and, if not, which personal characteristics and experiences contradict the negative self-image.
3. *Strengthening the positive self-image.* Then, the retrievability of the contradictory positive self-image is enhanced by strengthening its emotional load. In COMET, this is realized by (a) writing small self-referent stories of instances in which the positive qualities were and are manifest and distilling positive self-statements of these instances, (b) imagining oneself in positive personalized scenes, (c) purposefully manipulation body posture and facial expression, and (d) listening to music that is chosen by each patient personally because it is felt to be congruent with a positive self-image. These exercises are to be practiced during Sessions 2-5 as well as during daily homework assignments.
4. *Forming new associations between risk cues and positive self-image by counterconditioning*. In the last sessions of COMET, patients are trained to associate their new positive self-image with cues that normally provoke uncertainty and self-demeaning thoughts. The patient has to activate his/her positive self-esteem with the aid of imagination, posture and facial expression, music and positive self-statements. Then, the positive image is replaced by the image of a situation in which he/she normally feels insecure and worthless. Now, however, by keeping his/her positive feeling state activated, he/she tries to feel self-confident while being in the imagined difficult scene. Again, this has to be repeated several times and also has to be practiced in daily homework assignments. Once a difficult scene can be tolerated while retaining positive self-esteem, other scenes are practiced.

Treatment integrity

COMET sessions were observed by a trainee who was familiar with the COMET protocol; this observer made a checkmark on a list when the intended subjects of each therapy session had been dealt with adequately and noted whether any elements not in the protocol had been introduced.

Statistical analyses

On the basis of earlier findings (Korrelboom et al., 2009; Olij et al., 2006) large effect sizes were expected. In this randomized clinical trial design, we tested possible differences at baseline between both groups and between dropouts and completers (for continuous variables) with independent *t* tests or Mann-Whitney tests (when prerequisites for *t* tests were violated) and (for categorical variables) with chi-square tests. All differences between pre- and posttreatment measurements were tested with separate analyses of variance for repeated measures on an intention-to-treat basis by substituting the pretreatment scores of the 4 dropouts/no shows as posttreatment scores. Cohen's *d* was used to estimate the size of these differences, and 95% confidence intervals were calculated for all outcome measures. In all tests, a *p*-value of .05 was considered statistically significant. To assess the clinical significance of changes during treatment, we applied a method described by Jacobson and Truax (1991).

Results

One patient in the experimental condition was an outlier with extreme Z scores (<-3.19) far within the range of the normal population on two main indicators for having an eating disorder (Pursuit of Thinness and Body Dissatisfaction); she was considered to be misdiagnosed. Although this person was randomized, she never started COMET. Leaving this patient out of the analyses resulted in the experimental group and the control group having 26 patients each; all further calculations pertain to these 52 patients. For 1 patient in the experimental group, the pretreatment RSES was missing. Table 3.1 gives an overview of the pretreatment characteristics. There were no significant pretreatment differences between both groups. Compared with a functional Dutch female student norm group, these patients scored high to very high on the Pursuit of Thinness, Bulimia, and Body Dissatisfaction subscales of the EDI-II (van Strien, 2002). Compared with a non-clinical Dutch population (Schmitt & Allik, 2005) patients' scores on the RSES were extremely low (M = 21.2, SD = 5.3).

Table 3.1. Pretreatment status for the two treatment groups

	Experimental group			Control group			
Variable	**M**	**SD**	**n**	**M**	**SD**	**n**	**Significance**
Age (years)	25.5	5.3		25.4	5.7		ns
Diagnosis							ns
EDNOS			12			17	
BN			10			5	
AN			4			4	
Length of treatment before COMET (months)	9.8	7.7		10.7	9.3		ns
Intensity of TAU							ns
Outpatient			10			12	
LI day- treatment			11			7	
HI day-treatment			5			7	
Pursuit of thinness (EDI-II)	31.2	6.1		33.1	5.7		ns
Bulimia (EDI-II)	19.3	8.6		18.0	7.6		ns
Body dissatisfaction (EDI-II)	42.8	9.2		46.4	8.8		ns
Ineffectiveness (EDI-II)	41.6	8.6		41.4	9.5		ns
Self-esteem (RSES)	20.0	5.2		20.3	5.6		ns
Depressiveness (BDI)	22.1	11.8		22.7	11.8		ns

EDNOS = eating disorder not otherwise specified; BN = bulimia nervosa; AN = anorexia nervosa; COMET = competitive memory training; TAU = treatment as usual; LI day-treatment = low-intensity day-treatment (1 day per week); HI day-treatment = high-intensity day-treatment (3 days per week); EDI-II = Eating Disorders Inventory-II; RSES = Rosenberg Self-Esteem Scale; BDI = Beck Depression Inventory; ns = not significant

In the COMET group, 3 patients dropped out, and 1 did not show up for treatment (16%: 2 diagnosed with EDNOS, 1 with BN and 1 with AN; 3 of these patients had outpatient treatment as TAU, and 1 had high-intensity day-treatment), whereas all the patients in the control group filled in their posttreatment measurements. There were no significant differences in pretreatment measures between dropouts/no shows and completers. In addition, there were no important differences between the two groups for the number of therapy contacts or for the number of therapy hours received. During the research period, patients in TAU received on average 10.1 therapy contacts (SD = 13.2), whereas patients in COMET+TAU received 11.8 therapy contacts (SD = 7.1); this difference was not significant, $t(50) = 0.561$, $p = .58$. Measured in received hours of therapy, patients in COMET had on average

13.9 hr (*SD* = 13.5) of therapy during the research period, whereas patients in TAU received 10.5 hr (*SD* = 20.1). This difference was not significant, $t(50) = 0.56$, $p = .58$.

Treatment integrity was good. According to the observers, more than 90% of all the issues in the treatment protocol were adequately handled during COMET, and no new treatment elements were introduced.

Table 3.2 presents an overview of the interaction effects. Significant interaction effects (Treatment x Time) in favor of COMET were found for self-esteem (RSES), $F(1,49) = 7.58$, $p < .01$; EDI-II (Ineffectiveness), $F(1,50) = 4.4$, $p = .04$; and for depression (BDI), $F(1,50) = 5.17$, $p = .03$). The (between-subjects) effect size for the RSES was large, with Cohen's *d* being 0.8, $t(49) = 2.8$; the (between-subjects) effect size was intermediate for both the EDI-II (Ineffectiveness), Cohen's $d = 0.6$, $t(50) = 2.1$, and the BDI, Cohen's $d = 0.6$, $t(50) = 2.3$. All main effects for time were significant: RSES, $F(1,49) = 17.71$, $p < .00$; EDI-II (Ineffectiveness), $F(1,50) = 11.9$, $p < .00$; BDI, $F(1,50) = 16.00$, $p < .00$; and EDI-II (Body Dissatisfaction), $F(1,50) = 20.74$, $p < .00$). The within-subject effect sizes (Cohen's *d*) for the experimental group were intermediate: 0.7 for the RSES and 0.6 for the EDI-II (Ineffectiveness) and the BDI.

To make a clinically significant change, a patient has to fulfill two criteria: (a) he/she should progress from the problematic population to the normal population, and (b) the difference between his/her posttreatment score and pretreatment score should surpass the standard error of difference between these two scores (i.e. he/she should realize a reliable change score) (Jacobson & Truax, 1991). On the basis of the mean and standard deviation found by Schmitt and Allik (2005) in a functional Dutch population, a score of 23 was determined as the cutoff score between normal and pathological functioning on the RSES. On the basis of a reliability index of 0.87, found in that same study, an increase of at least 6 points between pre- and posttreatment was considered necessary to achieve a reliable change on this scale. In COMET + TAU, 6 patients (27% of the 22 patients who had completed COMET) achieved both the Jacobson and Truax's (1991) criteria and can be considered to have made a clinically significant change. In TAU, no patient realized a clinically significant change. In the two groups, no patient had a clinically significant change for the worse and no patient had a reliable change for the worse.

Table 3.2. Interaction effects between pre- and posttreatment: Intention to treat

		Pretreatment			Posttreatment				
Variable/Group	***N***	***M***	***SD***	**95% CI**	***M***	***SD***	**95% CI**	**Effect size (Cohen's *d*)**	**Significance**
RSES								0.8	.01
Exp	25[a]	20.0	5.2	17.8–22.1	23.6	5.5	21.4–25.9		
TAU	26	20.4	5.6	18.2–22.5	21.1	5.5	19.0–23.3		
BDI								0.6	.03
Exp	26	22.1	11.8	17.4–26.7	15.2	12.0	10.4–20.1		
TAU	26	22.7	11.8	18.0–27.4	20.8	12.7	16.0–25.7		
Body dissatisfaction (EDI-II)									.57 *(ns)*
Exp	26	42.8	9.2	39.3–46.4	39.8	11.3	35.5–44.1		
TAU	26	46.4	8.8	42.9–50.0	42.5	10.4	38.2–46.8		
Ineffectiveness (EDI-II)								0.6	.04
Exp	26	41.6	8.6	38.0–45.1	36.5	9.9	33.0–40.1		
TAU	26	41.4	9.5	37.8–44.9	40.2	8.0	36.6–43.7		

CI = confidence interval; ns = not significant; RSES = Rosenberg Self-Esteem Scale; Exp = experimental group (COMET + TAU); TAU = control group (treatment as usual); BDI = Beck Depression Inventory; EDI-II = Eating Disorders Inventory-II [a] One RSES missing

Discussion

The present study confirms earlier findings in two less rigidly controlled studies (Korrelboom et al., 2009; Olij et al., 2006) - that is, COMET as an add-on to regular therapy enhances self-esteem, at least in woman being treated for eating disorders. That the self-esteem of patients with eating disorders can be enhanced with a specific treatment procedure is of particular significance. Given that low self-esteem is an important aspect of the clinical picture of eating disorders and is considered a risk factor for relapse, interventions specifically aimed at the enhancement of self-esteem might be a valuable addition to the regular procedures used in treating these patients (Fairburn, Cooper, & Shafran, 2003). However, although 27% of the COMET completers had a clinically significant change, and none of the patients in TAU had a clinically significant change, it should be pointed out that the mean self-esteem score after COMET (M = 23.6, SD = 5.5) is still below the scores of a functional Dutch population (M = 31.6, SD = 4.5).

Having been performed in a (non-university) routine mental health setting, this study has several limitations. First, diagnoses and other inclusion and exclusion criteria were established in non-standardized clinical interviews. Second, there was no formal check on whether patients fulfilled their homework assignments, whereas doing so is considered an essential part of the COMET intervention. Third, it is debatable whether the Hawthorne effect might have played a role; in that case, the results could have been merely a reflection of the patients' or therapists' enthusiasm of being part of something new. Although this is a real possibility for the therapists, and although it cannot be ruled out completely for the patients, all control group patients knew that they too would receive COMET, albeit eight weeks later. Thus, it is unlikely that there has been a differential effect between patients in both groups concerning the Hawthorne effect. Fourth, all COMET therapies were applied by the same cotherapists, leaving the question open whether the outcome was a therapist effect or a treatment effect; however, in other studies on COMET protocols, similar results with many different therapists were found. Finally, although therapists conducting TAU were instructed not to apply interventions specifically aimed at enhancing self-esteem, no formal check on treatment integrity was made regarding this issue. On the other hand, had patients in TAU indeed received self-esteem enhancement procedures, COMET would still have outperformed the effects of these procedures.

To summarize, COMET seems to be an effective additional intervention for eating disorders and low self-esteem. The promising results of the current study warrant further investigation of this intervention among this and other psychiatric populations, with a sufficiently long follow-up period and with better control of several methodological aspects of the study.

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Chapter 4

Enhanced cognitive behavioral therapy for patients with eating disorders: a systematic review

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Abstract

Purpose of review: The aim of this study was to provide an update of the most recent (since January 2014) enhanced cognitive behavioral therapy (CBT-E) effectiveness studies (randomized controlled trials and open trials) on bulimia nervosa, binge eating disorder, and transdiagnostic samples.

Recent findings: Of 451 screened studies, seven effectiveness studies (five randomized and two open trials) were included in this review: of these, three had a bulimia nervosa sample and four a transdiagnostic sample (all conducted in an outpatient setting). Substantial differences in posttreatment remission rates were found (range: 22.2% to 67.6%) due, in part, to differences in samples and operationalization of clinical significant change.

Summary: There is robust evidence that CBT-E is an effective treatment for patients with an eating disorder. However, more studies on differential effects and working mechanisms are required to establish the specificity of CBT-E.

Keywords

cognitive behavioral therapy, eating disorders, effectiveness, transdiagnostic, treatment

Introduction

Eating disorders are severe mental disorders, which often begin in adolescence (Mitchison et al., 2012), frequently have a chronic course (Steinhausen, 2009) and can have considerable impact on quality of life (Jenkins et al., 2011). Eating disorders make a substantial contribution to the global burden of disease, especially among young women (Erskine, Whiteford, & Pike, 2016). Although anorexia nervosa is a relatively rare disorder in many non-western countries, bulimia nervosa and binge eating disorder (BED) are common disorders worldwide (Hoek, 2016). Previous reviews showed that, among young women in Europe, Asia, Africa and Latin America, bulimia nervosa is reported by 1-2% and BED by 1-4% (Keski-Rahkonen & Mustelin, 2016; Kolar et al., 2016; Perez, Ohrt, & Hoek, 2016; Thomas, Lee, & Becker, 2016; van Hoeken, Burns, & Hoek, 2016). Recent studies show that eating disorders (especially bulimia nervosa and BED) are also common among older persons; according to the DSM-5 criteria, the prevalence of all eating disorders combined is around 3.5% in older (aged >40 years) women and around 1-2% in older men (Mangweth-Matzek & Hoek, 2017). Despite that increasing numbers of individuals with eating disorders are receiving treatment, European samples show that only about one-third are detected via health care (Keski-Rahkonen & Mustelin, 2016).

In terms of the DSM-IV, the most common eating disorder diagnosis in both clinical and community samples was 'Eating disorder not otherwise specified' (EDNOS). With the introduction of the DSM-5 and concurrent changes in the eating disorder section (including the introduction of BED as an official category, and lowering the threshold for anorexia nervosa and bulimia nervosa) the percentage of 'Other specified feeding or eating disorder' (OSFED; DSM-IV EDNOS) was significantly reduced, even though this diagnosis might still be the most common one in this population (Keel et al., 2011; Machado, Goncalves, & Hoek, 2013; Smink, van Hoeken, & Hoek, 2013).

According to a recent international comparison between nine evidence-based clinical guidelines for eating disorders, cognitive behavioral therapy (CBT) is widely used as the preferred treatment for bulimia nervosa and BED (Hilbert, Hoek, & Schmidt, 2017). The major guidelines for the treatment of eating disorders (Hay et al., 2014; National Institute for Health and Care Excellence (NICE), 2017; Yager et al., 2014) recommend CBT as the psychological treatment of first choice for bulimia nervosa and BED. CBTE(nhanced) is a specific form of CBT and is designed to be suitable for the full range of

eating disorder diagnoses (Fairburn, 2008). It is based on the transdiagnostic theory of the maintenance of eating disorders, in which it is assumed that most of the mechanisms involved in the persistence of eating disorders are common to all eating disorders, rather than being specific to each diagnostic group separately. It asserts that central to all eating disorders is a dysfunctional evaluation of self-worth that is overly based on shape and weight (Fairburn, Cooper, & Shafran, 2003). CBT-E uses strategies and procedures to address this overevaluation of shape and weight by focusing on targeting these mechanisms (known as the 'focused' version of CBT-E). The treatment protocol can be extended with interventions that target additional maintaining mechanisms, that is core low self-esteem, clinical perfectionism, and interpersonal problems (known as the 'broad' version of CBT-E). For the OSFED diagnoses, CBT-E has an advantage over other CBT protocols because of its transdiagnostic reach. CBT-E has been investigated in several samples in which CBT-E for bulimia nervosa, BED and EDNOS proved to be a successful treatment in the first studies after development of the CBT-E protocol (Byrne et al., 2011; Fairburn et al., 2009).

This review provides an update of the most recent (i.e. published since 2014) CBT-E effectiveness studies (randomized controlled trials (RCTs) and open trials) on bulimia nervosa, BED and transdiagnostic samples. Studies on the transdiagnostic samples include bulimia nervosa, BED, OSFED and, sometimes (i.e. in studies with lower BMI inclusion criteria), anorexia nervosa. However, excluded from the present review were studies with an anorexia nervosa sample alone, due to differences in treatment duration and other treatment variables (e.g. a focus on weight gain).

In this review the characteristics of the included studies are described, possible explanations for the variability in outcome are proposed, recommendations are made for future research, and the methodological quality of the RCTs is described. Due to the small number of included studies, no meta-analysis was performed.

Materials and methods

Search strategy and study selection

The primary search strategy was made in Medline, PsycInfo and EMBASE; the search covered the period from January 2014 up to March 2018. The following concepts were combined and searched for in the title and abstract:

1. Eating Disorder OR disordered eat* OR binge eating disorder OR bulimia nervosa
2. Cognitive-behavioral OR CBT OR CBT-E

Articles had to meet the following criteria: i) a peer-reviewed study; ii) including a sample that meets the criteria for bulimia nervosa or BED, or a transdiagnostic sample with an eating disorder; and iii) an effectiveness study that includes (at least one condition of) manualized CBT-E.

After removing duplicates, 451 articles (published January 2014 to March 2018) were selected. The titles and abstracts of these articles were screened by the first author. The full-text versions of potential articles (n=35) were read to check for eligibility. The reference lists of the included articles and reviews were also examined for relevant studies.

Finally, seven articles met the inclusion criteria (Figure 4.1).

This review also includes an assessment of the methodological quality of the included RCTs. Tarrier and Wykes (Tarrier & Wykes, 2004) developed the Clinical Trials Assessment Test (CTAM), based on relevant features from the CONSORT guidelines (Moher et al., 2001), to assess the quality of trials of psychological treatments in mental health. This test contains 15 items grouped into six areas. Total scores range from 0 (no criterion is reached) to 100 (maximum score). The CTAM has good blind inter-rater agreement and adequate internal consistency (Tarrier & Wykes, 2004).

Ratings were done by the first author and one other independent rater. When required information was missing, the first author contacted the trial researchers for (possible) clarification.

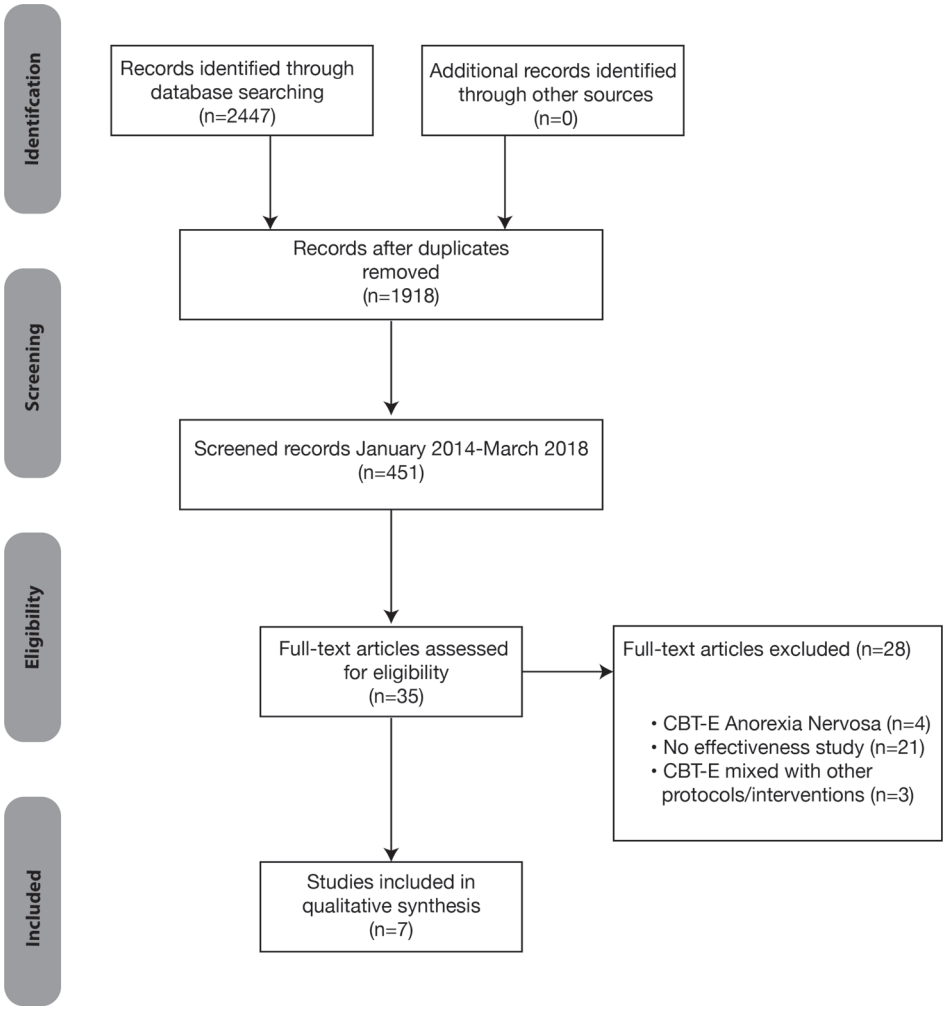

Figure 4.1. Flow diagram of inclusion of studies for this review

Results

If data were not reported, a calculation was made (when possible) based on the available data.

Design

Of the seven included studies, five were RCTs (Fairburn et al., 2015; Poulsen et al., 2014; Thompson-Brenner et al., 2016; Wade, Byrne, & Allen, 2017; Wonderlich et al., 2014), and two were open trials (Dalle Grave et al., 2015;

Signorini et al., 2018). Of the two open trials, one specifically aimed to find evidence that CBT-E is generalizable to treatment conducted in a non-controlled clinical context (Signorini et al., 2018).

Recruitment and population

All seven studies were conducted in an outpatient setting. Three studies included participants who were seeking help and had been referred (Dalle Grave et al., 2015; Fairburn et al., 2015; Signorini et al., 2018). Four studies also recruited participants through distribution of information in local papers, flyers, e-mails or (online) advertisements (Poulsen et al., 2014; Thompson-Brenner et al., 2016; Wade et al., 2017; Wonderlich et al., 2014). Four studies included a transdiagnostic sample (Dalle Grave et al., 2015; Fairburn et al., 2015; Signorini et al., 2018; Wade et al., 2017), two studies included participants with bulimia nervosa only (Poulsen et al., 2014; Wonderlich et al., 2014), and one study included participants with bulimia nervosa and comorbid (subthreshold) borderline personality disorder (Thompson-Brenner et al., 2016). Two transdiagnostic samples also included participants with anorexia nervosa (Signorini et al., 2018; Wade et al., 2017); this is explained by the use of a variable low-range cut-off for BMI, ranging substantially from 16 to 18.5. The Eating Disorder Examination (EDE) (Fairburn, Cooper, & O'Connor, 2008) is generally regarded as the gold standard in the assessment of an eating disorder. In five studies the diagnoses were assessed with the EDE (Fairburn et al., 2015; Poulsen et al., 2014; Thompson-Brenner et al., 2016; Wade et al., 2017; Wonderlich et al., 2014). In one study, the eating disorder was assessed by the treating therapists based on the DSM-IV criteria (Signorini et al., 2018), and in one study, no information was provided on how the eating disorder was diagnosed (Dalle Grave et al., 2015). Most studies included adults, although one study evaluated the effects of CBT-E in a cohort of non-underweight adolescents (Dalle Grave et al., 2015). There was a considerable difference in the number of participants per study (see Table 1).

Primary outcome measure and operationalization of clinical significant change

In all studies the EDE (Fairburn et al., 2008), or its self-report version (EDE-Q) (Fairburn & Beglin, 2008), was used as the primary outcome measure. Four studies used the EDE (Fairburn et al., 2015; Poulsen et al., 2014; Thompson-Brenner et al., 2016; Wonderlich et al., 2014) and three the EDE-Q (Dalle Grave et al., 2015; Signorini et al., 2018; Wade et al., 2017). In all four studies using the EDE as primary outcome measure, the EDE was assessed by independent blinded assessors (Fairburn et al., 2015; Poulsen et al., 2014;

Thompson-Brenner et al., 2016; Wonderlich et al., 2014). However, studies used different definitions of clinical significant change to indicate relevant change (e.g. remission, good outcome, abstinence, minimal residual eating disorder psychopathology, etc.) and different operationalizations of these concepts. In the studies with a bulimia nervosa sample (Poulsen et al., 2014; Thompson-Brenner et al., 2016; Wonderlich et al., 2014), abstinence from binges and purging was the main definition for clinical significant change. In the transdiagnostic samples, an global EDE-(Q) score less than 1 SD above the community mean (sometimes combined with BMI ≥18.5) was defined as clinical significant change (Dalle Grave et al., 2015; Fairburn et al., 2015; Signorini et al., 2018; Wade et al., 2017) (Table 1). The two studies conducted in Australia (Signorini et al., 2018; Wade et al., 2017) used different EDE-Q norms; although both studies refer to Mond et al. (2006) for the norms used to indicate clinical significant change (less than 1 SD above the community mean, i.e. ≤ 2.77), the EDE-Q norms reported by Signorini et al. (2018) were ≤ 2.46 or less.

Cognitive behavioral therapy enhanced variant

The seven included studies varied in: i) the setting in which therapy took place, ii) whether the focused or broad version of CBT-E was investigated, iii) the duration of therapy, and iv) whether extra sessions were planned involving significant others.

Four studies investigated the individual 20-session variant of the focused version of CBT-E (Fairburn et al., 2015; Poulsen et al., 2014; Thompson-Brenner et al., 2016; Wonderlich et al., 2014). In the study of Dalle Grave et al. (2015), parents were involved more closely, as participants were adolescents; the parental involvement consisted of five sessions of patients and parents together. Details about which version of CBT-E was investigated in this study were not reported. Wade et al. (2017) developed a treatment manual for group CBT-E based on the individual broad version of CBT-E including sessions to address the additional maintaining mechanisms (i.e. core low self-esteem, clinical perfectionism, and interpersonal problems). Eighteen group sessions of 2 h each were offered (with 5-10 min of individual work before each group session), and two additional individual sessions of 50 min each. In the study of Signorini et al. (2018), although CBT-E was investigated according to the manual (Fairburn, 2008), there was variability in the number of sessions (40 sessions for underweight participants, 20 sessions for nonunderweight participants) and also in the use of the focused or the broad version of CBT-E.

Control group

Of the five RCTs, three compared CBT-E to another active condition (Fairburn et al., 2015; Poulsen et al., 2014; Wonderlich et al., 2014). In one study CBT-E was compared with psychoanalytic psychotherapy (Poulsen et al., 2014). In the study of Wonderlich et al. (2014), CBT-E was compared with a new psychotherapeutic treatment for bulimia nervosa, that is integrative cognitive-affective therapy (ICAT). In the study of Fairburn et al. (2015), CBT-E was compared with another evidence-based treatment for bulimia nervosa: interpersonal psychotherapy (IPT) (Fairburn et al., 2015). In two of these three studies, the therapy dosage was the same in both groups (Fairburn et al., 2015; Wonderlich et al., 2014), but in one study the duration of therapy differed greatly due to the nature of psychoanalytic psychotherapy (Poulsen et al., 2014), that is the psychoanalytic psychotherapy involved weekly sessions of 50 minutes each over 2 years (mean number of sessions 72.3). Thompson-Brenner et al. (2016)compared the focused and broad version of CBT-E in persons with comorbid bulimia nervosa and borderline personality disorder. In the RCT of Wade et al. (2017), the control group was a waiting list group; however, in that study, only the first 8 weeks were controlled for; after this period, the control group had a delayed treatment start.

Therapist competence/treatment integrity

In four of the seven studies, the founder of CBT-E (Christopher Fairburn) or his colleague (Zafra Cooper) was closely involved in the training and supervision of the therapists (Dalle Grave et al., 2015; Fairburn et al., 2015; Poulsen et al., 2014; Thompson-Brenner et al., 2016). The remaining studies were supervised by experienced therapists (Signorini et al., 2018; Wade et al., 2017; Wonderlich et al., 2014). In six studies, the frequency of supervision was weekly or biweekly (Dalle Grave et al., 2015; Fairburn et al., 2015; Poulsen et al., 2014; Thompson-Brenner et al., 2016; Wade et al., 2017; Wonderlich et al., 2014). In the study of Signorini et al. (2018) the frequency of supervision was reported to be 'regular'. In three studies, the sessions were audio-recorded and a selection of these sessions was used and/or reviewed for purposes of supervision (Dalle Grave et al., 2015; Fairburn et al., 2015; Thompson-Brenner et al., 2016).

In three studies, treatment integrity was measured (Fairburn et al., 2015; Poulsen et al., 2014; Wonderlich et al., 2014).The quality of the delivery of the treatment condition was assessed by independent raters using diverse adherence scales. In these three studies, the raters scored adherence as 'good' (Wonderlich et al., 2014) or as 'high' (Fairburn et al., 2015; Poulsen et al., 2014).

Noncompleters

The operationalization of 'completion' also differs between studies. In four studies 'completion' was operationalized as finishing the complete treatment (Dalle Grave et al., 2015; Fairburn et al., 2015; Poulsen et al., 2014; Wade et al., 2017). Wonderlich et al. (2014) defined completion as attending at least 16 sessions (of 21). In two studies (Signorini et al., 2018; Thompson-Brenner et al., 2016), it is not clear how completion was operationalized. Noncompletion rates ranged from 22.2% to 50%. In the open trial of Signorini et al. (2018), an attrition rate of 50% was reported whereas the other open trial (Dalle Grave et al., 2015) reported a substantially lower rate (25%) of noncompleters. In four of the RCTs the rate of noncompleters was similar, ranging from 22.2% (Poulsen et al., 2014) to 26.2% (Fairburn et al., 2015). In the RCT of Wade et al. (2017), 30% of the participants did not complete treatment.

Analysis

All reported results are based on an intention-to-treat analysis.

Randomized controlled trials

Of the five RCTs, three reported significant differences between groups in favor of CBT-E (Fairburn et al., 2015; Poulsen et al., 2014; Wade et al., 2017). Wade et al. (2017) found that the first 8 weeks of group CBT-E were more effective in terms of reducing EDE-Q global scores compared with no treatment. In the study of Fairburn et al. (2015) the levels of eating disorder psychopathology decreased (global EDE score) in both conditions (CBT-E and IPT); however, the changes were significantly greater among CBT-E participants. The percentage of CBT-E participants in remission was almost twice as high as that in participants who received IPT (65.5% vs 33.3%). In the study of Poulsen et al. (2014), there was a large variation in treatment duration (5 months CBT-E vs. 24 months psychoanalytic psychotherapy). Significant differences were found between groups for binge eating and purging; 42% of the patients in CBT-E had ceased binge eating and purging (after 5 months) compared with 15% of the patients in psychoanalytic psychotherapy (after 24 months). By the end of both treatments, although there were substantial improvements in eating disorder psychopathology (global EDE scores), these changes took place more rapidly in CBT-E. In two out of five RCTs, no significant differences were found. In the study of Thomson-Brenner et al. (2016), two versions of CBT-E were compared (focused version vs. broad version). The groups did not differ in primary

outcome and the remission rate of the total sample was 42%. In addition, in the study of Wonderlich et al. (2014), comparing CBT-E with ICAT, no significant differences in treatment outcome were found between groups.

Open trials

In both open trials, there was a significant decrease in EDE-Q scores (Dalle Grave et al., 2015; Signorini et al., 2018) (Table 2). Dalle Grave et al. (2015) reported a remission rate of 67.6%; however, a substantial percentage of their patients (25%) met the criteria for remission before treatment started. Signorini et al. (2018) used two different definitions of remission and reported a remission rate of 42.2% and 35.4%, respectively. As mentioned, in the study of Wade et al. (2017), a control condition was included only in the first 8 weeks; after having received a full dosage of CBT-E, the remission rate for all patients (whether in the experimental or control group) was 66.7% (Table 1).

Differences in outcome, in RCTs and open trials, are explained in part by differences in the definition of clinical significant change and in the level of the EDE-Q community mean (Table 1).

Follow-up

Of the seven included studies, five had a follow-up assessment period varying from: 3 months (Wade et al., 2017), 4 months (Wonderlich et al., 2014), 20 weeks (Signorini et al., 2018), 6 months (Thompson-Brenner et al., 2016) to 60 weeks (Fairburn et al., 2015). Generally, in most studies, the posttreatment results were maintained during follow-up. In the study of Wade et al. (2017), during follow-up, the percentage 'good outcome' decreased from 66.7% to 46.2%. In the study of Fairburn et al. (2015), the proportion of participants meeting the criteria for remission during follow-up increased in the IPT condition (33.3% to 49.0%), but the rate remained higher (69.4%) in CBT-E.

Assessing quality and variability in psychological treatment trials: the Clinical Trial Assessment Measure (CTAM)

We used the CTAM (Tarrier & Wykes, 2004) to assess the methodological quality of the included RCTs (see Materials and methods). Three of the five RCTs had a similarly high CTAM score of 89 (Fairburn et al., 2015; Poulsen et al., 2014; Wonderlich et al., 2014), indicating good methodological quality. One of the RCTs described the process of assessor blinding (Thompson-Brenner et al., 2016), but none of them verified the blinding of assessors at

Table 4.1. CBT-E studies (published Jan 2014-March 2018): study characteristics and operationalization of clinical significant change

First author	Country	Design	N	Sample	BMI	Measure	Condition
Poulsen et al., 2014	Denmark	RCT	70	BN	-	EDE	CBT-Ef psychoanalytic psychotherapy
Wonderlich et al., 2014	USA	RCT	80	BN	≥18	EDE	CBT-Ef ICAT
Fairburn et al., 2015	UK	RCT	130	BN; 40.8% BED; 6.2% EDNOS; 53.1%	17.5-40	EDE	CBT-Ef IPT
Thompson-Brenner et al., 2016	USA	RCT	50	BN & BPS	-	EDE	CBT-Ef CBT-Eb
Wade et al., 2017	Australia	RCT[b]	40	AN; 20% BN; 57.5% BED; 5% OSFED; 17.5%	17.5-30	EDE-Q	Group CBT-Eb waiting list
Dalle Grave et al., 2015 [a]	Italy	Open trial	68	BN; 29.4% BED; 20.6% EDNOS; 50%	≥18.5	EDE-Q	CBT-E[c]
Signorini et al., 2018	Australia	Open trial	114	AN; 20.8% BN; 36.8% EDNOS; 42.5%	≥16	EDE-Q	CBT-Ef/Eb

AN = anorexia nervosa; BED = binge eating disorder; BMI = body mass index; BN = bulimia nervosa; BPS = borderline personality disorder; CBT-Eb = cognitive behavioral therapy enhanced broad version; CBT-Ef = cognitive behavioral therapy enhanced focused version; EDE = Eating Disorder Examination; EDE-Q = Eating Disorder Examination Questionnaire; EDNOS = eating disorder not otherwise specified; ICAT = integrative cognitive-affective therapy; IPT = interpersonal psychotherapy; ns = not significant; OSFED = other specified feeding or eating disorder; RCT = randomized controlled trial; WT = waiting list

[a] Sample: adolescents

[b] First eight weeks controlled

[c] Version not defined

[d] Criterion: abstinence of binging/purging in the past 4 weeks

[e] Global EDE(-Q) score less than 1 SD above the community mean and BMI ≥18.5

[f] Global EDE(-Q) score less than 1 SD above the community mean

Operationalization of clinical significant change			Clinical significant change posttreatment	Result
Global EDE(-Q) less than 1 SD above community mean	**BMI ≥18.5**	**Binging and/or purging[d]**		
no	no	yes	42% 15%	CBT-E > psychoanalytic psychotherapy
no	no	yes	22.5% 37.5%	ns
yes (i.e. ≤1.74)	no	no	65.5% 33.3%	CBT-E > IPT
no	no	yes	44% 40%	ns
yes (i.e. ≤2.77)	yes	no	66.7%[e]	CBT-E > WT[b]
yes (i.e. ≤2.77)	no	no	67.6%	-
yes (i.e. ≤2.46)	yes	no	42.2%[f] 35.4%[e]	-

the end of the study. In the study of Thompson-Brenner et al. (2016), due to the small sample size and lack of measurement of treatment quality, the CTAM score was 7 points lower. Compared with the other four RCTs, the trial of Wade et al. (2017) had a lower CTAM score; this latter study had a small sample size, no independent randomization, no description of randomization, no active control condition, and no assessment of treatment quality.

A full description and ratings of the CTAM are available on request from the first author.

Table 4.2. Changes in EDE-Q global score in open trials: intention-to-treat analysis

First author	N	Pre-treatment Mean Global EDE(-Q) (SD)	Post-treatment Mean Global EDE(-Q) (SD)	Follow-up Mean Global EDE(-Q) (SD)
Dalle Grave et al., 2015	68	3.6 (1.5)	1.8 (1.8)[a]	–
Signorini et al.i, 2018	108	4.03 (1.29)	3.09 (1.76)[a]	3.10 (1.76)
Wade et al., 2017	39	4.37 (1.19)	2.36 (1.31)[a]	2.67 (1.44)

EDE = Eating Disorder Examination; EDE-Q = Eating Disorder Examination Questionnaire; SD = standard deviation
[a] significant at $p < 0.05$

Discussion

The findings of this systematic review of seven effectiveness studies (five RCTs and two open trials) replicate and extend findings from two earlier studies (Byrne et al., 2011; Fairburn et al., 2009), demonstrating that CBT-E is an effective treatment for bulimia nervosa, BED and transdiagnostic samples of adult patients with an eating disorder. Since 2014, several RCTs made a direct comparison between CBT-E and other active treatment conditions, such as interpersonal psychotherapy (IPT), psychoanalytic psychotherapy, and integrative cognitive-affective therapy (ICAT). Although IPT is also an established evidence-based treatment for bulimia nervosa and BED (Kass, Kolko, & Wilfley, 2013), the first direct comparison made between IPT and CBT-E in a transdiagnostic eating disorder sample, showed that CBT-E was more effective (Fairburn et al., 2015). In another comparison in a bulimia nervosa sample, 20 weeks of CBT-E was compared with two years of psychoanalytic psychotherapy (Poulsen et al., 2014). At the end of treatment, the considerable difference in remission rates of binge eating and purging in favour of CBT-E (in combination with the substantial differences

in treatment duration), demonstrates that CBT-E for bulimia nervosa is highly cost-effective compared with psychoanalytic psychotherapy. One study was the first to show that ICAT (a new psychotherapeutic treatment for bulimia nervosa) might be as effective as CBT-E (Wonderlich et al., 2014). Furthermore, group CBT-E seems to be an acceptable alternative to individual CBT-E (Wade et al., 2017). In a bulimia nervosa sample with comorbid borderline personality disorder, no difference in effect was found between the focused and the broad version of CBT-E (Thompson-Brenner et al., 2016). The study of Dalle Grave et al. (2015) showed that CBT-E might be a potential treatment approach for nonunderweight adolescents with an eating disorder. Although Family-Based Treatment (FBT) is the preferred treatment for adolescents with bulimia nervosa (Le Grange et al., 2015), CBT-E might be a possible alternative when, for example, FBT is not sufficiently effective or not available. Finally, the study of Signorini et al. (2018) showed that CBT-E is generalizable to a noncontrolled clinical context. However, that study had a high attrition rate of up to 50%, possibly due to the high percentage of participants with anorexia nervosa (20.8%) in their sample. In an earlier open trial (Byrne et al., 2011) with a transdiagnostic sample including anorexia nervosa, the attrition rate was also high (40%).

In this review, substantial differences were found in posttreatment remission rates (22.2% to 67.6%); when interpreting these differences, several issues need to be considered. First, studies are difficult to compare due to variation in the included samples, differences in the definition of clinical significant change, and differences in the methodological quality of the studies. For example, in the study of Dalle Grave et al. (2015), the high proportion that met the criteria for remission at baseline (25%) biases the relatively high posttreatment remission rate (67.6%). Also, the difference in 'good outcome' between the studies of Wade et al. (2017) and Signorini et al. (2018), both carried out in Australia, can be explained, in part, by the different EDE-Q community mean used for the definition of clinical significant change. Signorini et al. (2018) found a posttreatment remission rate of 42.2% (EDE-Q score ≤ 2.46), whereas Wade et al. (2017) reported 66.7% (EDE-Q score ≤2.77).

Moreover, differences between the studies are not always easy to explain. For example, the substantial difference in outcome of CBT-E between the study of Poulsen et al. (2014), with a posttreatment abstinence rate of 42% compared with the 22.5% reported by Wonderlich et al. (2014) is puzzling, as both studies are similar regarding their samples, operationalization of

clinical significant change (abstinence of binge eating/purging), and both are of good quality. One difference between these studies is that, in the study of Poulsen et al. (2014), the founder of CBT-E was closely involved in the training and supervision of the therapists. Another is how completion was operationalized. Poulsen et al. (2014) defined completion as finishing the complete treatment, whereas Wonderlich et al. (2014) defined completion as attending at least 16 sessions.

A strong point of the present study is that it is the first review on CBT-E to assess the methodological quality of the included RCTs. Moreover, the results of this assessment indicate that, overall, the quality of the studies was high.

Taken together, the effectiveness studies of CBT-E for bulimia nervosa, BED and transdiagnostic samples (published since January 2014), of which four RCTs with high methodological quality, provide additional and robust evidence that CBT-E is indeed an effective treatment for patients with eating disorders.

This systematic review excluded CBT-E trials which studied patients with anorexia nervosa alone; however, the two open studies with transdiagnostic samples also included patients with anorexia nervosa (Signorini et al., 2018; Wade et al., 2017). Although these latter studies show positive effects of CBT-E in these samples, the anorexia nervosa subgroups were not analysed separately. Also, although CBT-E has been described as promising for the treatment of anorexia nervosa (Fairburn et al., 2013), the results are not consistent (Calugi, El Ghoch, & Dalle Grave, 2017; Dalle Grave et al., 2016; Egger et al., 2016; Frostad et al., 2018). In an open trial, preliminary support was found for the use of CBT-E for anorexia nervosa (Fairburn et al., 2013). In a subsequent implementation study of CBT-E for outpatients with anorexia nervosa, half of the patients did not complete CBT-E whereas the remaining patients achieved a significant increase in BMI at 1-year follow-up (Frostad et al., 2018). In an open study among inpatients with anorexia nervosa, Calugi et al. (2017)found that CBT-E was well accepted and might be a viable and promising treatment, even for those with severe and enduring anorexia nervosa. Overall treatment results of CBT-E for anorexia nervosa were poorer than results of CBT-E for other eating disorders; however, this finding needs to be interpreted in the broader context of treatment studies on anorexia nervosa with overall poor posttreatment outcome (Waller, 2016).

Some recommendations can be made for future research. A trial with a direct comparison between CBT-E and another CBT protocol might help unravel the differential effects of CBT-E, and studies on the working mechanisms of CBT-E could strengthen its theoretical foundation. On the basis of our results, we also recommend that researchers facilitate comparability between CBT-E studies. Agreement should be reached concerning, for example, what outcome variable to use to establish clinical significant change, what level of competence is needed for a CBT-E therapist, what tool should be used to measure treatment integrity, and what specifically constitutes 'not completed' therapy.

This review has some limitations. First, the literature search and identification of relevant studies was done by one researcher (first author), implying that studies might have been missed and/or study characteristics or results may have been misinterpreted. Second, for practical reasons, only studies in the English language were included. Finally, the literature search was restricted to Medline, PsycINFO and Embase; although we tried to address this limitation by examining the reference lists of earlier meta-analyses and of the articles in this review, eligible articles may unintentionally have been missed.

Conclusion

There is robust evidence that CBT-E is an effective treatment for adult patients with an eating disorder, especially for bulimia nervosa, BED and OSFED. Future research on the working mechanisms and differential effects of CBT-E compared with other CBT protocols might reveal the theoretical foundations and specificity of CBT-E. To establish good comparability between studies, we recommend that agreement be made between researchers, in particular regarding the operationalization of clinical significant change and the use of standard definitions.

KEY POINTS

- There is robust evidence that CBT-E is an effective treatment for adult patients with an eating disorder, especially for bulimia nervosa, BED and OSFED.
- The substantial range in remission rates between studies is partly due to differences in study samples and the definition used for clinical significant change.
- Although IPT is an evidence-based treatment for bulimia nervosa and BED, the first direct comparison between IPT and CBT-E showed CBT-E to be more effective.
- CBT-E is a far more (cost-)effective treatment for bulimia nervosa than psychoanalytic treatment on the main parameters of bulimia nervosa, that is binge eating and purging.
- Future research should focus on the working mechanisms and differential effects of CBT-E compared with other CBT protocols to establish the specificity of CBTE.

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Conflicts of interest

There are no conflicts of interest.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ▪ of special interest
- ▪▪ of outstanding interest

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Egger, N., Wild, B., Zipfel, S., Junne, F., Konnopka, A., Schmidt, U., *et al.* (2016). Cost-effectiveness of focal psychodynamic therapy and enhanced cognitive-behavioural therapy in out-patients with anorexia nervosa. *Psychological Medicine, 46*(16), 3291-3301. https://doi.org/10.1017/S0033291716002002

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In this RCT, 20 weeks of CBT-E for BN was compared with 2 years of psychoanalytic psychotherapy; CBT-E appeared a far more (cost-)effective treatment for BN than psychoanalytic treatment on the main parameters of bulimia nervosa, that is binge eating and purging.

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Chapter 5

Effectiveness of enhanced cognitive behavioral therapy (CBT-E) for eating disorders: study protocol for a randomized controlled trial

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Abstract

Background: While Eating Disorder Not Otherwise Specified (EDNOS) is the most common eating disorder (ED) diagnosis in routine clinical practice, no specific treatment methods for this diagnosis have yet been developed and studied. Enhanced cognitive behavioral therapy (CBT-E) has been described and put to the test as a transdiagnostic treatment protocol for all EDs, including EDNOS. Initial research in the UK suggests that CBT-E is more effective for eating disorders, especially bulimia nervosa (BN) and EDNOS, than the earlier version of CBT. These positive results of CBT-E have to be replicated in more detail, preferably by independent researchers in different countries. Being the first Dutch study into CBT-E, the results from this national multi-center study – with three sites specialized in EDs – will deliver important information about the effectiveness of CBT-E in several domains of ED pathology, while providing input for the upcoming update of the Dutch Multidisciplinary Guideline for the Treatment of Eating Disorders.

Methods/Design: A multi-center randomized controlled trial will be conducted. One hundred and thirty-two adult outpatients (aged 18 years and older) with an ED diagnosis and a Body Mass index (BMI) of between 17.5 and 40 will be randomly allocated to the control or intervention group. Subjects in the control group will receive treatment as usual (standard outpatient treatment provided at the participating sites). Subjects in the intervention group will receive 20 sessions of CBT-E in 20 weeks. The design is a 2 (group) x 5 (time) repeated measures factorial design in which neither therapists nor patients will be blinded for treatment allocation. The primary outcome measure is recovery from the ED. Secondary outcome measures include ED psychopathology, common mental disorders, anxiety and depressive symptoms, health-related quality of life, health care use and productivity loss. Self-esteem, perfectionism and interpersonal problems will be examined as putative predictors and mediators of the effect of treatment. Also, an economic evaluation from a societal perspective will be undertaken. All relevant effects, direct, and indirect costs will be included. Utility scores will measure the effects. Measurements will take place at pre-treatment, 6 weeks, 20 weeks, 40 weeks and 80 weeks.

Discussion: This effectiveness study into CBT-E has the aim to broaden the scope and generalizability of former studies. If CBT-E appears to be at least as effective as traditional diagnosis-specific treatments for a broad range of ED patients, training in one protocol would be sufficient for clinicians to treat patients with different kinds of EDs. It gives the opportunity to offer treatment for a severe mental disorder with fewer resources, thereby increasing the accessibility of specialized care for patients with an ED.

Trial registration: Netherlands Trial Register, NTR4485. Registered on 2 April 2014.

Keywords

eating disorders, transdiagnostic treatment, cognitive-behavioral therapy, CBT-E, treatment outcome, cost-effectiveness, RCT

Background

Eating disorders (EDs) are severe mental disorders, which typically begin in adolescence (Hudson et al., 2007; Jenkins et al., 2011; Mitchison et al., 2012; Stice, Marti, & Rohde, 2013). In the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association, 1994) three EDs are recognized: anorexia nervosa (AN), bulimia nervosa (BN) and a residual diagnostic category called eating disorder not otherwise specified (EDNOS), including binge eating disorder (BED). In the new edition, DSM-5 (American Psychiatric Association, 2013), BED has been added as a new official diagnosis (Attia et al., 2013). Prior to the official recognition of BED as a specific DSM-5 ED, several studies into the efficacy of specific BED interventions have been performed (Wilson et al., 2010), utilizing DSM-IV research criteria. In DSM-5, the remaining EDs from the DSM-IV EDNOS category have been redefined into two categories: other specified feeding or eating disorder (OSFED) and unspecified feeding or eating disorder (USFED).

These developments have complicated direct comparisons between research data on the DSM-IV EDNOS and the DSM-5 BED, OSFED and USFED categories.

The effectiveness research on EDs has focused on BN and, more recently, BED. Studies of good quality on DSM-IV EDNOS (with the exception of BED) and AN are limited. This paucity of research on eating disorder symptoms summarized in the DSM-IV EDNOS category is a serious problem, as EDNOS has been the most common ED diagnosis (50-77%) in routine clinical practice (Fairburn & Bohn, 2005; Machado et al., 2007), and is responsible for severe morbidity, loss of quality of life and even an annual mortality rate of 3.3 per 1000 person years (Arcelus et al., 2011). General health care utilization among this group of patients is high (van Son et al., 2012), and about 62% are referred to mental health care by their GPs (van Son et al., 2010).

EDNOS often refers to ED psychopathology that does not meet the full diagnostic criteria of one of the specific eating disorders (i.e., AN or BN). Examples are: (in women) all symptoms of AN except amenorrhea, and compensatory behavior by individuals of normal weight after eating small amounts of food. Although the use of DSM-5 criteria effectively reduces the frequency of the residual diagnosis EDNOS (for example, by lowering the threshold for AN and BN and adding BED as a specified ED), the magnitude of this reduction varies across studies (Smink, van Hoeken, & Hoek, 2013).

The three most prominent guidelines – from the UK National Institute for Health and Care Excellence in 2004 (National Institute for Health and Care Excellence (NICE), 2004), from the American Psychiatric Association in 2006 (American Psychiatric Association, 2006) and the most recent from the Royal Australian and New Zealand College of Psychiatrists in 2014 (Hay et al., 2014) – recommend cognitive behavior therapy (CBT) as the psychological treatment of first choice, specifically for BN and BED. Specific treatment recommendations for AN are less forthcoming due to the paucity of positive outcome data in this area. These recommendations concur with those from the Dutch Multidisciplinary Guideline for the treatment of Eating Disorders in 2006 (Landelijke Stuurgroep Multidisciplinaire Richtlijnontwikkeling in de GGZ, 2006).

Fairburn (Fairburn, 2008) developed a relatively short transdiagnostic CBT, CBT-E(nhanced), designed to be suitable for the full range of ED diagnoses. CBT-E is based upon the transdiagnostic theory of the maintenance of EDs, in which it is assumed that most of the mechanisms involved in the persistence of EDs are common to all three EDs, rather than being specific to each diagnostic group separately (Fairburn, Cooper, & Shafran, 2003). According to Fairburn and colleagues, EDs have more similarities than differences, especially the core psychopathology (over-evaluation of shape and weight) and expression in attitudes and behavior (dietary restriction, dietary rules, binges, self-induced vomiting etc.). CBT-E, the enhanced version of CBT, uses new strategies and procedures to address mechanisms that are central to the maintenance of all EDs, including the diversity of eating disorder psychopathology that until recently comprised the DSM-IV EDNOS category. CBT-E is characterized by increased focus on engagement, greater emphasis on the modification of concerns about shape and weight, and the development of skills to deal with setbacks. Regardless of ED diagnosis, CBT-E is designed as an individualized and "modular" form of treatment, in which specific modules may be directed at the particular maintaining mechanisms operating in the individual patient's case.

There are two forms of CBT-E: a focused form (CBT-Ef) that targets ED psychopathology exclusively (e.g., procedures directed at over-evaluation of shape and weight), and a more complex broad form (CBT-Eb) that also addresses additional problems that appear to maintain EDs or complicate their treatment. Fairburn et al. (Fairburn, Cooper, Shafran, et al., 2008) state that additional mechanisms as clinical perfectionism, low self-esteem and interpersonal problems maintain the ED psychopathology and thereby

obstruct change during the treatment with CBT-E. The broad version of CBTE was designed to focus on these mechanisms. For both versions of CBT-E two variants of intensity have been developed: 20 sessions in 20 weeks for the patients who are not significantly underweight (Body Mass Index (BMI) above 17.5), and 40 sessions in 40 weeks for the patients who are significantly underweight (BMI below 17.5).

First studies have found CBT-E to be more efficacious than other psychological approaches (Byrne et al., 2011; Fairburn et al., 2009; Poulsen et al., 2014). It seems feasible to treat a broad range of ED patients with CBT-E, but more evidence is required according to a recent meta-analysis (Spielmans et al., 2013) and the most recent guidelines (Hay et al., 2014). The current study will not only evaluate the effectiveness of CBT-E in terms of the reduction of ED psychopathology and additional comorbid psychopathology and enhancement of quality of life and health status, but also the cost-effectiveness of CBT-E relative to regular ED therapy. Treatment as usual (TAU) for patients with an ED varies per ED category. For BN and BED there are well-described and evaluated CBT protocols (Dingemans, 2005; Vanderlinden et al., 2011). For AN and EDNOS (except BED) evidence-based treatment protocols are lacking and treatments vary greatly. There are no empirical data about duration, intensity and costs of regular therapy for eating disorders in the Netherlands. However, consulted independent ED experts in the Netherlands and Belgium have estimated that TAU for EDs is probably more intensive, long-term and less effective than CBT-E. Therefore, we expect CBT-E to be more cost-effective compared to regular treatment.

If CBT-E indeed appears to be at least as effective as traditional diagnosis-specific treatments for a broad range of ED patients, this unified transdiagnostic approach for all eating disorders would give the opportunity to offer treatment for a severe mental disorder with fewer resources and, therefore, increase the accessibility of an evidence based treatment for patients with an ED.

In this study we only use the focused version (CBT-Ef) for patients with a BMI above 17.5. BMI above 17.5 is considered by Fairburn as the critical limit for the 20-session CBT-E variant. Additional measurements on top of the outcome measures and those for quality of life and health status involve perfectionism, self-esteem and interpersonal problems. These are believed to be possible clinical and research indications for obstruction in change and progress. Measurements will be taken before, during, and after treatment to explore the predictive and mediating effects on treatment outcome.

Methods/design

Design

We will execute a multi-center randomized controlled trial (RCT) with two equal-sized parallel groups at three specialized ED treatment centers from three regions in The Netherlands. Participants will be randomized into two groups (CBT-E versus TAU) stratified by eating disorder center and type of eating disorder. Measurements will take place at pre-treatment, 6 weeks, 20 weeks, 40 weeks and 80 weeks, resulting in a 2 (group) x 5 (time) repeated measures factorial design. For an overview of the proposed flow of participants, see Figure 5.1. The present study protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) (Chan et al., 2013.

Participants

Participants will consist of 132 adult outpatients aged from 18 years with an ED diagnosis according to DSM-5 and a BMI between 17.5 and 40. They are recruited at the participating mental health centers: PsyQ/ Parnassia Psychiatric Institute in The Hague will include 60 patients and PsyQ/ Lentis Psychiatric Institute in Groningen and Rintveld/Altrecht Mental Health Institute in Zeist both 36 patients.

Inclusion criteria

In order to be eligible to participate in this study, a participant must meet all of the following criteria:

1. Adult outpatients (from age 18 years) with an ED diagnosis: AN, BN, BED, OSFED (EDNOS), according to an adapted version of the SCID-I (see "Measurement" section) and a BMI of between 17.5 and 40
2. Provision of Informed consent
3. Ability to understand Dutch (speaking, listening, reading)

Exclusion criteria

A potential participant who meets any of the following criteria will be excluded from participation in this study:

1. Prior treatment that closely resembles CBT-E or another evidence-based intervention for eating pathology in the past 2 years
2. A severe Axis-I or -II psychiatric disorder or other psychosocial circumstances that require priority in clinical attention and other support, and therefore

impedes immediate treatment of the ED (e.g. psychoses, addiction, suicidality, homelessness)
3. Receiving ongoing psychiatric treatment (except for antidepressant medication)
4. Intellectual disability
5. Medical instability or pregnancy
6. Not available over the coming 20 weeks

Procedure

Each patient will be recruited at the site at which they were referred to for treatment. All assessors have been trained in the adjusted SCID-I ED section which will be used to diagnose Axis-I ED. During intake potential participants receive information about the research (treatment conditions, procedure, randomization process, confidentiality) from the local assessors. The assessment staff of each site will decide whether a patient meets the inclusion- or exclusion criteria and whether they are definitely eligible for the study. If this is considered to be the case, the research assistant (who is located at the logistic center of the study, PsyQ The Hague) will, for each site, randomly assign the patient to TAU or CBT-E and send an e-mail (in attachment) to the assessor. Randomization is done by making use of a random allocation program, stratified by center and type of ED. Participation will be discussed with the patient during a second appointment with the assessor. If the patient is willing to participate and has signed the Informed Consent Form, the assessor will open the email to inform the patient of the condition they are assigned to. Data will be obtained mainly by online questionnaires, with exception of the SCID-I ED section, which will be conducted by telephone, and the IAT computer task which will be conducted on a stand alone computer. Prior to the first treatment session, patients will be asked to fill out the online questionnaires and complete the IAT computer task. After 6, 20, 40 and 80 weeks the online questionnaires are obtained. After 20 and 80 weeks the SCID-I will be repeated. After 20 weeks the IAT task will be repeated (for an overview of the assessments see Figure 5.1). Participants who do not complete the online questionnaires within 1 week will be contacted by means of personalized emails and/or telephone calls. If they decide to discontinue study participation, efforts will be made to retain them in the trial, while respecting their right to withdraw from participation at any time without further consequences. Patients will not receive any monetary compensation for their involvement, but treatment will be delivered free of charge.

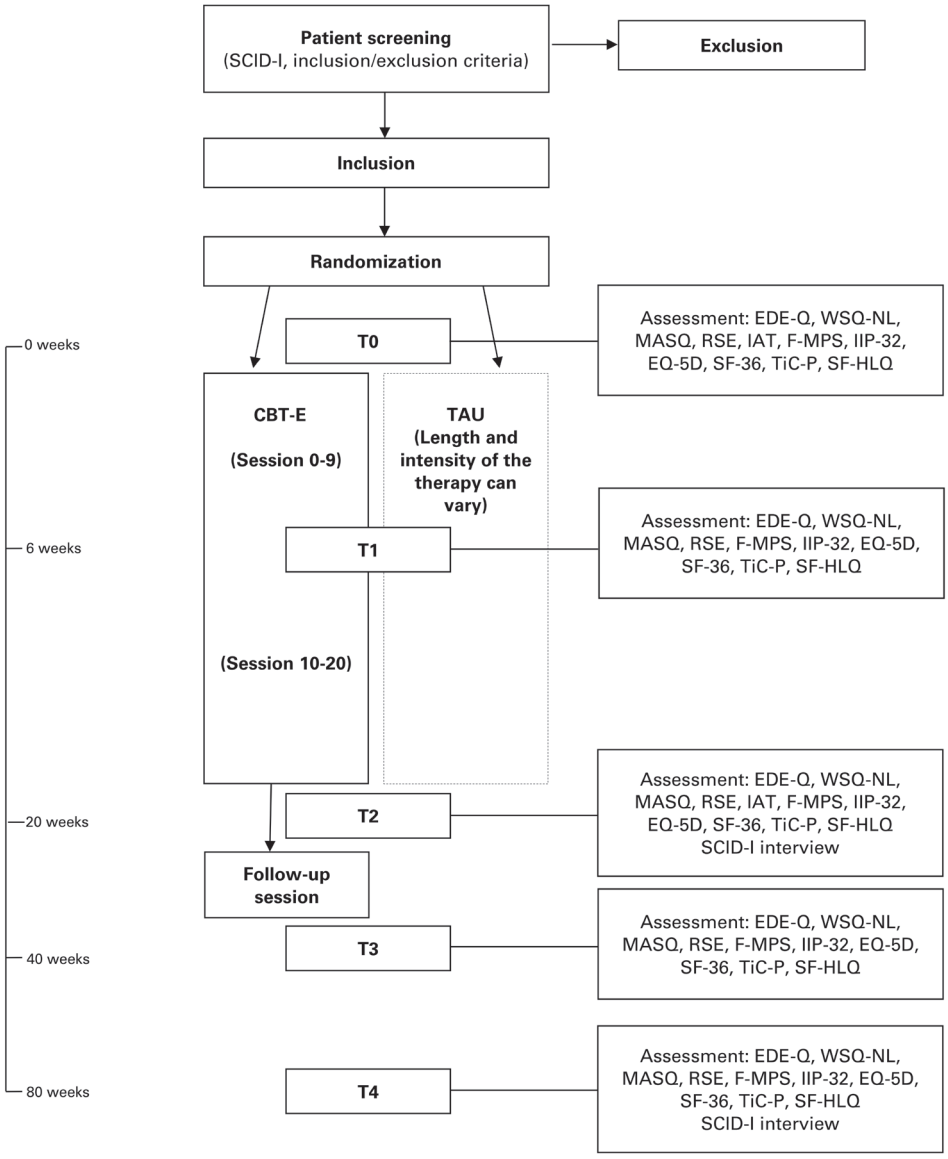

Figure 5.1. Proposed flow of participants

T0 = Baseline, T1 = Week 6, T2 = End of treatment Week 20, T3 = Follow up Week 40, T4 = Follow Up Week 80 SCID-I = Structured Clinical Interview for DSM Axis-I disorders; EDE-Q = The Eating Disorder Examination- Questionnaire; WSQ = Web screening Questionnaire for common mental disorders; MASQ = Mood and Anxiety Questionnaire; EQ-5D = EuroQoL five dimensions questionnaire; SF-36 = Short Form Health Survey; TiCP = Trimbos/ iMTA questionnaire for Costs associated with Psychiatric illness; RSE = Rosenberg Self-Esteem Scale; IAT = Implicit Association Test Self-Esteem; FMPS = Frost Multidimensional Perfectionism Scale; IIP-32 = Inventory of Interpersonal Problems

Study conditions

***CBT-E*:** a transdiagnostic 20-sessions version of CBT, CBT-E(nhanced). In this study we use the focused version for patients with a BMI above 17.5, designed to be suitable for the full range of ED diagnoses. CBT-E is a treatment for ED psychopathology, rather than for a specific eating disorder diagnosis. The strategy underpinning CBT-E is to construct a transdiagnostic formulation (or set of hypotheses) of the processes that are maintaining the patient's psychopathology and to use this formulation to identify the features that need to be targeted in treatment. This formulation is constructed at the beginning of treatment, but will be revised, if needed, during therapy. In this way a tailor-made treatment is created.

Stage 1 (sessions 1-7) is an intensive initial stage, with appointments twice a week. The therapist and the patient together set up the formulation of the underlying maintaining factors , which will be used as a base for the remainder of the treatment. The aims of this stage are to engage the patient in treatment.

Stage 2 (sessions 8-9) are weekly appointments. This stage is a brief stage in which the therapist and patient take stock, review progress, identify any emerging barriers to change, modify the formulation and plan stage 3. This stage is important to identify problems with the therapy, to remove barriers and adjust treatment if needed. After Stage 2 the treatment will become more personalized.

Stage 3 (sessions 10-17) is the main body of treatment. There are eight weekly appointments. The aim is to address the main mechanisms that are supposed to maintain the patient's ED. How this is done precisely varies from patient to patient. The therapist can choose to pay attention to one or more defined maintaining factors.

Stage 4 (sessions 18-20) is the final stage of treatment and the focus shifts to the future. The appointments are scheduled at 2-week intervals. There are two aims: the first one is to ensure that the changes are maintained (over the subsequent 20 weeks until a review appointment is held), and the second one is to minimize the risk of relapse in the long-term.

After 20 weeks there is a review session. The most important aim in this session is to review what is learned and achieved during treatment and what risk factors are to be taken into account when therapy has ended.

***TAU*:** the usual treatment given at the participating treatment sites is in general based on CBT, individually or in a group with elements of existing CBT treatment protocols (Dingemans, 2005; Vanderlinden et al., 2011). Depending on the site's treatment policy, this may vary from low-intensity care (weekly sessions) to high-intensity care. This high-intensity care consists of two group sessions a day for 2 days of the week, sometimes supplemented with individual sessions due to coexisting psychopathology. Most of the times more than one discipline (psychologist, dietitian, psychiatrist) is involved in applying the treatment. The type of treatment provided is registered.

Selection and training of therapists

All CBT-E therapists are psychologists/psychiatrists or registered nurses/social workers (n = 10). All have at least 2 years of experience as a therapist in the field of EDs and have been working at least 2 years according to CBT principles. All CBT-E therapists in the participating centers were trained as a group by Christopher G. Fairburn and had 20 supervision sessions through videoconferencing from Zafra Cooper. A Dutch treatment manual was developed and will be used by all CBT-E participating therapists. All participating CBT-E therapists have treated at least 3 ED patients with CBT-E under supervision before entering the trial.

All TAU therapists are psychologists/psychiatrists or registered nurses/social workers who have at least 2 years of experience as a therapist in the field of EDs. TAU did not include training or supervision of the therapists. TAU therapists have regularly standard, local collegial consultation.

The treatment integrity in CBT-E will be evaluated by recording all CBT-E sessions. Two audiotaped sessions of every CBT-E patient will be randomly selected (from respectively, stages 1/2 and stages 3/4) and the use of specific therapeutic interventions according to the treatment manual will be scored on several 7-point Likert scales. The first 20 audiotapes will be double rated to assess interrater reliability. Evaluation of the CBT-E sessions will be executed by psychologists who are familiar with the treatment protocol (trained through the online training in CBT-E developed by Fairburn), by ticking on prearranged checklists whether all due aspects of specific therapy stages have been handled adequately by the therapist.

Objectives

The primary objective of this study is to assess whether CBT-E is more optimal in terms of a higher percentage of recovery from EDs compared to TAU.

The secondary objectives are to assess whether CBT-E is more effective in (1) reducing important aspects of ED psychopathology, (2) reducing indications for the presence of comorbid psychopathological conditions and additionally comorbid symptoms of anxiety and depression, (3) improving health-related quality of life and (4) effectuating a better cost-effectiveness, compared to TAU.

Moreover, self-esteem, perfectionism and interpersonal problems are repeatedly measured during this RCT to examine their possible predictive and mediating effects on treatment outcome.

Measurements

Screening and primary treatment outcome

Structured Clinical Interview for DSM Axis-I Disorders (SCID-I). The SCID-I (First et al., 1996; van Groenestijn et al., 1998) will be used to assess the presence of an ED. Only the section about EDs will be administered. Because the SCID-I only covers AN, BN, and EDNOS-BED, skip rules were changed or omitted and parts of the *Eating Disorder Examination (EDE)* (Fairburn, Cooper, & O'Connor, 2008) were added in order to diagnose DSM-5 AN, BN, BED and OSFED (Smink et al., 2014). The interview will be used both to obtain a DSM-5 diagnosis for inclusion and as a treatment outcome measure at T2 (at the end of treatment, 20 weeks after treatment had started) and T4 (80 weeks after the start of treatment). Several studies found moderate to excellent interrater agreement for determining presence of Axis-I disorders using the original SCID-I (Lobbestael, Leurgans, & Arntz, 2011) and good test-retest reliability (Zanarini & Frankenburg, 2001; Zanarini et al., 2000).

Secondary study parameters

The Eating Disorder Examination-Questionnaire (EDE-Q) (Fairburn & Beglin, 2008; van Furth, 2000). This questionnaire is a self-report measure that was adapted from the interview-based EDE (Cooper, Cooper, & Fairburn, 1989) and measures ED pathology. It consists of 36 items that are scored on a 7-point scale. The total score is used as an indicator for the level of ED pathology, with a higher score denoting more pathology. Good concurrent validity (Black & Wilson, 1996; Fairburn & Beglin, 1994; Mond et al., 2004; Wilfley et al., 1997), discriminant validity (Wilson, Nonas, & Rosenblum, 1993) and acceptable criterion validity (Mond et al., 2004) have been demonstrated with adults. Moreover, the EDE-Q has been found to have good internal consistency and test-retest reliability in adults (Luce & Crowther, 1999). In studies comparing the EDE interview and EDE-Questionnaire the overall correlation coefficient ranged from .68 to .76. In general, participants obtain higher scores in the questionnaire than in the

interview mode of administration (Berg et al., 2011; Binford, Le Grange, & Jellar, 2005).

Web Screening Questionnaire for common mental disorders (WSQ) (Donker et al., 2009). This self-report screening instrument will be used to screen for Axis-I disorders. It is a short screening instrument for depressive disorder, alcohol abuse/dependence, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), social phobia, panic disorder, agoraphobia, specific phobia, and obsessive compulsive disorder (OCD). The questionnaire consists of 15 questions. The sensitivity of the WSQ is 0.72-1.00 and specificity is 0.44-0.77 (Donker et al., 2009).

Mood and Anxiety Symptom Questionnaire (MASQ) (de Beurs, van Hemert, & Goekoop, 1991). The MASQ is a self-report questionnaire to assess the severity of symptoms of anxiety and depression. It is based on the tripartite model of anxiety and depression symptoms, which can be separated into three groups: global discomfort (anxiety and depression), anhedonia (specific for depression) and physiological hyper arousal (specific for anxiety). The questionnaire consists of 90 items, with an answering scale from 1 to 5 ("not" to "very much"). The scores of the subscales are measured by summating the scores of the items of the subscales. The subscales have sufficient discriminant validity, especially the depression scales (Boschen & Oei, 2007; Buckby et al., 2007; de Beurs et al., 2007). Subscales seem to have sufficient internal consistency (de Beurs et al., 1991).

EuroQoL five dimensions questionnaire (EQ-5D) (Rabin & de Charro, 2001). The EQ-5D aims to measure health-related quality of life. The EQ-5D is a short questionnaire that consists of five questions with three answer levels, reflecting "no problem", "some problem" and "extreme problem" in relation to specific dimensions (i.e., mobility, self-care, usual activity, pain and mood). In addition the EQ-5D also includes a visual analogue scale (VAS) to value the respondent's health state, labeled from "best imaginable health" (100) to "worst imaginable health" (0). The EQ-5D can be used to assess sociodemographic differences in health status. Research provides support for the validity of the EQ-5D as a measure for health status (Johnson & Coons, 1998).

Short Form Health Survey (SF-36) (Ware, 2000). We will use the SF-36 to assess health related quality of life and health status. The SF-36 was developed for a wide range of chronic diseases (Ware, 2000). It

is a multidimensional instrument, with 36 questions to measure eight dimensions: physical functioning, social functioning, role limitations (physical and emotional), mental health, vitality, pain, general health perception and health change. The scores per dimension will be transformed to a scale from 0 to 100 and a higher score denotes a better health status. The Dutch translation has good reliability (Cronbach's alpha coefficients above .70) and validity (Aaronson et al., 1998).

Trimbos/iMTA Questionnaire for Costs associated with Psychiatric Illness (TiC-P), including the Short Form – Health and Labour Questionnaire (SF-HLQ) (Hakkaart-van Roijen, Donker, & Tiemens, 2002). The TiCP is a validated tool commonly applied in economic evaluations of treatments in mental health care. The TiC-P is a paper and pencil self-report questionnaire that consists of two parts. The first part obtains information about the volume of health care consumption (direct costs) and the production losses relative to the health problem in question (indirect costs), and some general questions. The second part of the TiC-P, which measures the indirect costs, is the SF-HLQ. The SF-HLQ, an abbreviated version of the HLQ, is a generic and validated measurement instrument to collect data on productivity losses related to health problems in individuals with paid or unpaid work (Hakkaart-van Roijen et al., 2002). By multiplying the volumes by the cost prices, it is possible to calculate the costs (Tan, Bouwmans-Frijters, & Hakkaart-van Roijen, 2012).

Putative predictors/mediators

The Rosenberg Self-Esteem Scale (RSE) (Rosenberg, 1965). The RSE is a widely-used 10-item Likert scale to measure self-esteem. Items are answered on a 4-point scale – from "strongly agree" to "strongly disagree" – measuring positive and negative feelings towards the self. The Dutch version of the RSE is found to be a one-dimensional scale with high internal consistency (Cronbach's alpha of 0.89) and congruent validity (Franck et al., 2008).

Implicit Association Test Self-Esteem (IAT) (Greenwald, McGhee, & Schwartz, 1998). The IAT will be used to assess implicit self-esteem. The IAT is a computer-administered task, which measures the automatic associations between concepts. The IAT is based on a double discrimination task in which participants are asked to assign single stimuli as fast as possible to a given pair of target categories. The internal consistency has an average score of 0.70 (Greenwald et al., 1998).

Frost Multidimensional Perfectionism Scale (F-MPS) (Frost et al., 1993). We will use the F-MPS to assess perfectionism. The scale contains 35 questions with a 5point Likert scale from "strongly disagree" to "strongly agree". When the scale was developed it measured six subscales of perfectionism. It is regarded as internally consistent, reliable over time and displays sound concurrent validity (Frost et al., 1993; Frost et al., 1990). However, in practical applications, the six-factor structure appeared to be unstable and an alternate four-factor structure was proposed by several others (Hawkins, Watt, & Sinclair, 2006; Stöber, 1998).

Inventory of Interpersonal Problems (IIP-32) (Vanheule, Desmet, & Rosseel, 2006). The IIP is a self-report questionnaire that measures the interpersonal problems that people experience. The instrument was first developed as a 127-item questionnaire on the basis of a list of common interpersonal difficulties raised by persons seeking psychotherapy. The 64-item version was created by Alden et al. (Alden, Wiggins, & Pincus, 1990) specifically to provide a circumplex measure (originally called the IIP-C). For this research we will use the shorter 32-item version (IIP-32), which was developed with the aim of providing a more rapid assessment with a good reliability and validity (Barkham, Hardy, & Startup, 1996). All items are rated on a 5-point Likert scale ranging from 0 ("not at all") to 4 ("extremely"). The questionnaire has good internal consistency, the coefficient alpha for the scales of the IIP-32 are above 0.70 (Vanheule et al., 2006).

Sample size

In order to detect an absolute difference in recovery rate from ED of 25% (CBT-E: 50% versus TAU: 25%), a sample size of 66 patients per treatment condition is required to provide 80% power at two-sided $p<0.05$ (intention-to-treat analysis). This means that at least 132 patients are needed for this study.

Randomization, treatment allocation and blinding

Randomization takes place after screening of the inclusion/exclusion criteria and signing of informed consent. The research assistant will randomly assign the participating patients to CBT-E or TAU, stratified by centre and type of eating disorder (AN, BN, BED, OSFED). Within each of the twelve strata, a research assistant will randomize participants using a permuted block design. Given the nature of the psychological treatment neither the therapists nor participants can be blinded for the delivered treatment.

Data management and storage

All study-related data and other study material will be stored securely at the study site (PsyQ The Hague). Participant information and study data will be kept in locked cabinets in areas with limited public access. After obtaining informed consent, participants will be allocated a unique code. The file that links participants to their codes is stored on a secure server hosted by PsyQ and is only accessible by the researcher and research-assistant. Any study material concerning participant information will not be released outside the study without written permission of the participant. Online questionnaires will be collected using an authorized Surveymonkey account and downloaded and added to the database. The SurveyMonkey security and privacy statements for internet security and handling personal information and data can be found at respectively https://www.surveymonkey.com/mp/policy/security/ and https://www.surveymonkey.com/mp/policy/privacy-policy/.

Data collected on paper (SCID-I), will be manually entered into a database. Data collected by the IAT computer task will be transcripted and added to the database. Data integrity will be enforced through several ways, including valid values, range checks and consistency checks. The master database will be held on a secure server hosted by PsyQ, only accessible for authorized personnel involved in the trial. All obtained data and administrative forms (e.g., informed consent) will be stored in accordance with the data storage protocol for 15 years.

Statistical analysis

All participants who are randomized will be included in the comparison and analysed according to their randomized allocation (intent-to-treat analysis). Wherever possible, we will continue to collect follow-up data from participants after any dropout of treatment or the study, in order to keep the dataset as complete as possible. In addition, baseline differences in study completers and dropouts will be analyzed with *t* tests for independent samples or chi-square analyses if appropriate. Moreover, we will perform a per-protocol analysis by including only those participants who completed at least 70% of the scheduled therapy sessions. All analyses will be carried out using SPSS 23 (IBM Corporation, 2014).

Primary study parameter(s)

To test the hypothesis that CBT-E is more effective than TAU, post-treatment differences in recovery rate (based on SCID-I diagnosis) between conditions will be analysed with chi-square analysis. Using logistic regression analysis

with recovery at post treatment as outcome and treatment condition and baseline EDE-Q scores as predictors, whether differences in recovery rate between conditions are independent of severity of ED pathology at pre-treatment will also be investigated. Moreover, the course of scores from pre-, mid- and post-treatment to follow-ups I and II on the EDE-Q will be analyzed with multilevel analyses (MLA). MLA is especially suitable to analyze repeated measures data because it takes into account the dependencies among observations nested within individuals. Another advantage of this methodology is its ability to handle missing data, a problem often occurring in longitudinal research (Twisk et al., 2013). The data have a three-level hierarchical (multilevel) structure: repeated measures at the first level, individuals at the second level and treatment at the third level. Besides main effects for treatment and time, whether groups differ in their course of EDE-Q scores will be investigated by including a treatment x time interaction term. Differences between treatment centers will be investigated likewise.

Secondary study parameter(s); indirect clinical effectiveness

Three-level MLA will also be used to study the relative efficacy of CBT-E versus TAU in reducing scores on the secondary outcome measures.

Putative mediators

To test the hypothesis that the effects of the CBT-E/TAU on the EDE-Q scores are mediated by the putative mediators investigated (i.e. self-esteem, perfectionism, and interpersonal problems), first, standardized residualized gain scores are calculated by removing the portion of mid-treatment scores on the mediators that can be predicted linearly by corresponding pre-treatment scores and the portion of post-treatment EDE-Q scores that can be predicted linearly by mid-treatment EDE-Q scores. Next, following the analytic steps outlined by Baron and Kenny (Baron & Kenny, 1986) and Kraemer et al. (Kraemer et al., 2002) we will test the significance of the following paths using linear regression analyses: path a: the independent variable (i.e., CBT-E/TAU) must affect the mediator (i.e., pre- to mid-residualized change scores for self-esteem, perfectionism or interpersonal problems); path b: the mediator must affect the dependent variable (i.e., mid- to post-residualized EDE-Q change scores); path c: the independent variable must affect the dependent variable; and path c': the direct effects of treatment on the dependent variable must be meaningfully reduced when including a hypothesized mediator in the model. When early process changes predict later outcome changes, it will be further tested whether this prediction remains significant also after controlling for autocorrelations (i.e.,

the correlations between early and late process changes) and synchronous correlations (i.e., the correlations between early process and early outcome changes) (Burns et al., 2003). The significance of the indirect effect of treatment on EDE-Q scores through the putative mediators will be determined using a bootstrap approximation with 5000 iterations to obtain biased-controlled confidence intervals. In case of multiple significant mediators, the independent contribution of these mediators will be further explored using multiple mediation models.

Cost-effectiveness analysis

We will apply a cost-utility analysis (CUA). The results will be expressed as cost per Quality adjusted Life Year (QALY). The economic evaluation will be undertaken from a societal perspective. Hence, all relevant effects and costs due to resource utilization within and outside the healthcare (direct costs) and costs due to production losses (indirect costs) will be included. To examine the cost-effectiveness of CBT-E compared to TAU the EQ-5D, the SF-36 and the TiC-P will be used.

The cost utility will be calculated as an incremental cost-effectiveness ratio (ICER) which is the ratio between the difference in costs and the difference in QALYs. The budget impact analysis (BIA) will be conducted from a health care payer perspective according to the ISPOR guidelines (Tan et al., 2012). So, we will compare total health care costs when applying the intervention compared to the standard treatment for the target population in The Netherlands. Cost-effectiveness analyses will be performed using the ICEinfer package (Obenchain, 2014) within the R environment (R Core Team, 2015).

Dissemination

Results of the study will be presented at international scientific congresses and published in international scientific journals. Also, if applicable, the practical implications of the study outcome will be published in professional journals and can provide input for the Dutch Multidisciplinary Guideline for the treatment of eating disorders. Moreover, depending on the outcome of the study, research findings will be used in the training of professionals.

Ethical considerations

Ethical approval is obtained from the Ethical Review Board of the Leiden University Medical Center. The Board of Directors at PsyQ agreed to support the

execution of the study. The Boards of Directors of the three psychiatric regional centers that take part in the study also gave their consent. All participants will be extensively informed about the study, addressing confidentiality and the right to abort their participation at any time and without clarification; quitting the research program will by no means affect the course of treatment. No harm is expected from the intervention. In case of clinical deterioration (for any reason), the responsible clinical psychologist/psychiatrist can advise discontinuation of trial participation at any time. Written information will be given. When the patient is willing to continue, written consent is required. An independent physician is appointed, to whom subjects can address questions about the research before, during and after a study. The independent physician is not involved in the study itself.

Discussion

In this study we assess the effectiveness of CBT-E. In addition to the assessment of changes in eating pathology and comorbid other psychopathology, we will also assess the differential cost-effectiveness of CBT-E compared to that of TAU. This is an important strength of this study because to our knowledge this has not been done yet. In a time were resources in health care are limited this question becomes more and more important. If CBT-E appears to be cost-effective for a broad range of ED patients, it would give the opportunity to offer treatment for a severe mental disorder with fewer resources, thereby increase the accessibility of specialized care for patients with an ED.

A large sample will be recruited and the sample is a clinically relevant one as it will be recruited among consecutive patients from three outpatient centers and few exclusion criteria are applied.

The follow up will take place until 60 weeks after the end of treatment which gives the opportunity to look for long-term results. This is an important strength because there are a few effectiveness studies in de field of EDs with long term follow-up.

Low self-esteem, dysfunctional perfectionism and interpersonal problems have been identified in clinical practice and in research as possible factors for obstruction in change and progress. Therefore, these three factors are measured during this RCT before, during and after treatment to explore their possible predictive and/or mediating effects on treatment outcome.

There are, however, also some limitations to consider given the chosen research design.

Firstly, most of the measurements are conducted online which gives a reduction in research costs and maximization of the accessibility of participation. However, this also could be a limitation because of the non-standardized assessment situation and possible delay in collection of data between the moment the questionnaires are sent and the moment of completion.

Secondly, we include participants according to DSM-5 criteria while at the same time we use the SCID-I which is validated to assess the presence of an ED according to the DSM-IV. Because the SCID-I only covers AN, BN, and EDNOS-BED, skip rules were changed or omitted and parts of the *Eating Disorder Examination (EDE)* (Fairburn, Cooper, & O'Connor, 2008) were added in order to diagnose DSM-5 AN, BN, BED and OSFED. Although these adjustments have also been used in a recent epidemiological study, they (Smink et al., 2014) have not yet been validated.

Thirdly, the present study uses TAU as control condition; no alternative control conditions such as a no-treatment, waiting-list or placebo condition are included. This could be a limitation especially when we do not find a difference in outcome between the two active treatment conditions. When no difference in outcome will be found, it will be difficult to determine to what extent the effect of treatment has to be ascribed to non-specific factors, the effect of testing or the passage of time.

Fourthly, we designed our RCT as a superiority trial with enough statistical power to detect a difference in outcome between treatments (if present) with a medium effect size. However, it could be considered a limitation of the study that the power analysis was only based on detecting such difference in recovery rate because, with the therefore necessary 132 participants, only medium to large mediation effects can be tested with a power of 80% using bias-corrected bootstrapping procedures (Fritz & Mackinnon, 2007).

Fifthly, although we will determine treatment integrity, therapist competence in delivering the experimental intervention will not be assessed. However, because all participating CBT-E therapists will be trained in CBT-E, and will have treated at least three ED patients with CBT-E under supervision before entering the trial, a sufficient level of competence may be assumed.

Finally, the sample size is too small to allow subgroup analyses and consequently the possible differential effectiveness of CBT-E for AN, BN, BED, and EDNOS cannot be assessed. Moreover, the changes in thresholds for AN and BN in DSM-5, the addition of BED as a new official diagnosis, and the redefinition of the remaining EDs from the DSM-IV EDNOS category into two categories complicates investigations of the differential effectiveness of CBT-E for diagnostic subcategories.

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Chapter 6

Effectiveness of enhanced cognitive behavior therapy for eating disorders: a randomized controlled trial

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Abstract

Objective: Enhanced cognitive behavior therapy (CBT-E) is a transdiagnostic treatment suitable for the full range of eating disorders (EDs). Although the effectiveness of CBT(-E) is clear, it is not being used as widely in clinical practice as guidelines recommend. The aim of the present study was to compare the effectiveness of CBT-E with treatment as usual (TAU), which was largely based on CBT principles.

Method: We conducted a randomized controlled trial on a total of 143 adult patients with an ED who received either CBT-E or TAU. The primary outcome was recovery from the ED. Secondary outcome measures were levels of ED psychopathology, anxiety and depressive symptoms. Self-esteem, perfectionism and interpersonal problems were repeatedly measured to examine possible moderating effects. We explored differences in duration and intensity between conditions.

Results: After 80 weeks, there were no differences between conditions in decrease in ED psychopathology, or symptoms of anxiety and depression. However, in the first six weeks of treatment there was a larger decrease in ED psychopathology in the CBT-E condition. Moreover, when the internationally most widely used definition of recovery was applied, the recovery rate at 20 weeks of CBT-E was significantly higher (57.7%) than of TAU (36.0%). At 80 weeks , this difference was no longer significant (CBT-E 60.9%; TAU 43.6%). Furthermore, CBT-E was more effective in improving self-esteem and was also the less intensive and shorter treatment.

Discussion: With broader use of CBT-E, the efficiency, accessibility and effectivity (on self-esteem) of treatment for EDs could be improved.

Keywords

CBT-E, cognitive behavior therapy, eating disorders, RCT, transdiagnostic, treatment outcome

Introduction

Prevailing guidelines for the treatment of eating disorders (ED) endorse cognitive behavior therapy (CBT) as psychological treatment of first choice, especially for bulimia nervosa (BN) and binge eating disorder (BED) (Hay et al., 2014; Hilbert, Hoek, & Schmidt, 2017; National Institute for Health and Care Excellence (NICE), 2017; Yager et al., 2014). The effectiveness of CBT for anorexia nervosa (AN) is less pronounced, however this should be understood in the context of similar, somewhat disappointing, outcomes of other therapies for AN (van den Berg et al., 2019; Waller, 2016). CBT-Enhanced (CBT-E) is a specific form of CBT suitable for the full range of eating disorder diagnoses (Fairburn, 2008). It is based on a transdiagnostic theory of the maintaining mechanisms involved in the persistence of ED, which assumes that most mechanisms are common to all EDs, rather than being specific for one diagnostic category. According to this theory, a dysfunctional evaluation of self-worth, overly based on shape and weight, is central to all eating disorders (Fairburn, Cooper, & Shafran, 2003). The focused version of CBT-E (CBT-Ef) consists of interventions to modify this over-evaluation of shape and weight. The treatment protocol can be adjusted when additional maintaining mechanisms are expected to obstruct change (low self-esteem, clinical perfectionism, and interpersonal problems). This extended protocol is known as the 'broad' version of CBT-E (CBT-Eb). For both versions of CBT-E, two variants of intensity have been developed involving either 20 sessions in 20 weeks for patients who are not significantly underweight (body mass index (BMI) >17.5), or 40 sessions in 40 weeks for patients who are significantly underweight (BMI <17.5). On account of its transdiagnostic reach, CBT-E has an advantage over other CBT protocols for the otherwise specified feeding and eating disorder (OSFED). A systematic review in 2018 showed robust evidence for the effectiveness of CBT-E in adult patients with an ED, especially those with BN, BED and OSFED (de Jong, Schoorl, & Hoek, 2018).

Although there is clear evidence of the effectiveness of CBT(-E) for EDs, it is not being used as widely in clinical practice as guidelines recommend (Tobin, Banker, Weisberg, & Bowers, 2007; von Ranson & Robinson, 2006). In a 2018 Dutch study among 139 clinicians who delivered CBT for eating disorders, the use of specific CBT techniques was below the level one would expect if following treatment manuals (Mulkens, de Vos, de Graaff, & Waller, 2018). Moreover, there are no empirical data about the content, effectiveness and efficiency of treatments as usual (TAU). Independent ED experts in Belgium and the Netherlands have estimated that TAU for EDs is probably more

intensive, longer-term and less effective than CBT-E (de Jong et al., 2016). If time-limited CBT-E is indeed at least as effective as TAU for a broad range of ED patients, then the effectiveness, efficiency and accessibility of an evidence-based treatment for patients with an ED could be improved.

Therefore, the primary objective of this study was to assess whether the focused version of CBT-E for patients with an ED and a BMI >17.5 was more optimal in terms of a higher percentage of recovery compared to TAU. The secondary objectives were to assess whether CBT-E was more effective in reducing important aspects of ED psychopathology, and comorbid symptoms of anxiety and depression. Although the effect of the focused version of CBT-E was assessed, according to the rationale of the broad version of CBT-E, participants with more self-esteem problems, perfectionism and interpersonal problems at baseline were expected to respond less on the focused version of CBT-E. Consequently, these variables were examined as possible moderating variables. Finally, to test the hypothesis that CBT-E is a less intensive and shorter treatment than TAU, possible differences in the duration and intensity between CBT-E and TAU were explored.

Method

Design

A multicenter randomized controlled trial (RCT) was conducted at three specialized eating disorder treatment centers in three different regions in the Netherlands. Participants were randomized into two groups (CBT-E vs. TAU), stratified by type of ED (AN, BN, BED, OSFED), gender (male/female), BMI range (17.5-20, 20-25, 25-30, 30-40), and psychotropic medication (yes/no). They were all assessed pre-treatment (T0) and at 6 weeks (T1), 20 weeks (T2), 40 weeks (T3) and 80 weeks (T4), resulting in a 2 (treatment) × 5 (time) repeated measures factorial design. Given the nature of the psychological treatment, neither the therapists nor participants were blinded for the treatment given. Ethical approval was obtained from the Institutional Review Board of Leiden University Medical Centre (NL39205.058.12). The trial was also registered in the Netherlands Trial Register (NTR4485). For details of the rationale, design, methods and procedure, we refer to De Jong et al. (2016).

Recruitment

The patient sample (N = 143) was recruited at three specialized departments for eating disorders: PsyQ/Parnassia Psychiatric Institute in The Hague,

PsyQ/Lentis Psychiatric Institute in Groningen, and Rintveld/Altrecht Mental Health Institute in Zeist. Figure 6.1 shows the CONSORT flow diagram. The inclusion criteria were: having an ED that required treatment (determined using SCID-I) (First, Spitzer, Gibbon, & Williams, 1996; van Groenestijn, Akkerhuis, Kupka, Schneider, & Nolen, 1998); aged 18 years or older; a BMI >17.5 and <40 (because of possible medical complications); and giving written informed consent after receiving a detailed description of the study. The exclusion criteria were: prior CBT-E or very similar treatment (N = 2); a co-existing general psychiatric disorder that precluded eating disorder-focused treatment (N = 9); medical instability or pregnancy (N = 5); intellectual disability (N = 0); insufficient command of the Dutch language to fill in the research questionnaires (N = 3); ongoing psychiatric treatment (except for antidepressant or attention deficit hyperactivity disorder medications) (N = 4) or not being able to attend the scheduled therapy sessions (N = 24).

Treatments

Enhanced cognitive behavior therapy (CBT-E)

CBT-E is psychological treatment of 20 sessions, preceded by one preparatory session and followed by one review session 20 weeks after treatment. The sessions were held twice a week for the first 4 weeks, weekly for the next 10 weeks, and then biweekly in the last 6 weeks. CBT-E is personalized to match the eating disorder psychopathology of the individual patient. In this study the focused version was used for patients with a BMI >17.5. Up to three additional sessions with significant others could be planned. A detailed manual in Dutch was developed based on the CBT-E protocol (Fairburn, 2008) and was used by the participating therapists.

Treatment as usual

Because there are no empirical data about TAU in the Netherlands, clinician teams were asked about the content, intensity and duration of their TAU. The usual treatment given at the participating locations was based on CBT principles, given individually or in a group and containing elements of existing CBT treatment protocols (Dingemans, 2005; Vanderlinden, Pieters, Probst, & Norré, 2011). Depending on the center's treatment policy, this varied from low-intensity care (weekly sessions) to high-intensity care, which consisted of several group sessions a day for 2-4 days per week, and sometimes supplemented with individual sessions for coexisting psychopathology. The duration of the treatment was variable. Quite often more than one discipline (psychologist, dietitian, psychiatrist) was involved in providing treatment. The type of treatment provided was registered.

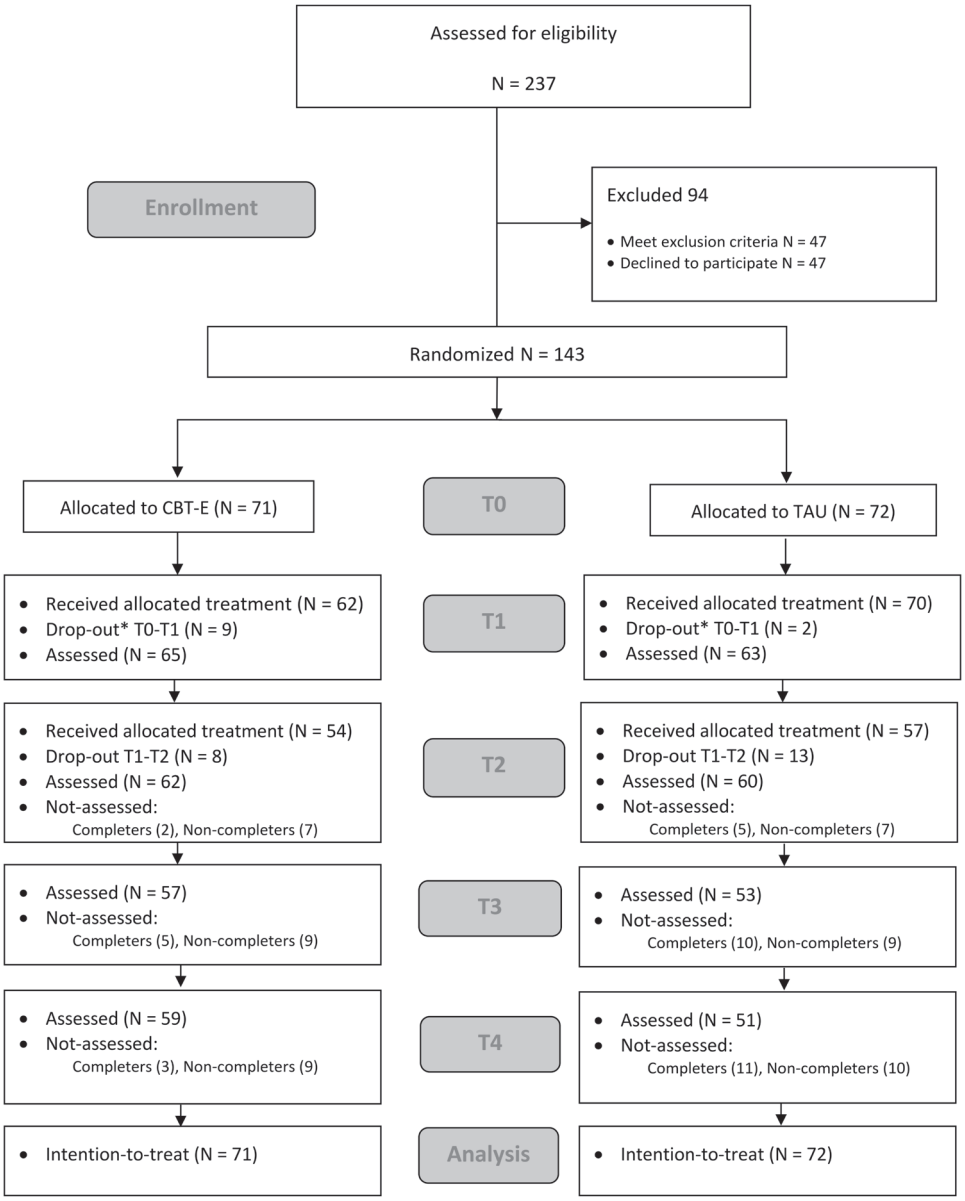

Figure 6.1. CONSORT Flow diagram

*Operationalization of drop-out differs between conditions

Therapists and treatment integrity

All the CBT-E therapists were psychologists, psychiatrists, registered nurses or social workers. They had at least two years of experience as a therapist in the field of EDs and had worked for at least two years according to CBT principles. CBT-E therapists in the participating centers were trained by the founder of CBT-E, Professor Christopher Fairburn, and had 20 supervision sessions via videoconferencing from his co-worker, Professor Zafra Cooper. All the CBT-E therapists treated at least three ED patients with CBT-E under supervision before entering the trial. All the TAU therapists were psychologists/psychiatrists or registered nurses/social workers who had at least two years of experience as therapists in the field of EDs. TAU therapists had regular (mostly weekly), standard, local collegial consultation led by experienced eating disorder clinicians.

The quality of delivery of CBT-E was assessed by independent raters (after an online CBT-E training) who listened to the recorded sessions. In general, two recorded sessions for every CBT-E patient were randomly selected (from, respectively, stages 1/2 and stages 3/4). The use of specific interventions according to the treatment manual was scored on several 3-point Likert scales reflecting phase-specific interventions and the use of interventions outside the scope of CBT-E. This resulted in a total score for treatment adherence (0-25%, 25-50%, 50-75%, 75-100%). Of 121 recorded sessions, 52 were double-rated to assess interrater reliability. For interrater reliability, Gwet's agreement coefficient (Gwet, 2008) with linear weights was calculated as an alternative to Cohen's Kappa for ordinal data (which is known to lead to paradoxical results when there is high agreement among raters) (Feinstein & Cicchetti, 1990; Warrens, 2010). There were five raters, one of whom was part of the rating pair on all occasions. This led to four rating pairs.

Assessment

Data was obtained via online questionnaires (using SurveyMonkey), with the exception of the SCID-I ED section, which was conducted by telephone.

Screening and primary treatment outcome

Structured Clinical Interview for DSM Axis-I Disorders (SCID-I). SCID-I (First et al., 1996; van Groenestijn et al., 1998) is a structured interview used to assess the presence of an ED. Because SCID-I only covers DSM-IV AN, BN and EDNOS-BED, skip rules were changed or omitted, and parts of the Eating Disorder Examination (EDE) (Fairburn, Cooper, & O'Connor, 2008) were added in order to diagnose DSM-5 AN, BN, BED and OSFED (Smink, van Hoeken, Oldehinkel, & Hoek, 2014).

Web Screening Questionnaire for common mental disorders (WSQ). The WSQ (Donker, van Straten, Marks, & Cuijpers, 2009) was used to screen for Axis-I disorders.

Secondary study parameters

The Eating Disorder Examination-Questionnaire (EDE-Q). The EDE-Q (van Furth, 2000) is a self-reported measure of ED psychopathology. Three outcome variables were created from the EDE-Q: (a) severity of ED features as measured by the mean EDE-Q item score (continuous), (b) a recovery rate defined as a global EDE-Q score <1 standard deviation (SD) above community mean (categorical) (an internationally often used measure (Dalle Grave, Calugi, Sartirana, & Fairburn, 2015; Wade, Byrne, & Allen, 2017)), i.e. ≤2.77 (Mond, Hay, Rodgers, & Owen, 2006), (c) a global EDE-Q score ≤2.77 + the reliable change index using Jacobson and Truax's method (Jacobson & Truax, 1991) assuming a test-retest correlation of .76 (Reas, Grilo, & Masheb, 2006). A change greater than 1.41 was considered as reliable change.

Mood and Anxiety Symptom Questionnaire (MASQ). The MASQ (de Beurs, van Hemert, & Goekoop, 1991) was used to assess the severity of symptoms of anxiety and depression.

Treatment duration. To measure treatment intensity and duration, treatment minutes (registered by the therapists) of every participant were collected between T0-T1, T1-T2 and T2-T3.

Moderating variables

The *Rosenberg Self-Esteem Scale (RSE)* (Rosenberg, 1965) is a widely-used instrument used to assess global self-esteem. A higher score refers to a better self-esteem; the *Frost Multidimensional Perfectionism Scale (FMPS)* (Frost, Heimberg, Holt, Mattia, & Neubauer, 1993) was used to assess perfectionism, and the *Inventory of Interpersonal Problems (IIP-32)* (Barkham, Hardy, & Startup, 1996) was used to measure interpersonal problems.

Power and sample size

In order to detect an absolute difference in recovery rates from ED of 25% (CBT-E: 50% versus TAU: 25%), a sample size of 66 patients per treatment condition was required to provide 80% power at two-sided p <0.05 (intention-to-treat analysis). This means that at least 132 patients were needed for this study.

Randomization

Randomization took place after screening of the inclusion/exclusion criteria and signing of the informed consent. Stratified randomization was achieved by generating a separate block for each combination of covariates (i.e., type of ED, gender, BMI range, and use of psychotropic medication) and assigning participants to the appropriate block of covariates. After the research assistant has allocated a participant to one of the strata, participants were assigned to CBT-E or TAU using a permuted block randomization list, based on a computer generated outcome, blinded to the research assistant until the allocation to one of the strata.

Statistical methods

Pre-treatment differences between conditions and between participants who completed the intended treatment and those who did not, were analyzed using *t* tests and Pearson's chi-squared tests or Fisher's exact tests (if necessary).

Intention-to-treat analysis

Primarily, generalized estimating equations (GEE) were used to analyze the repeated measurement data for the presence of an eating disorder (SCID-I) at T0, T2 and T4. The model consisted of main effects for time and type of treatment, as well as their interaction. Linear mixed models were used to analyze the repeated measurement data for eating disorder psychopathology (EDE-Q), interpersonal problems (IIP-32), perfectionism (FMPS), self-esteem (RSE), lack of positive affect, somatic arousal, and negative affect at all five time points. The fixed part of each model consisted of main effects for treatment and time, as well as their interaction. Time was included in the analyses as a categorical variable, with the baseline measurement as reference category. The random part of each model contained a random intercept and a random slope for time, which were assumed to be correlated. For SCID-I and EDE-Q, it was investigated whether there was any difference in time effect between the three treatment locations, by incorporating a fixed effect for location and an interaction between location and time. Restricted maximum likelihood estimation was used in all mixed models. When an overall F test indicated the presence of a significant *time x treatment* interaction, fixed effects were reported for all parameters.

Mixed models were used to investigate the possible moderation of RSE, FMPS and IIP-32 baseline scores on the *time x treatment* interaction in the analysis concerning EDE-Q, by including an interaction between the already present *time x treatment* interaction and RSE, FMPS and IIP-32, respectively.

Per protocol analysis

In an ITT analysis the effect of being assigned to a specific treatment is estimated, irrespective of whether or not participants started or completed the treatment. To estimate the true effect of the experimental condition taking into account effects of non-adherence, a per-protocol (PP) analysis was conducted (Oncioiu et al., 2017). For the PP analysis, not receiving CBT-E as intended was defined as premature termination of treatment (i.e. patient had received less than 70% of the allocated treatment, <14 of the 20 sessions), or when additional treatment for the ED or comorbid psychopathology was provided. As there was no manualized protocol for TAU as control group, not receiving TAU as intended was defined as termination of the indicated treatment before T2, either against the therapist's advice or when participants were transferred to another department before T2 for another treatment as originally intended. GEE and mixed models were repeated for participants who completed the intended treatment and only findings that deviated from previous findings in the intention-to-treat analyses will be reported. Subsequently, group differences in recovery rates (based on SCID-I diagnosis, EDE-Q ≤2.77 and EDE-Q ≤2.77 + reliable change index (Jacobson & Truax, 1991)) were analyzed at 20 and 80 weeks using Pearson's chi-squared tests. Analyses regarding recovery (based on the EDE-Q) were repeated, after omitting participants with scores below the cut-off at baseline (EDE-Q ≤2.77). Differences between conditions in treatment intensity (T0-T1, T1-T2, T2-T3 and T0-T3) were analyzed using Mann-Whitney *U* test.

Results

Patient sample

A total of 143 participants were enrolled from three Dutch mental health centers between 2013 and 2016 (89 from PsyQ/Parnassia Psychiatric Institute in The Hague, 34 from PsyQ/Lentis Psychiatric Institute in Groningen, and 20 from Rintveld/Altrecht Mental Health Institute in Zeist). Their diagnoses were as followed: 13 AN; BMI range 17.1-19.0 (9.1%), 50 BN; BMI range 18.8-39.3 (35%), 38 BED; BMI range 20.1-41.2 (26.6%) and 42 OSFED; BMI range 18.4-38.7 (29.4%). 71 were randomized to CBT-E and 72 to TAU. Except for age ($t(133.83) = -2.11$, $p = .04$, $d = 0.35$), there were no significant differences in relevant baseline variables between the two treatment conditions and between the three locations. The demographic characteristics of the sample are summarized in Table 6.1. Given the recovery cut-off for the EDE-Q (Mond et al., 2006), there were nine participants with scores below the cut-off at baseline in the total sample of the TAU group, and seven in the CBT-E group.

Treatment integrity

Due to a malfunctioning voice recorder, 8% of the recorded interview sessions were missing. According to the nomenclature proposed by Landis and Koch (1977), the interrater reliability was fair for the first couple (AC_2 = .36), and almost perfect for the second and third couples (AC_2 = .83 respectively .86). For the fourth couple, there was an absolute agreement on all ratings, which meant we could not calculate Gwet's AC (theoretically, however, this AC was 1.00). 93% of the recorded sessions were scored in the highest rating range (75-100%), indicating there was good delivery of CBT-E.

Table 6.1. Baseline characteristics of the patient sample

	CBT-E (N = 71)		TAU (N = 72)	
	M	***SD***	***M***	***SD***
Age (years)	28.9	8.6	26.2	6.9
Duration of eating disorder in years (N = 123)	9.2	8.5	7.7	6.3
BMI	26.3	7.0	25.6	6.7
EDE-Q global score	4.1	1.0	4.0	1.1
FMPS	86.5	22.2	83.1	22.2
IIP-32	1.5	0.6	1.3	0.6
RSES	22.3	5.1	23.6	5.2
MASQ-PA	2.4	0.7	2.3	0.7
MASQ-SA	1.8	0.6	1.9	0.7
MASQ-NA	2.7	0.8	2.8	0.8
WSQ	3.8	2.2	3.4	2.1
	N	***%***	***N***	***%***
Female	69	97.2	68	94.4
Currently in a relationship	32	45.1	31	43.1
Children	16	22.5	11	15.3
Live with parents	11	15.5	10	13.9
Anorexia nervosa	5	7.0	8	11.1
Bulimia nervosa	27	38.0	23	31.9
Binge-eating disorder	18	25.4	20	27.8
Other specified feeding and eating disorders	21	29.6	21	29.2
Binges (during the past 28 days)	51	71.8	53	73.6
Purging (during the past 28 days)	30	42.2	28	38.9

CBT-E = cognitive behavior therapy enhanced, EDE-Q = Eating Disorder Examination-Questionnaire, F-MPS = Frost Multidimensional Perfectionism Scale, IIP-32 = Inventory of Interpersonal Problems, MASQ = Mood and Anxiety Questionnaire, NA = negative affect, PA = positive affect, RSE = Rosenberg Self-Esteem Scale, SA = somatic anxiety, TAU = treatment as usual, WSQ = Web Screening Questionnaire for common mental disorders

Characteristics of TAU

The type of treatment provided in TAU was registered (see Table 6.2). All treatments were based on CBT principles (i.e., registrations, cognitive techniques and behavioral experiments). However, there was a great variety in interventions, intensity, duration, setting and treatment of comorbidity.

TAU differed from CBT-E in two specific ways: (a) the content of the group treatments in TAU was based on CBT principles for specific diagnoses (for example; BN group or BED group) as opposed to CBT-E that is a (individual) transdiagnostic treatment. (b) the content of individual treatments in TAU is best described as more freely applied CBT compared to manual based CBT-E.

In addition to CBT for eating disorder psychopathology, a variety of additional interventions were integrated in TAU, including; nutritional interventions and psychomotor therapy (i.e. body awareness, emotion regulation). Furthermore, 29 % of the treatments in TAU included interventions for comorbid psychopathology (i.e., EMDR for post-traumatic stress disorder, CBT for depression and schema therapy for personality disorder). In most treatments (85%) more than one discipline was involved.

Differences between participants treated as intended vs not treated as intended

In the CBT-E group 17 participants (24%) did not complete treatment as intended; in the TAU group this involved 15 participants (21%). The 32 participants who were not treated as intended did not differ from the 111 patients who completed treatment in their baseline measurements on the EDE-Q, RSE, FMPS and IIP-32, their SCID diagnosis, treatment location or treatment condition (results available on request).

Table 6.2. Characteristics of treatment as usual (TAU) groups

Location (N)	CBT	Group therapy	Individual therapy	Combination therapy [a]	≥2 disciplines involved [b]	With treatment for comorbidity [c]
The Hague (43)	43	8	24	11	40	14
Groningen (19)	19	5	5	9	11	5
Zeist (10)	10	2	4	4	10	2
Total	72 (100%)	15 (21%)	33 (46%)	24 (33%)	61 (85%)	21 (29%)

[a] Combination of group and individual therapies
[b] For example, dietician, psychologist, psychiatrist, psychomotor therapist
[c] including ADHD, depression, personality disorder, PTSS

Intention-to-treat analysis

There was no significant interaction between group and time regarding recovery from SCID diagnosis (OR = 1.01, 95% CI [0.81, 1.26]). However, there was a main effect for time (OR = 2.33, 95% CI [1.98, 2.74]). Treatment locations did not differ in the overall presence of SCID diagnoses, nor was there an interaction with the time variable. Estimates and confidence intervals for this analysis are presented in Table S6.1 in the supplementary material.

For EDE-Q, there was a significant main effect for time ($F(4, 441) = 51.66$, $p < .001$) and a significant interaction between group and time ($F(4, 441) = 2.85$, $p = .02$). The fixed effects in Table 6.3 show that this effect is particularly significant between T0 and T1. There was no main effect for location ($F(2, 139) = 0.98$, $p = .38$), nor an interaction effect between time and location ($F(8, 433) = 1.06$, $p = .39$). The left panel of Figure 6.2 show the development of EDE-Q scores over time for both groups. Parameter estimates for fixed effects can be found in Table 6.3.

For RSE, a main effect was present for time ($F(4, 452) = 20.14$, $p < .001$) as well as a group x time interaction ($F(4, 452) = 2.49$, $p = .04$). Fixed effects are presented in Table 6.3. In general, RSE showed a positive trend over time, and CBT-E showed it had an extra time effect on self-esteem. The development of RSE scores over time for both groups are depicted in the right panel of Figure 6.2, and parameter estimates are reported in Table 6.3.

For FMPS, only a significant main effect for time was found ($F(4, 446) = 5.03$, $p < .001$), but no significant *group x time* interaction ($F(4, 446) = 1.71$, $p = .15$).

For IIP-32, significant main effects were found for time ($F(4, 445) = 13.17$, $p < .001$) and group ($F(1, 141) = 4.19$, $p = .04$), but no *group x time* interaction ($F(4, 445) = 1.73$, $p = .14$).

For the MASQ, there was a main effect for time regarding negative affect ($F(4, 456) = 17.57$, $p < .001$), positive affect ($F(4, 456) = 13.30$, $p < .001$) and anxiety ($F(4, 456) = 11.84$, $p < .001$), but no *group x time* interactions were found for negative affect ($F(4, 456) = 0.34$, $p = .85$), positive affect ($F(4, 456) = 0.62$, $p = .65$) or anxiety ($F(4, 456) = 0.67$, $p = .61$). For all seven outcome measures, test statistics from the overall F tests are presented in Table S6.2 in the supplementary material.

Table 6.3. Fixed effects for mixed models with EDE-Q and RSE

	Estimate	*SE*	*df*	*t*	*p*
EDE-Q					
Intercept	4.07	0.12	441	33.23	<.001
Time					
6 weeks	-0.49	0.10	441	-5.00	<.001
20 weeks	-1.20	0.18	441	-6.68	<.001
40 weeks	-1.28	0.17	441	-7.49	<.001
80 weeks	-1.76	0.19	441	-9.24	<.001
Condition	0.06	0.17	141	0.36	0.72
Condition x Time					
6 weeks	-0.31	0.14	441	-2.22	0.03
20 weeks	-0.29	0.25	441	-1.18	0.24
40 weeks	-0.42	0.24	441	-1.77	0.08
80 weeks	0.11	0.26	441	0.43	0.67
RSE					
Intercept	23.57	0.61	452	38.64	<.001
Time					
6 weeks	0.41	0.47	452	0.88	0.38
20 weeks	1.70	0.61	452	2.79	0.01
40 weeks	2.37	0.80	452	2.94	<.001
80 weeks	3.73	0.84	452	4.43	<.001
Condition	-1.27	0.87	141	-1.47	0.14
Condition x Time					
6 weeks	1.64	0.66	452	2.48	0.01
20 weeks	2.30	0.86	452	2.69	0.01
40 weeks	2.36	1.12	452	2.10	0.04
80 weeks	2.29	1.15	452	1.99	0.048

EDE-Q = Eating Disorder Examination Questionnaire, RSE = Rosenberg Self-Esteem Scale, Condition = CBT-E (cognitive behavior therapy enhanced)

Per protocol analysis

The recovery rates at 20 weeks (end of CBT-E) and 80 weeks, as measured with the SCID were comparable for both treatment conditions (see Table 6.4). When using the international EDE-Q recovery norm (global sore ≤1 SD above community mean; i.e., ≤2.77, and EDE-Q≤2.77 + RCI), the post-treatment recovery rates for CBT-E at 20 weeks (57.7% and 46.2%) were significantly higher than that for TAU (36.0% and 26.0%). However, at 80 weeks this difference was no longer significant.

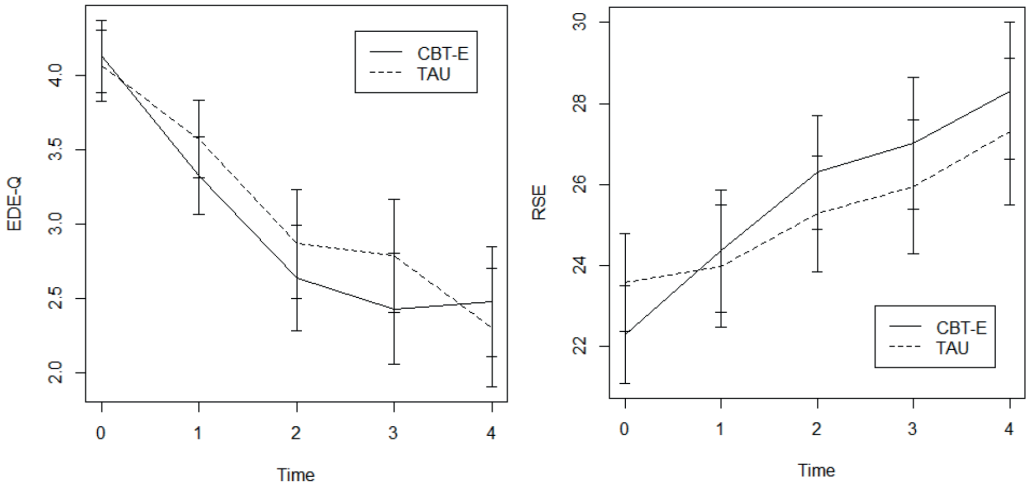

Figure 6.2. EDE-Q and RSE scores for the CBT-E and TAU groups
CBT-E = cognitive behavior therapy enhanced, EDE-Q = Eating Disorder Examination Questionnaire, RSE = Rosenberg Self-Esteem Scale, TAU = treatment as usual

For IIP, the main effect for treatment was non-significant ($F(1, 109) = 1.69$, $p = .20$), but the *time x treatment* effect became significant ($F(4, 381) = 3.29$, $p = .01$). CBT-E shows an extra decline at 20 and 40 weeks compared to TAU. The overall F test statistics and fixed effects for IIP in the per protocol analysis are presented in the supplementary material, respectively in Tables S6.3 and S6.4.

Moderators

The *time x treatment* interaction for EDE-Q global was moderated by the RSE baseline score ($F(4, 433) = 2.56$, $p = .04$). Between baseline and 6 weeks, participants receiving CBT-E reported an additional decrease in EDE-Q scores, when the RSE baseline score was higher. Overall *F* test statistics and fixed effects for this moderator analysis are presented in Tables S6.5 and S6.6 in the supplementary material.

Treatment intensity

Significant differences in treatment intensity between T0–T1 and T2–T3 were found. Between T0 and T1, CBT-E was more intensive (Mann-Whitney: $p < .001$), while between T2–T3 TAU consisted of more treatment minutes (Mann-Whitney: $p < .001$). Overall, between T0–T3, CBT-E appeared a significantly less intensive treatment than TAU (Mann-Whitney: $p = 0.01$) (see Table 6.5 and Figure S6.1 in the supplementary material).

Discussion

The first two aims in this study were to compare the focused version of CBT-E with TAU for patients with an ED (BMI >17.5) in terms of differences in recovery from the ED, and reduction of important aspects of ED psychopathology and comorbid symptoms of anxiety and depression. Systematic registration of TAU showed that all these treatments were based on CBT principles, however with a great variation in interventions, setting, treatment intensity, number of involved disciplines, and treatment of co-morbidity. After 80 weeks, there were no differences between conditions in recovery from the ED, or in decrease in global ED psychopathology and comorbid symptoms of anxiety and depression. However, significant differences in effect were found in the first six weeks of treatment, with the CBT-E condition showing a larger decrease in ED psychopathology. Moreover, when the internationally most widely used definition of recovery was applied, the recovery rate at 20 weeks of CBT-E was significantly higher (57.7%) than of TAU (36.0%). At 80 weeks (60 weeks follow-up for the CBT-E condition), this difference was no longer significant (CBT-E 60.9%; TAU 43.6%). Compared to other RCTs examining CBT-E with similar transdiagnostic samples (Fairburn et al., 2015; Fairburn et al., 2009) these recovery results are slightly lower, although the differences are small and direct comparisons are complicated by differences in study characteristics, instruments and data analysis. Furthermore, 24% of the participants in the present study did not complete CBTE as intended which is comparable to the Fairburn et al. study (2009) with a drop-out rate of 22.1%. CBT-E for non-underweight patients with an ED is known to be more efficacious than interpersonal psychotherapy (Fairburn et al., 2015) and psychoanalytic therapy (Poulsen et al., 2014) in terms of a faster treatment response. This is the first study showing that CBT-E also reaches these results faster than a less formal protocol of CBT (i.e. TAU). Although in this study therapists' considerations and exact treatment interventions (in the TAU group) were not registered, earlier studies have shown that in clinical practice, the integrity of applying CBT techniques (even in CBT eating disorder therapies) is below the level one would expect if treatment manuals were followed (Mulkens et al., 2018; Waller, Stringer, & Meyer, 2012). Together with the clear focus of CBT-E on early behavioral change, it is likely that offering twice-weekly sessions at the start could explain the faster response to CBT-E in the first phase of treatment.

The third aim was to examine the possible moderating effects of self-esteem, perfectionism and interpersonal problems. No differences between conditions

Table 6.4. Participants treated as intended; rates at 20 and 80 weeks for CBT-E and TAU using three different definitions of recovery

	At 20 weeks						At 80 weeks					
	CBT-E		TAU		Test statistics		CBT-E		TAU		Test statistics	
	N	%	N	%	$\chi^2(1)$	p	N	%	N	%	$\chi^2(1)$	p
Including participants with scores below the cut-off at baseline												
Remitted (SCID)	22	42.3	17	32.7	1.03	0.31	32	64.0	23	50.0	1.92	0.17
EDE-Q ≤2.77	30	57.7	18	36.0	4.81	0.03	32	62.7	22	50.0	1.56	0.21
EDE-Q ≤2.77 & RCI	24	46.2	13	26.0	4.48	0.03	30	58.8	18	40.9	3.03	0.08
Excluding participants with scores below the cut-off at baseline												
Remitted (SCID)	22	42.3	17	32.7	1.03	0.31	32	64.0	23	50.0	1.92	0.17
EDE-Q ≤2.77	26	55.3	14	31.8	5.09	0.03	28	60.9	17	43.6	2.53	0.11
EDE-Q ≤2.77 & RCI	23	48.9	12	27.3	4.51	0.03	26	56.5	17	43.6	1.41	0.23

CBT-E = cognitive behavior therapy enhanced, TAU = treatment as usual
RCI (Reliable Change Index) was based on a test-retest correlation of .76 and baseline pooled SD of 1.037 for both groups. Bold face values are significant.

Table 6.5. Treatment intensity of participants treated as intended

	CBT-E		TAU	
	Mdn	IQR	Mdn	IQR
T0–T1[a]				
Treatment intensity (minutes)	560	148	270	255
T1–T2				
Treatment intensity (minutes)	587	143	630	822
T2–T3[a]				
Treatment intensity (minutes)	87	125	570	1100
Total (T0–T3)[a]				
Treatment intensity (minutes)	1272	249	1860	2280

CBT-E = cognitive behavior therapy enhanced, IQR = interquartile range, Mdn = Median, TAU = treatment as usual [a] Significant Mann-Whitney *U* test

were found on reduction of perfectionism or interpersonal problems, but CBT-E proved more effective in improving self-esteem than TAU. While it is often thought that amelioration of psychopathology symptoms during psychotherapy is associated with the enhancement of self-esteem (Fennell & Jenkins, 2004), the precise mechanisms underpinning these effects are not known (Linardon, Kothe, & Fuller-Tyszkiewicz, 2019). However, some potential explanations for the overall superior effect of CBT-E on self-esteem can be hypothesized. The main focus of CBT-E is to modify the over-evaluation of shape and weight by establishing self-worth based on other aspects (friends, work, hobbies, etc.). It is assumed that by enhancing attention to other domains of self-worth, self-esteem can be improved (Fairburn, 2008). Interestingly, the difference in effect on self-esteem was found to be largest in the first six weeks of treatment, which were not explicitly focused on modifying the over-evaluation of shape and weight. However, this first phase is intensive (twice-weekly sessions) and focuses mainly on understanding the processes that maintain the eating problems and on early behavioral change. This approach could also have secondary effects. For example, creating hope that change is possible, can enhance self-confidence and self-esteem (Fairburn, 2008).

Moreover, in the CBT-E condition, changes in ED psychopathology during the first six weeks of treatment, were moderated by self-esteem. When, at baseline, self-esteem problems were less severe, there was an additional effect of CBT-E on decreasing ED psychopathology in this first phase. This enhancing effect of self-esteem disappears from week 20 onwards. Changes in ED psychopathology were not moderated by the degree of perfectionism or interpersonal problems. This means that, in this study, we found no support for the hypothesis that more severe self-esteem problems, higher levels of perfectionism, or more interpersonal problems (the supposed additional maintaining mechanisms of ED) would obstruct long-term improvement and would therefore need extra attention in an extended protocol.

The last aim of this study was to explore possible differences in the duration and intensity of CBT-E and TAU. Although for non-underweight ED patients, the current standard is to administer around 20 sessions of CBT in 20 weeks, there are no studies that have mapped the duration and intensity of TAU. In general CBT-E was completed in 20 weeks and was significantly more intensive for the first six weeks of treatment, whereas TAU was significantly more intensive between 20 and 40 weeks of treatment. Overall (between start and 40 weeks of treatment) CBT-E was significantly less intensive, which can have a major effect on health care costs.

This study has several limitations. The SCID was conducted by the research assistant. She was not blind for condition or previous SCID outcome because the outcome of the SCID was necessary for randomisation and there was only one research assistant available. However, the EDE-Q could be administered by Survey Monkey which had the benefit of unbiased data collection. Although the content of TAU was registered, there was no detailed description. For example, the way self-esteem was addressed in TAU was unclear, which complicates interpretation of the differences in effect on self-esteem between the two conditions. Furthermore, therapists and patients may be more interested in the effect of an intervention delivered as intended rather than in the effect of the assigned intervention. The results of our PP analysis closely replicated the results of our ITT analysis. However, as there is no univocal definition of TAU, and therefore no manualized protocol for the control group, TAU as intended had to be defined somewhat different from CBT-E as intended with at least 14 sessions as a minimal requirement for attendance. Consequently, results have to be interpreted with caution. Moreover, because of the nature of the RCT, TAU was not limited in its duration. Therefore, we cannot draw any conclusions on the follow-up results of TAU. Lastly, this study was restricted to participants with a BMI >17.5. Although it included a small percentage of participants with AN, we cannot generalize these findings to patients with AN.

A recommendation can be made for future research: although this study strengthens the evidence on the effectiveness of CBT-E, little is known about the working mechanisms. Studies on these mechanisms in CBT-E could strengthen its theoretical foundations.

Conclusion

After 80 weeks CBT-E and TAU both have comparable effects on patients' recovery from an ED and show a decrease of ED psychopathology, however, we found CBT-E reaches these results faster and is superior in enhancing self-esteem with significantly fewer sessions and within a shorter time. With a broader implementation of CBT-E in clinical practice, the efficiency, accessibility and effectivity (on self-esteem) of treatment for patients with an ED could be improved.

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Supplementary Material

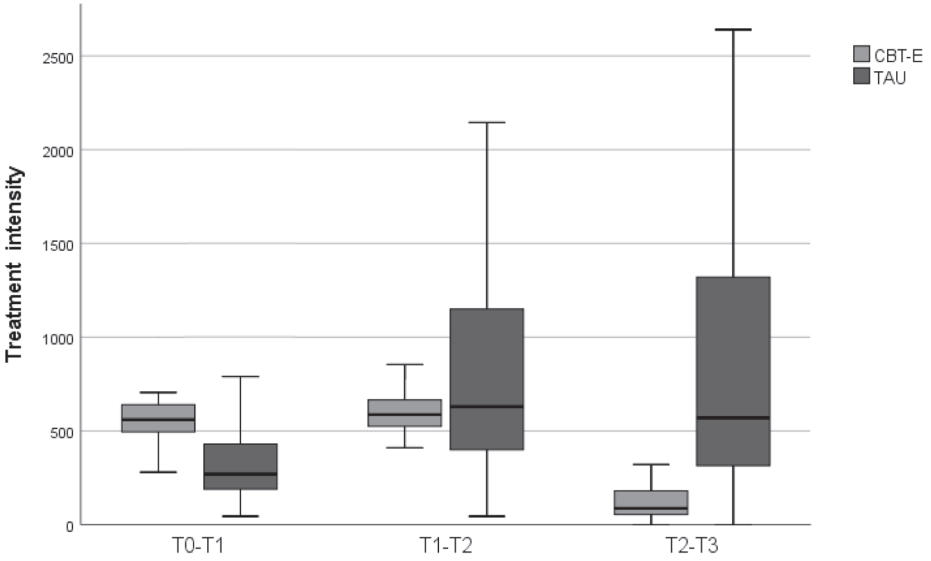

Figure s6.1. Box plots for treatment intensity in minutes for both conditions, between subsequent timepoints

Table s6.1. Estimates for Generalized Estimating Equations regarding SCID I diagnosis [a]

				95% CI	
	Estimate	***SE***	***Odds ratio***	***Upper***	***Lower***
(Intercept)	-3,08	0,29	0,05	0,03	0,08
Time	0,85	0,08	2,33	1,98	2,74
CBT-E	0,28	0,37	1,33	0,64	2,77
Time x CBT-E	0,01	0,11	1,01	0,81	1,26

CBT-E = cognitive behavior therapy enhanced, SCID I = Structured Clinical Interview for DSM Axis-I Disorders

[a] The Hague as reference category

Table s6.2. Overall F test statistics for model parameters in mixed models

	df1	*df2*	*F*	*p*
EDE-Q				
Intercept	1	441	2147,89	<.001
Time	4	441	51,66	<.001
CBT-E	1	141	0,02	0,90
Time x CBT-E	4	441	2,85	0,02
RSE				
Intercept	1	452	3660,84	<.001
Time	4	452	20,14	<.001
CBT-E	1	141	0,59	0,44
Time x CBT-E	4	452	2,49	0,04
F-MPS				
Intercept	1	446	2354,79	<.001
Time	4	446	5,03	0,001
CBT-E	1	141	0,00	0,99
Time x CBT-E	4	446	1,71	0,15
IIP-32				
Intercept	1	445	827,38	<.001
Time	4	445	13,17	<.001
CBT-E	1	141	4,19	0,04
Time x CBT-E	4	445	1,73	0,14
MASQ NA				
Intercept	1	456	664,84	<.001
Time	4	456	17,57	<.001
CBT-E	1	141	0,78	0,38
Time x CBT-E	4	456	0,34	0,85
MASQ PA				
Intercept	1	456	836,65	<.001
Time	4	456	13,30	<.001
CBT-E	1	141	1,97	0,16
Time x CBT-E	4	456	0,62	0,65
MASQ SA				
Intercept	1	456	214,56	<.001
Time	4	456	11,84	<.001
CBT-E	1	141	0,33	0,56
Time x CBT-E	4	456	0,67	0,61

CBT-E = cognitive behavior therapy enhanced,

EDE-Q = Eating Disorder Examination-Questionnaire,

RSE = Rosenberg Self-Esteem Scale,

F-MPS = Frost Multidimensional Perfectionism Scale,
IIP-32 = Inventory of Interpersonal Problems,
MASQ = Mood and Anxiety Symptom Questionnaire,
NA = negative affect, PA = positive affect, SA = somatic anxiety

Table s6.3. Overall F test statistics for model parameters in mixed model for IIP-32 in per protocol analyses

	df1	*df2*	*F*	*p*
Intercept	1	381	653,64	<.001
Time	4	381	12,86	<.001
CBT-E	1	109	1,69	0,20
Time x CBT-E	4	381	3,29	0,01

CBT-E = cognitive behavior therapy enhanced, IIP-32 = Inventory of Interpersonal Problems

Table s6.4. Fixed effects for mixed model with IIP-32 in per protocol analysis

	Estimate	***SE***	***df***	***t***	***p***
Intercept	1,24	0,08	381	16,17	<.001
Time					
6 weeks	-0,01	0,06	381	-0,13	0,89
20 weeks	-0,10	0,07	381	-1,45	0,15
40 weeks	-0,15	0,07	381	-2,31	0,02
80 weeks	-0,23	0,08	381	-2,75	0,01
CBT-E	0,20	0,11	109	1,78	0,08
CBT-E x Time					
6 weeks	-0,05	0,08	381	-0,63	0,53
20 weeks	-0,25	0,10	381	-2,56	0,01
40 weeks	-0,24	0,09	381	-2,56	0,01
80 weeks	-0,10	0,11	381	-0,86	0,39

CBT-E = cognitive behavior therapy enhanced, IIP-32 = Inventory of Interpersonal Problems

Table s6.5. Overall F test statistics for model parameters in mixed model for EDE-Q with baseline RSE as a moderator. Baseline RSE score was standardized

	df1	*df2*	*F*	*p*
Intercept	1	433	2895,82	<.001
Time	4	433	52,32	<.001
CBT-E	1	139	0,06	0,81
RSE baseline	1	139	46,97	<.001
Time x CBT-E	4	433	2,80	0,03
Time x RSE baseline	4	433	0,25	0,91
CBT-E x RSE baseline	1	139	0,34	0,56
Time x CBT-E x RSE baseline	4	433	2,56	0,04

CBT-E = cognitive behavior therapy enhanced,
EDE-Q = Eating Disorder Examination-Questionnaire,
RSE = Rosenberg Self-Esteem Scale

Table s6.6. Fixed effects in mixed model for EDE-Q with baseline RSE as a moderator. Baseline RSE score was standardized.

	Estimate	***SE***	***df***	***t***	***p***
Intercept	4,12	0,11	433	38,44	<.001
Time					
6 weeks	-0,51	0,10	433	-5,25	<.001
20 weeks	-1,23	0,18	433	-6,80	<.001
40 weeks	-1,29	0,17	433	-7,46	<.001
80 weeks	-1,78	0,20	433	-9,11	<.001
CBT-E	-0,05	0,15	139	-0,33	0,74
RSE Baseline	-0,60	0,10	139	-5,81	<.001
CBT-E x Time					
6 weeks	-0,31	0,14	433	-2,24	0,03
20 weeks	-0,27	0,25	433	-1,09	0,28
40 weeks	-0,41	0,24	433	-1,72	0,09
80 weeks	0,14	0,26	433	0,52	0,60
RSE Baseline x Time					
6 weeks	0,18	0,10	433	1,92	0,06
20 weeks	0,31	0,18	433	1,77	0,08
40 weeks	0,12	0,17	433	0,70	0,49
80 weeks	0,20	0,19	433	1,07	0,29
CBT-E x RSE Baseline	0,24	0,15	139	1,60	0,11
CBT-E x RSE Baseline x Time					
6 weeks	-0,32	0,14	433	-2,31	0,02
20 weeks	-0,38	0,25	433	-1,56	0,12
40 weeks	-0,02	0,24	433	-0,07	0,94
80 weeks	-0,25	0,27	433	-0,94	0,35

CBT-E = cognitive behavior therapy enhanced,
EDE-Q = Eating Disorder Examination-Questionnaire,
RSE = Rosenberg Self-Esteem Scale

Chapter 7

Summary and general discussion

Summary and general discussion

Eating disorders are severe mental disorders responsible for significant elevated mortality rates (Arcelus et al., 2011) and loss of quality of life (Jenkins et al., 2011). In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013) three specific eating disorders are specified: anorexia nervosa, bulimia nervosa and binge eating disorder. A large percentage of people with eating disorders, in both clinical and community samples, do not meet the full DSM-5 diagnostic criteria for these disorders and are diagnosed with 'otherwise specified feeding or eating disorder' (Keel et al., 2011; Machado, Goncalves, & Hoek, 2013; Smink, van Hoeken, & Hoek, 2013). Especially for bulimia nervosa and binge eating disorder there is strong empirical evidence for the effectiveness of cognitive behavioral therapy, more specifically cognitive behavioral therapy enhanced (CBT-E), a transdiagnostic treatment for eating disorders (Hay et al., 2014; Hilbert, Hoek, & Schmidt, 2017; National Institute for Health and Care Excellence (NICE), 2017; Netwerk Kwaliteitsontwikkeling GGz, 2017; Yager et al., 2014). This last mentioned treatment protocol has an advantage above other evidence-based eating disorder protocols because of its transdiagnostic reach and therefore its suitability for the treatment of all forms of eating disorders. There are two forms of CBT-E: a focused form (CBT-Ef) that targets eating disorder psychopathology exclusively (e.g. procedures directed at over-evaluation of shape and weight), and a more complex broad form (CBT-Eb) targeting additional maintaining mechanisms that are expected to obstruct change and improvement (low self-esteem, clinical perfectionism, and interpersonal problems). For both versions of CBT-E, two variants of intensity have been developed, involving either 20 sessions in 20 weeks for patients who are not significantly underweight (BMI >17.5), or 40 sessions in 40 weeks for patients who are significantly underweight (BMI ≤17.5).

Adherence of clinicians to empirically-based treatment protocols is rather poor and the content of eating disorder therapies varies greatly (Haas & Clopton, 2003; McAlpine et al., 2004; Mulkens et al., 2018; Mussell et al., 2000; Simmons, Milnes, & Anderson, 2008; Tobin et al., 2007; von Ranson & Robinson, 2006; Waller, Stringer, & Meyer, 2012). Therapists routinely use less well supported or non-evidence based approaches, however little is known about the exact content, effectiveness and efficiency of this "regular" eating disorder treatment, referred to as treatment as usual or TAU (Waller, 2016a). Independent eating disorder experts in Belgium and the

Netherlands have estimated that TAU for eating disorders is probably more intensive, longer-term and less effective than CBT-E (de Jong et al., 2016). If CBT-E indeed appears to be at least as effective as traditional diagnosis-specific treatments for a broad range of eating disorders patients, this unified transdiagnostic approach for all eating disorders would give the opportunity to offer treatment for a severe mental disorder with fewer resources and, therefore, increase the accessibility. Although CBT-E is considered an evidence-based treatment, RCTs that studied the effectiveness of CBT-E were mainly performed by the research group in Oxford that developed this intervention. To increase generalizability, there is a need for RCTs conducted independently from the original research group.

We performed an RCT in order to compare the effectiveness of the evidence-based treatment for eating disorders (CBT-Ef) with TAU. In relation to the content and application of TAU no specifications were made in advance, with the only provision that TAU should be performed by specialized eating disorder therapists. To gain understanding of the content of TAU and to allow for comparisons with CBT-Ef, several aspects of this treatment condition such as content, duration and intensity were monitored. Although the founder of CBT-E (Christopher Fairburn) and his colleague (Zafra Cooper) were involved in the training and supervision of the therapists that participated in the trial, they had no role in the design and implementation of the study.

Furthermore, identifying moderators of treatment outcome is crucial for identifying which treatments work best for whom and under what conditions. In the field of eating disorders, minimal research has been done toward testing moderators of treatment outcome in samples other than BED (Linardon, de la Piedad Garcia, & Brennan, 2017). As mentioned above, in the broad version of CBT-E, three additional maintaining mechanisms for severe eating disorders have been described (Fairburn, 2008). Patients with core low self-esteem, clinical perfectionism and interpersonal problems are expected to respond less on the focused version of CBT-E because these mechanisms obstruct change and improvement. Therefore, the possible moderating effects of these maintaining mechanisms for severe eating disorders were also studied.

As an important maintaining factor in severe eating disorder psychopathology and because of its association with the aetiology of eating disorders, self-esteem was an additional important topic of this thesis. The objective of one of the studies was to gain more insight in the relationship between explicit and implicit self-esteem and eating disorder psychopathology. Finally,

because competitive memory training (COMET) is described as a promising intervention (Korrelboom et al., 2009; Korrelboom, Maarsingh, & Huijbrechts, 2012; Korrelboom, Marissen, & van Assendelft, 2011; Olij et al., 2006; Staring et al., 2016; van der Gaag et al., 2012) specifically targeting low self-esteem as a relevant maintaining mechanism, we tested the effectiveness of COMET in an eating disorder population.

To summarize, the research presented in this thesis has a twofold focus; one on the effectiveness and efficiency of eating disorder treatment in general and one on the role of low self-esteem in the manifestation and treatment of eating disorders. In this discussion we will first summarize and reflect on our main findings. We will then describe the results in the broader context of the existing literature, followed by the strengths and limitations of our research, the recommendations for future research and the clinical implications of the findings.

Main findings

The study reported in **chapter two** examined whether explicit self-esteem, implicit self-esteem and the discrepancy between these two constructs – discrepant self-esteem – were associated with (the severity of) eating disorders. Although both explicit and implicit self-esteem were lower in patients with an eating disorder than in the comparison group, there was no unique contribution of implicit self-esteem in predicting eating disorder status. Moreover, only explicit self-esteem was a significant predictor for the severity of eating disorder psychopathology. The way discrepant self-esteem was related to eating disorder status depended on which operationalization of the concept and statistical method was used. Therefore, no conclusions were drawn regarding the relationship between discrepant self-esteem and eating disorder status.

In conclusion, especially low explicit self-esteem seems to be associated with eating disorder psychopathology.

Chapter three reported on the effectiveness of a cognitive behavioral intervention, competitive memory training (COMET), for the treatment of low self-esteem in patients with eating disorders. In this RCT patients were randomized to either eight weeks of COMET + treatment as usual (TAU) or

to eight weeks of only TAU. The results indicated that COMET as an add-on intervention to regular eating disorder therapy had a significant effect in enhancing self-esteem compared to TAU only.

COMET seemed to be an effective additional intervention for patients with eating disorders and low self-esteem.

The evidence for the effectiveness of CBT-E for patients with an eating disorder (BMI >17.5) was shown in a systematic review described in **chapter four;** it contains an update of the CBT-E effectiveness studies from January 2014 – March 2018. However, in this study a substantial range in remission rates between studies was found. We concluded that this was partly due to differences in study samples and the definition used for clinical significant change.

In the main study of this thesis we tested the effectiveness of the focused version of CBT-E compared to TAU in a large RCT in patients with eating disorders and a BMI >17.5. The study protocol of this trial was presented in **chapter five**. The results after 80 weeks, described in **chapter six**, showed no differences between conditions in decrease in eating disorder status, eating disorder psychopathology, symptoms of anxiety and depression or reduction of perfectionism or interpersonal problems. However, in the first six weeks of treatment there was a larger decrease in eating disorder psychopathology in the CBT-Ef condition. Moreover, when the internationally most widely used definition of recovery was applied, the recovery rate at 20 weeks of CBT-Ef was significantly higher than of TAU. At 80 weeks, this difference was no longer significant. Furthermore, at all time points CBT-Ef was more effective in improving self-esteem and was the less intensive and shorter treatment.

In the CBT-Ef condition, changes in eating disorder psychopathology during the first six weeks of treatment were moderated by self-esteem. When, at baseline, self-esteem problems were less severe, there was an additional effect of CBT-Ef on decreasing eating disorder psychopathology in this first phase. This enhancing effect of self-esteem disappears from week 20 onwards. Changes in eating disorder psychopathology were not moderated by the degree of perfectionism or interpersonal problems.

Effectiveness of CBT-E in the context of existing literature

The outcome of our RCT on CBT-Ef added relevant information to the existing literature on the effectiveness of CBT-Ef for patients with an eating disorder and a BMI >17.5. CBT-Ef is already considered an evidence-based treatment for eating disorders, moreover the current study provided information that increases generalizability of CBT-Ef to other treatment settings and populations. Compared to other RCTs examining CBT-E with similar transdiagnostic samples (Fairburn et al., 2015; Fairburn et al., 2009), the recovery results regarding eating disorder psychopathology (Table 7.1) were slightly lower, although the differences were small and comparisons are complicated by differences in study characteristics, instruments and data analysis.

Table 7.1. Recovery rates completers from three studies with comparable transdiagnostic samples

	Recovery rates 20 weeks	Recovery rates 60 weeks follow up
Fairburn et al., 2009	66.4%	50%[a]
Fairburn et al., 2015	75%	70%
De Jong et al., 2020	57.7%	60.9%

[a] Recovery rate overall sample

Furthermore, the results of our study showed that CBT-Ef reaches treatment results faster than a less formal protocol of CBT (i.e. TAU). The clear focus of CBT-E on early behavioral change together with the twice-weekly sessions at the start of CBTE could explain the faster response in the first phase of treatment.

On all time points (after 6, 20, 40 and 80 weeks) CBT-Ef proved more effective in improving self-esteem than TAU. Initially this seemed to be an unexpected result because the focused version of CBT-E does not aim directly on enhancing self-esteem. However, some potential explanations for the overall superior effect of CBT-Ef on self-esteem can be hypothesized. The main focus of CBT-Ef is to modify the over-evaluation of shape and weight by establishing self-worth based on other aspects (friends, work, hobbies, etc.). It is assumed that by enhancing attention to other potential sources of self-worth, self-esteem can be improved (Fairburn, 2008). Interestingly, the difference in effect on self-esteem was found to be largest in the first six weeks of treatment, a treatment phase which is not explicitly focused on

modifying the over-evaluation of shape and weight. However, this first phase is intensive (twice-weekly sessions) and focuses mainly on understanding the processes that maintain the eating problems and on early behavioral change. This approach could also have secondary effects. For example, creating hope that change is possible, can enhance self-confidence and self-esteem (Fairburn, 2008).

We found no support for the hypothesis that more severe self-esteem problems, higher levels of perfectionism, or more interpersonal problems would obstruct long-term improvement and would therefore need extra attention in an extended protocol. Minimal research has been done toward testing moderators in eating disorders samples and the existing publications suggest that we have limited ability to match manualized CBT to individual profiles (Linardon et al., 2017). One exception is a study where the focused version (in this study without the module mood intolerance) of CBT-E was compared to the broad version for patients with bulimia nervosa and comorbid borderline personality disorder (Thompson-Brenner et al., 2016). Overall the outcome suggested that the focused version of CBT-E was associated with better eating disorder outcome, however the severity of affective and interpersonal problems moderated treatment outcome. Participants with higher severity of affective and interpersonal problems showed better eating disorder outcomes in the broad version of CBT-E, whereas those with lower severity showed better outcomes in the focused version of CBT-E.

Outcome self-esteem studies in the context of existing literature

The importance of self-esteem in eating disorders has been demonstrated in numerous previous studies, with low self-esteem being strongly associated with the severity of eating disorder pathology, psychotherapy dropout, poor treatment response, symptom persistence, and long-term relapse (Cockerham et al., 2009; Collin et al., 2016; Halmi et al., 2005; La Mela et al., 2013; Linardon et al., 2017; Masheb & Grilo, 2008; Sassaroli, Gallucci, & Ruggiero, 2008; Vall & Wade, 2015; Wilson et al., 2010). However, most studies on self-esteem and eating disorders focused mainly on the role of explicit self-esteem in eating disorders. The association between explicit self-esteem and eating disorder psychopathology was confirmed in this thesis. Furthermore, we found that implicit self-esteem was significantly lower in an eating disorder population than in the comparison group. This finding is in line with most recent studies of implicit self-esteem in relation to psychopathology: when an association was found, lower implicit self-esteem was related to more psychopathology (Franck et al., 2007; Glashouwer et

al., 2013; Risch et al., 2010; Ritter et al., 2013). In our study, however, when explicit and implicit self-esteem were investigated jointly, only explicit self-esteem remained a significant predictor of eating disorder status. The less robust association of implicit self-esteem with eating disorder psychopathology could be related to characteristics of the measures used. The association of the self-report measures that were used to investigate explicit self-esteem and eating disorder psychopathology may be overinflated because of common-method variance or criterion contamination (as low self-esteem may express itself in e.g. a negative body image).

In particular, definitions and measures of implicit cognitive processes relative to explicit cognitive processes need further refinement and validation, both in their psychometric properties and in their specific applications to psychopathology (De Houwer et al., 2009; Fiedler, Messner, & Bluemke, 2006).

The study described in chapter three showed that COMET is an effective intervention for improvement of self-esteem, in addition to regular treatment for patients with eating disorders and low self-esteem. This is of particular relevance because, although low self-esteem is associated with the aetiology and persistence of eating disorders, at the start of this study no evidence-based treatment protocol was available to treat low self-esteem. Since then, COMET has been tested in various RCTs. It was found to be effective in reducing low self-esteem in patients with depression (Korrelboom et al., 2012), personality disorders (Korrelboom et al., 2011) and anxiety disorders (Staring et al., 2016). Together, the results yield strong evidence of the effectiveness of COMET in treating low self-esteem, irrespective of the nature of the mental disorder.

Self-esteem improvements after CBT-E and COMET

In the meta-analysis of Linardon et al. (2019) of the effects of psychotherapy for bulimia nervosa and binge eating disorder on self-esteem, some support was found for the beneficial effects of eating disorder therapy on self-esteem, although these effects were small. The authors suggest that most of the examined interventions did not directly target low self-esteem, possibly resulting in these relatively small effects. This raises the question if integrating additional therapeutic interventions designed to directly address low self-esteem into existing treatment protocols would result in larger improvements in self-esteem. In this thesis the effects of COMET (directly targeting low self-esteem) + TAU and CBT-Ef (not directly targeting low

self-esteem) on self-esteem were studied in two different trials. As this complicates comparisons, we calculated the within group effect size, using Cohen's *d* (Cohen, 1992), for both the effect of COMET and CBT-Ef on self-esteem in order to increase comparability between these studies. Although COMET did directly address low self-esteem, COMET and CBT-Ef led to similar (significant) improvements in self-esteem with comparable large within group effect sizes (Table 7.2). This is in line with the conclusion of Fairburn that for the majority of patients with eating disorders and self-esteem problems, the focused version of CBT-E will suffice (Fairburn et al., 2009) and no additional attention for self-esteem is needed. However, in contrast to the CBT-E study, participants in the COMET study were included after at least two months of eating disorder treatment and low self-esteem (as reported by the patients and their referring therapists and confirmed in an informal clinical interview by the researchers) was a specific inclusion criterion. As to be expected this difference in recruitment resulted in the inclusion of patients with more severe self-esteem problems in the COMET study (illustrated by a small difference in pre-treatment self-esteem scores on the RSES in Table 7.2 (Cohen's $d = 0.44$)). Only a direct comparison of CBT-Ef vs CBT-Ef + COMET can answer the question more specifically whether both treatments have a comparable effect on self-esteem and whether level of self-esteem moderates the effects of CBT-E and COMET.

Table 7.2. RSES means, standard deviations and effect sizes of COMET and CBT-E

	Pre-treatment		**Post-treatment**		
	M	***SD***	***M***	***SD***	**Effect size Cohen's *d***
COMET	20.0	5.2	23.6	5.5	0.80
CBT-Ef	22.3	5.1	26.6	6.0	0.86

RSES = Rosenberg Self-Esteem Scale; COMET = competitive memory training; CBT-Ef = cognitive behavior therapy enhanced focused version
Possible range 10-40. Higher scores are indicative of more positive self-esteem

Effectiveness, content and duration of TAU for eating disorders

To enhance understanding of the regular eating disorder treatment in routine clinical practice (TAU), the content, duration and intensity of this treatment condition was registered in the RCT described in chapter six where TAU and CBT-E were compared in terms of effectiveness and efficiency. All treatments in TAU showed to be based on CBT principles, however mostly not according to an evidence-based CBT protocol and with a great variation in interventions,

setting, treatment intensity, duration, number of involved disciplines, and treatment of comorbidity. These results support findings from earlier studies that indicate that the adherence of clinicians to evidence-based protocols is poor and the integrity of applying CBT techniques is below the level one would expect if treatment manuals were followed (Mulkens et al., 2018; Waller et al., 2012). Even when patients report that they have had CBT (as labelled by their therapist) for their eating disorder, probably few received an evidence-based version of CBT (Cowdrey & Waller, 2015). Clinicians report that they often use a mixture of (un-tested or un-supported) techniques (Tobin et al., 2007; von Ranson & Robinson, 2006). In the existing literature this phenomenon is referred to as "therapist drift" (Waller, 2009). A common belief among clinicians is that the results from research trials are not applicable to their patients, for example due to the idea that patients in research settings are carefully selected (e.g. exclude comorbidity) and not representative for the patients with more complex psychopathology who they see in routine clinical practice (Waller, 2016a). However, so far there was no evidence that an individual-centered approach is more effective than a standardized protocol-based approach. Although in this thesis we found (after 80 weeks) that TAU and CBT-E yield similar effects on reducing eating disorder psychopathology, CBT-E reached these results faster and was the less intensive and shorter treatment. This finding is in line with a recent published study about the implementation of CBT-E in a routine clinical setting (van den Berg et al., 2020). In this study CBT-E for adult eating disorder patients and a BMI>17.5 was found to be superior to TAU from a cost effectiveness perspective.

Strengths and limitations

The results of the research presented in this thesis should be considered in the light of several strengths and limitations.

As far as the CBT-E effectiveness studies are concerned, most RCTs were performed by the research group that developed the treatment protocol. In the CBT-E trial part of this thesis the founder of CBT-E and his colleague (Christopher Fairburn and Zafra Cooper) were only involved in the training and supervision of the therapists that participated in the trial, but had no role in the design and implementation of the study. This strengthens the generalizability of the results. Furthermore this study is the first study that provided information about the content, effectiveness and efficiency of the regular eating disorder treatment (TAU) in the Netherlands. The direct comparison between TAU and CBT-E gives important information about the differential effects between an individualized treatment approach and a

protocol based approach. This is of value in the dissemination of evidence-based interventions like CBT-E. Moreover, self-esteem, perfectionism and interpersonal problems, the supposed additional maintaining mechanisms for severe eating disorder psychopathology, have been examined as possible moderating variables in the effect of the focused version of CBT-E. Identification of these patient characteristics help to answer the question for whom the focused version of CBT-E is effective.

As far as the topic of self-esteem is involved, this thesis contains the first randomized controlled trial that evaluates COMET for the treatment of low self-esteem in patients with eating disorders. As an important maintaining factor in eating disorder psychopathology and because of its association with the aetiology of eating disorders, the search for an evidence-based intervention specifically aimed at the enhancement of self-esteem is of great value.

In this thesis we report about two RCTs. Both trials pertain to "real world" patients while few exclusion criteria were applied. The inclusion of this "real world" patients enhances the external validity of the findings because of the close resemblance to everyday practice, including patients with various eating disorders and comorbidities, thereby increasing the generalizability of the findings. Furthermore, to make sure that the investigated interventions in this thesis (COMET and CBT-E) were performed as intended, both RCTs were subject to a thorough check of treatment fidelity.

The studies included in this thesis had several limitations. An important limitation of both RCTs was the lack of information about if and how self-esteem was addressed in the TAU condition. Due to the lack of a step-to-step protocol in this condition, therapists were free to address low self-esteem whenever they considered this necessary and they could do this in the way they considered appropriate. This complicates interpretations of differences in effect on self-esteem between the two conditions. Furthermore in both trials no non-treatment condition and/or placebo condition was included. Not comparing what happens in similar participants facing similar conditions without getting treatment or getting a placebo, complicates attribution of changes to the effect of the investigated treatment. However, a trial with a no treatment or placebo condition in an eating disorder population would give ethical problems because of the serious risks of not treating an eating disorder.

In the CBT-E trial there was no univocal definition of TAU, and therefore no manualized protocol for the control group. Consequently TAU as intended had to be defined somewhat differently from CBT-E as intended. Therefore results had to be interpreted with caution. Moreover, no conclusions could be drawn on the follow-up results of TAU, because TAU was not limited in its duration.

Finally, although attention was given to treatment fidelity and treatment integrity was assessed in the trials, we did not include an existing validated instrument to measure therapist competence like the Revised Cognitive Therapy Scale (CTS-R; (Blackburn et al., 2001)).

Recommendations future research

Although this thesis strengthens the evidence on the effectiveness of CBT-Ef, little is known about its working mechanisms. A trial with a direct comparison between CBT-E and another evidence-based CBT protocol might help unravel the differential effects of CBT-E, and studies on the working mechanisms of CBT-E could strengthen its theoretical foundation.

The CBT-E RCT studied individual moderators or – in other words – single variables interacting with treatment type. Although common in the past two decades, this type of research rarely resulted in solid answers about which patient characteristics predict treatment response. This has led to a shift in research towards a more multivariate approach which can help to answer the question how information from multiple variables can be combined to offer meaningful treatment recommendations (DeRubeis, 2019). This is not only interesting in answering the question "which treatment works best for whom?" but also "which treatment technique within a treatment protocol is the most promising?" (Lutz et al., 2019). Although in this thesis (with a single variable approach) we did not find the predictive value of low self-esteem, perfectionism and interpersonal problems in CBT-Ef treatment outcome, a multivariable approach with a combination of these and other patient characteristics could lead to a more differentiated outcome. In these questions about treatment matching big data research and more specifically machine learning algorithms could allow predictions of clinical outcomes at the level of an individual patient or a subgroup of patients. This kind of approach could ultimately enable personalized treatment decisions and improve treatment response rates (Passos, Mwangi, & Kapczinski, 2016).

Results of the two RCTs presented in this thesis show positive effects on self-esteem improvement after both COMET (directly targeting low self-esteem) and CBT-Ef (not directly targeting low self-esteem) with similar effect sizes. However, the included eating disorder sample in the COMET study is characterized by lower self-esteem scores. It remains unclear if COMET has additional effects in improving self-esteem especially in patients with more severe self-esteem problems. Only a direct comparison of CBT-Ef vs CBT-Ef + COMET can answer the question whether both treatments have comparable effects on self-esteem and whether level of self-esteem moderates the effects of CBT-E and COMET.

To facilitate comparability between CBT-E studies, agreement should be reached concerning, for example definitions of clinical significant change, what level of competence is needed for a CBT-E therapist, what tool should be used to measure treatment integrity and what specifically constitutes "not completed" therapy.

Clinical implications

The results described in this thesis support the strong empirical evidence for the effectiveness of CBT-Ef for patients with an eating disorder and a BMI >17.5. When compared to TAU, we found comparable effects on eating disorder psychopathology, however CBT-Ef is superior in enhancing self-esteem with significantly fewer sessions and within a shorter time. We can conclude that a broader use of CBT-Ef in clinical practice could result in more efficient and accessible treatment for patients with an eating disorder. However, many studies that investigate the use and implementation of evidence-based treatments in routine clinical practice show that this is a major challenge. This is often referred to as the "research-practice" gap (Lilienfeld et al., 2013) resulting in supply of suboptimal treatments in clinical practice. Several reasons for clinicians not to adhere to evidence-based protocols are described in the literature. One of these reasons is that clinicians often are unaware of and untrained in evidence-based treatments (Waller, 2016a). Furthermore, while research showed that the therapeutic alliance does not drive change in behaviors in eating disorder therapies (Graves et al., 2017), non-delivery of CBT for eating disorders has been associated with clinicians' beliefs about the power and importance of the therapeutic alliance in achieving good therapy outcome (Mulkens et al., 2018). Moreover, clinicians report that evidence-based protocols are not applicable to their patients because of "more complex" psychopathology than addressed in clinical trials. Consequently they decide to use an individualized

mixture of techniques (Tobin et al., 2007; von Ranson & Robinson, 2006) and expect that this leads to better treatment outcome. However as mentioned above, in this thesis no superior effects of the more diverse, intensive and longer TAU condition was found. Furthermore, in contrast to what clinicians often think, we found no support for the hypothesis that more severe self-esteem problems, higher levels of perfectionism, or more interpersonal problems (the supposed additional maintaining mechanisms that indicate more complex eating disorder psychopathology) would obstruct long-term improvement in CBT-Ef and would therefore need extra attention.

This raises the question how eating disorder clinicians could be encouraged to use evidence-based methods also for the patients they consider "complex", for example because of the severity of the eating disorder or the presence of comorbid psychopathology? Having training and supervision can help therapists to be better equipped to deliver evidence-based treatments (Schoenwald & Garland, 2013; Wright & Waller, 2020). Moreover, providing the intervention in written form facilitates uniform and reliable training and supervision. Standard part of training should be an up-to-date overview about relevant research findings and teaching clinicians how research is essential and serves as a safeguard against pervasive biases (Lilienfeld et al., 2013). Furthermore, Shafran et al. (Shafran et al., 2009) suggest that ongoing supervision clearly improves treatment outcome. Patients can benefit if supervisors focus more on the implementation of protocols (Waller, 2016b). However, it is important that the supervisor has the necessary evidence-based knowledge and skills to be able to teach the supervisee to be adherent. Obviously not every patient will benefit from treatment (among which CBT-E), even when applied with rigour by highly experienced clinicians (Waller, 2009). It is of considerable relevance to identify this as early as possible in the therapy process. In CBT-E, Fairburn (Fairburn, 2008) describes the importance to be responsive to early indicators that the patient is not changing and taking stock, rather than waiting until the end to see if change has occurred. Advances in new technologies and software has led to the development of promising feedback systems to support clinicians to make these treatment considerations in a more systematic way (Lutz et al., 2019). With such feedback systems, actual treatment progress can be compared to the expected course of treatment and signals can be provided to the therapist in case of negative developments (Hooke et al., 2018). Additional clinical problem solving tools can provide suggestions about which treatment adaptations can be considered (Whipple et al., 2003). This gives clinicians the opportunity of a more empirical supported method to personalize treatment.

We did not find the predictive value of low self-esteem in CBT-Ef treatment outcome and CBT-Ef had a significant better effect on enhancing self-esteem than TAU. What does this mean for the need to integrate COMET as an additional intervention aimed at enhancing self-esteem in an eating disorder treatment? In the CBT-E trial, patients were not selected on the basis of low self-esteem (e.g. the more extreme group). In the COMET trial, where low self-esteem was an inclusion criterion, we found positive effects of COMET on enhancing self-esteem when compared to TAU. Until the outcome of a direct comparative study is available between CBT-E and CBT-E + COMET, we suggest using COMET as an additional intervention only when in phase two (taking stock) core low self-esteem is pronounced and appears to be maintaining the eating disorder and interferes with making progress.

Conclusion

This thesis strengthens the evidence of the effectiveness of the focused version of CBT-E for a broad range of patients with an eating disorder and a BMI>17.5. When compared to the regular eating disorder treatment, CBT-Ef is more effective in enhancing self-esteem, leads to a faster decrease in eating disorder psychopathology and is the less intensive and shorter treatment. Although recovery rates show that not every patient benefits from CBT-Ef, at this point research has not resulted in answers as to which patients benefit most from CBT-Ef and for which patients this treatment is less suitable.

In another study we found COMET to be effective in enhancing self-esteem in patients with an eating disorder. Since we did not find the predictive value of low self-esteem in CBT-E treatment outcome, we suggest to integrate COMET in an eating disorder treatment only when low self-esteem is pronounced and interferes with making progress. A multivariable approach in future big data research could be helpful in answering questions around more empirical-based treatment matching. With a broad implementation of CBT-Ef, the effectiveness, efficiency and accessibility of an eating disorder treatment in the Netherlands can be improved. Furthermore, training and ongoing supervision of eating disorder clinicians is important to enhance adherence of clinicians to evidence-based protocols like CBT-E. Advances of promising feedback systems can support clinicians to make more systematic treatment considerations and prevent "therapist drift".

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Abbreviations and measurements

AN	anorexia nervosa
BDI	Beck Depression Inventory
BED	binge eating disorder
BMI	body mass index
BN	bulimia nervosa
CBT	cognitive behavioral therapy
CBT-E	cognitive behavioral therapy – enhanced
CBT-Eb	cognitive behavioral therapy – enhanced broad
CBT-Ef	cognitive behavioral therapy – enhanced focused
COMET	competitive memory training
CTAM	Clinical Trials Assessment Test
DED	department of eating disorders
DSE	discrepant self-esteem
DSM	Diagnostic and Statistical Manual of Mental Disorders
ED	eating disorder
EDE	Eating Disorder Examination
EDE-Q	Eating Disorder Examination-Questionnaire
EDI-II	Eating Disorder Inventory-II
EDNOS	eating disorder not otherwise specified
EQ-5D	a measure of health status from the EuroQoL Group
ESE	explicit self-esteem
F-MPS	Frost Multidimensional Perfectionism Scale
IAT	Implicit Association Test
ICAT	integrative cognitive-affective therapy
IIP-32	Inventory of Interpersonal Problems
IPT	interpersonal psychotherapy
ISE	implicit self-esteem
MASQ	Mood and Anxiety Symptom Questionnaire
MINI	Mini-International Neuropsychiatric Interview
OSFED	other specified feeding or eating disorder
RCT	randomized controlled trial
RSE	Rosenberg Self-Esteem Scale
SCID-I	Structured Clinical Interview for DSM Axis I Disorders
SCL-90	Self-report Symptom Checklist-90
SCOFF	a screening tool for eating disorders
SF-36	Short Form Health Survey 36-item

SF-HLQ	Short Form – Health and Labour Questionnaire
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
TAU	treatment as usual
TiC-P	Trimbos/iMTA questionnaire for Costs associated with Psychiatric illness
USFED	unspecified feeding or eating disorder
WSQ	Web Screening Questionnaire for common mental disorders

Bijlagen

Nederlandse samenvatting

Inleiding

Eetstoornissen zijn ernstige psychiatrische aandoeningen die gekenmerkt worden door verstoringen in het eetgedrag en daaraan gerelateerde cognities en emoties. Mensen met een eetstoornis raken in beslag genomen door gedachten over voedsel en hun lichaamsvorm en gewicht. Daarnaast zijn eetstoornissen verantwoordelijk voor significant verhoogde sterftecijfers en verlies van kwaliteit van leven. Hoewel het hebben van een eetstoornis meest voorkomend is onder jonge vrouwen, kan het op elke leeftijd optreden, zowel bij vrouwen als bij mannen. In de DSM-5 worden drie specifieke eetstoornissen beschreven: anorexia nervosa, boulimia nervosa en de eetbuistoornis. Een groot percentage van de mensen met een eetstoornis, zowel in de klinische praktijk als in de algemene bevolking, voldoet niet aan de volledige diagnostische criteria van de DSM-5 voor deze aandoeningen en wordt gediagnosticeerd met een 'anders gespecificeerde voedings- of eetstoornis'.

Ten aanzien van de behandeling van boulimia nervosa en de eetbuistoornis is overtuigend bewijs voor de effectiviteit van cognitieve gedragstherapie meer specifiek CBT-E (cognitive behavior therapy- enhanced; Fairburn, 2008), een transdiagnostische behandeling geschikt voor alle eetstoornissen. Er bestaan twee vormen van CBT-E. Een gefocuste vorm (CBT-Ef) die zich met name richt op het behandelen van de eetpathologie waaronder een reeks aan interventies gericht op de beïnvloeding van de overwaardering van lichaamsvormen en gewicht. En daarnaast is er de uitgebreide vorm (CBT-Eb) die zich aanvullend richt op bijkomende factoren die de eetstoornis in stand houden zoals een extreem laag zelfbeeld, disfunctioneel perfectionisme en interpersoonlijke problemen. Voor beide vormen van CBT-E zijn er twee varianten; 20 sessies in 20 weken voor patiënten die geen extreem ondergewicht hebben (BMI>17.5) en een variant van 40 sessies in 40 weken voor patiënten met ondergewicht (BMI≤17.5).

Hoewel er voor boulimia nervosa en de eetbuistoornis meerdere effectief gebleken protocollen beschikbaar zijn, worden deze in de praktijk in veel gevallen niet door clinici gebruikt en zijn er grote verschillen in het behandelaanbod voor eetstoornis patiënten. Behandelaren gebruiken vaak minder of zelfs in het geheel niet empirisch onderbouwde behandelmethoden. Er is echter weinig bekend over de exacte inhoud, effectiviteit en efficiëntie van deze "reguliere" eetstoornis behandelingen (ook wel treatment as

usual of TAU genoemd). In een kleine informele enquête hebben een aantal eetstoornis experts uit België en Nederland die niet betrokken waren bij de onderzoeken uit dit proefschrift ingeschat dat deze "reguliere" behandelingen naar alle waarschijnlijkheid intensiever, langer durend en minder effectief zijn dan CBT-E. Een belangrijke doelstelling van dit proefschrift is om te onderzoeken of de gefocuste versie van CBT-E inderdaad op zijn minst even effectief, korter en minder intensief is dan TAU in de behandeling van eetstoornissen. Wanneer deze hypothese bevestigd wordt, kan een brede implementatie van deze transdiagnostische relatief korte behandelmethode leiden tot kortere wachtlijsten en verbetering van de toegankelijkheid van zorg voor eetstoornis patiënten. Daarnaast zijn de reeds eerder uitgevoerde gerandomiseerde studies naar het effect van CBT-E met name gedaan door de onderzoeksgroep vanuit Oxford die deze behandelmethode ontwikkeld heeft. Een onafhankelijke replicatie studie kan de generaliseerbaarheid van de resultaten vergroten.

Om een directe vergelijking te kunnen maken tussen de effecten van CBT-Ef en TAU voor eetstoornis patiënten hebben we een gerandomiseerde studie (RCT) uitgevoerd. Daarbij werden de inhoud, duur en intensiteit van TAU zorgvuldig gemonitord. Om de kwaliteit van CBT-Ef te borgen werden de grondlegger van CBT-E (Christopher Fairburn) en zijn collega (Zafra Cooper) gevraagd de betrokken behandelaren te trainen en te superviseren. Beiden waren niet betrokken bij de opzet en implementatie van de studie.

In het eetstoornissen veld is er weinig bekend over welke behandeling het beste werkt voor wie. Binnen de uitgebreide vorm van CBT-E worden drie factoren beschreven die vooruitgang kunnen belemmeren wanneer ze in extreme mate aanwezig zijn en onvoldoende aandacht krijgen in een eetstoornis behandeling. De verwachting is dat patiënten die last hebben van een extreem laag zelfbeeld, disfunctioneel perfectionisme en/of interpersoonlijke problemen minder profiteren van de gefocuste versie van CBT-E. Om dit te kunnen toetsen is het moderatie effect van deze factoren onderzocht.

Het hebben van een laag zelfbeeld speelt een belangrijke rol bij het ontstaan en in stand houden van een eetstoornis en is derhalve gekozen als aanvullend thema van dit proefschrift. Het doel van een van de studies was om meer inzicht te verkrijgen in de relatie tussen expliciet en impliciet zelfbeeld en eetstoornis psychopathologie. Daarnaast is COMET (competitive memory training; Korrelboom, 2011) beschreven als een veelbelovende

transdiagnostische interventie in de behandeling van een negatief zelfbeeld. Om het effect van COMET ten aanzien van het verbeteren van het negatief zelfbeeld in een eetstoornis populatie te onderzoeken hebben we een tweede gerandomiseerde studie uitgevoerd.

Belangrijkste bevindingen

In de studie uit **hoofdstuk 2** werd de relatie tussen expliciet zelfbeeld, impliciet zelfbeeld, discrepant zelfbeeld (discrepantie tussen expliciet en impliciet zelfbeeld) en (de ernst van) eetstoornissen onderzocht. Alhoewel zowel expliciet als impliciet zelfbeeld lager bleken in de eetstoornisgroep dan in de vergelijkingsgroep, kon er geen unieke bijdrage van impliciet zelfbeeld (los van expliciet zelfbeeld) vastgesteld worden in het voorspellen van een eetstoornis. Expliciet zelfbeeld bleek ook als enige een voorspellende waarde te hebben voor de ernst van de eetpathologie. Of er wel of geen relatie tussen eetstoornisstatus (wel of geen eetstoornis) en een discrepant zelfbeeld werd gevonden hing af van de manier waarop het discrepant zelfbeeld geoperationaliseerd was en welke statistische methode gebruikt werd. Om die reden werd er geen conclusie getrokken ten aanzien van de relatie tussen een discrepant zelfbeeld en eetstoornisstatus.

Concluderend blijkt vooral een laag expliciet zelfbeeld geassocieerd te zijn met eetstoornis psychopathologie.

In **hoofdstuk 3** worden de resultaten van de studie naar de effectiviteit van COMET, een interventie gericht op het verbeteren van een laag zelfbeeld bij eetstoornis patiënten, beschreven. In deze RCT werden 52 patiënten gerandomiseerd over acht weken COMET aanvullend aan TAU en acht weken enkel TAU. De resultaten van deze studie tonen aan dat COMET een effectieve aanvullende interventie is voor het verbeteren van een negatief zelfbeeld bij eetstoornissen patiënten.

De effectiviteit van CBT-E voor patiënten met een eetstoornis en een BMI > 17.5 werd bevestigd in een review artikel, beschreven in **hoofdstuk 4**, die een overzicht geeft van de CBT-E effectiviteitsstudies uit de periode Januari 2014 – Maart 2018. Er bleek echter sprake van een behoorlijke spreiding in herstelpercentages tussen de diverse studies, mogelijk samenhangend met de verschillen in geïncludeerde populaties en de gehanteerde definities van significante verandering.

De hoofdstudie van dit proefschrift betreft een grote RCT (N=143) uitgevoerd in drie eetstoornissencentra in Nederland naar de effectiviteit van CBT-Ef vergeleken met TAU bij patiënten met een eetstoornis en een BMI > 17.5. De opzet van deze studie is beschreven in **hoofdstuk 5**. De resultaten na 80 weken, beschreven in **hoofdstuk 6**, laten geen verschillen tussen condities zien ten aanzien van herstel van de eetstoornis, afname van eetpathologie, afname van angst en depressieve klachten of reductie van perfectionisme en interpersoonlijke problemen. Echter in de eerste zes weken van de behandeling was er sprake van een sterkere afname van eetpathologie in de CBT-Ef conditie in vergelijking met TAU. En wanneer de internationaal meest gebruikte definitie van herstel (EDE-Q score ≤ 2.77) werd toegepast, waren de herstelpercentages bij 20 weken (einde CBT-Ef behandeling) significant hoger in CBT-Ef dan TAU. Na 80 weken was dit verschil echter niet meer significant. Wel bleek CBT-Ef op alle meetmomenten effectiever in het verbeteren van het zelfbeeld. Bovendien was het de minder intensieve en kortere behandeling.

In deze studie vonden we geen bewijs voor de hypothese dat meer zelfbeeld problemen, een grotere mate van perfectionisme of meer interpersoonlijke problemen bij start behandeling (de veronderstelde complicerende factoren in een eetstoornis behandeling) lange termijn vooruitgang belemmeren. Hiermee hebben we dus geen aanwijzingen gevonden dat deze factoren extra aandacht zouden behoeven in een uitgebreider protocol bij eetstoornis patiënten met een BMI > 17.5.

Effectiviteit van CBT-E in de context van de bestaande literatuur

Alhoewel CBT-Ef reeds bewezen effectief is voor patiënten met een eetstoornis en een BMI > 17.5, draagt de uitkomst van onze studie bij aan de generaliseerbaarheid van de resultaten naar andere behandelcentra en eetstoornispopulaties. Daarnaast veronderstellen we dat de duidelijke focus van CBT-Ef op snelle gedragsverandering in combinatie met de intensieve start (twee sessies per week) waarschijnlijk heeft geleid tot snellere klachten reductie vergeleken met de minder geprotocolleerde vorm van CBT (TAU). Omdat de gefocuste versie van CBT-E zich niet direct richt op het verbeteren van het zelfbeeld was het gegeven dat op alle meetmomenten (na 6, 20, 40 en 80 weken) CBT-Ef een sterkere verbetering van het zelfbeeld liet zien dan TAU een onverwacht resultaat. Hier zijn diverse mogelijke verklaringen voor. CBT-Ef is voor een belangrijk deel gericht op het beïnvloeden van de overwaardering van lichaamsvorm en gewicht door patiënten te helpen hun zelfbeeld aan andere terreinen (los van lichaamsvorm en gewicht) te leren

ontlenen (vriendschappen, werk, hobby's etc.). Er wordt verondersteld dat door het verleggen van de aandacht naar andere mogelijke bronnen van eigenwaarde, het zelfbeeld kan worden verbeterd. Interessant in dit licht is echter dat het verschil in effect op zelfbeeld het grootst bleek na de eerste fase van de behandeling (na zes weken), een fase waarin nog geen aandacht besteed wordt aan de overwaardering van lichaamsvorm en gewicht. Deze eerste fase is een intensieve behandelfase die zich vooral richt op het leren herkennen van factoren die de eetstoornis in stand houden en is gericht op vroege gedragsverandering. De snelle inzet op gedragsverandering zou het bijkomende effect kunnen hebben dat, wanneer ervaren wordt dat verandering mogelijk is (bijvoorbeeld door een reductie van eetbuien), dit een positieve boost geeft in zelfvertrouwen ("ik kan dit") en het derhalve een positief effect heeft op het zelfbeeld.

Uitkomst van de zelfbeeld studies in de context van de bestaande literatuur

Het belang van een laag zelfbeeld bij het ontstaan en in stand houden van een eetstoornis is in veel studies aangetoond waarbij een laag zelfbeeld in verband is gebracht met de ernst van een eetstoornis, voegtijdig stoppen met behandeling, slechter behandelverloop en terugval. De meeste studies hebben zich hierbij gericht op de rol van expliciet zelfbeeld bij eetstoornissen. De relatie tussen expliciet zelfbeeld en eetpathologie werd in dit proefschrift bevestigd. Aanvullend vonden we dat ook impliciet zelfbeeld lager was in een eetstoornis populatie vergeleken met een vergelijkingsgroep. Deze bevinding ligt in lijn met andere studies die de rol van impliciet zelfbeeld bij psychopathologie hebben onderzocht en waarbij, wanneer een relatie gevonden werd, een laag impliciet zelfbeeld gerelateerd bleek aan meer psychopathologie. Wanneer expliciet en impliciet zelfbeeld gezamenlijk werden onderzocht vonden we echter geen unieke bijdrage van impliciet zelfbeeld in de voorspelling van de eetstoornis status. De minder overtuigende relatie tussen impliciet zelfbeeld en eetstoornis pathologie zou te maken kunnen hebben met de eigenschappen van de instrumenten die we gebruikt hebben. De relatie tussen expliciet zelfbeeld en eetpathologie kan versterkt zijn doordat beide constructen onderzocht werden met zelf-rapportage instrumenten (i.t.t. het instrument wat gebruikt is om impliciet zelfbeeld te meten). Daarnaast is er een inhoudelijke overlap tussen beide zelf-rapportage instrumenten (bijvoorbeeld een laag zelfbeeld dat ook uitgedrukt wordt in een negatief lichaamsbeeld).

Definities en meetinstrumenten om impliciete cognitieve processen ten opzichte van expliciete cognitieve processen in kaart te brengen hebben een verdere verfijning en validering nodig, zowel in hun psychometrische kwaliteiten alsook ten aanzien van de specifieke toepassingen bij psychopathologie.

De COMET studie heeft aangetoond dat, aanvullend aan de reguliere eetstoornis behandeling (TAU), COMET een effectieve interventie is om het negatieve zelfbeeld te verbeteren. Dit is een klinisch relevante bevinding in het licht van de eerder beschreven rol van een negatief zelfbeeld bij het ontstaan en in stand houden van een eetstoornis en het ontbreken van een evidence based behandelmethode bij de start van deze studie. De afgelopen jaren is de effectiviteit van COMET in diverse RCTs onderzocht. Daarbij werd gevonden dat deze interventie effectief is in het verbeteren van het zelfbeeld bij patiënten met een depressie, persoonlijkheidsstoornissen en angststoornissen. Deze onderzoeken hebben geleid tot een sterke empirische onderbouwing van de effectiviteit van COMET als een transdiagnostische interventie bij diverse psychiatrische stoornissen.

Zelfbeeld verbeteringen na CBT-E en COMET

In dit proefschrift wordt in twee verschillende studies het effect van COMET (een interventie direct gericht op het verbeteren van het negatief zelfbeeld) en van CBT-Ef (een interventie niet direct gericht op het verbeteren van het zelfbeeld) met betrekking tot het verbeteren van het negatief zelfbeeld bij eetstoornis patiënten onderzocht. Om deze effecten met elkaar te kunnen vergelijken hebben we de sterkte van de effecten met Cohen's *d* (Cohen, 1992) berekend voor zowel COMET als CBT-Ef. We vonden vergelijkbare grote effect sizes hetgeen de conclusie van Fairburn en collega's (2009) onderbouwt dat voor het overgrote deel van de patiënten met een eetstoornis en zelfbeeld problemen, de gefocuste versie van CBT-E voldoet en er geen aanvullende aandacht nodig is voor de behandeling van een negatief zelfbeeld. Echter, in tegenstelling tot de CBT-E studie, werden de patiënten in de COMET studie pas geïncludeerd wanneer ze minstens twee maanden in behandeling waren voor hun eetstoornis en er daarnaast sprake was van een negatief zelfbeeld (zoals gerapporteerd door de patiënt en verwijzende behandelaar). Zoals verwacht heeft dit verschil in inclusie criteria geleid tot de inclusie van patiënten met meer zelfbeeld problemen in de COMET studie. Alleen een studie met een directe vergelijking tussen CBT-Ef en CBT-Ef + COMET kan het antwoord geven op de vraag of beide behandelingen vergelijkbare effecten hebben op het verbeteren van het zelfbeeld en of de ernst van de zelfbeeld problemen het effect van CBT-E en COMET modereert.

Effectiviteit, inhoud en duur van TAU voor eetstoornissen

Om het inzicht te vergroten in de reguliere eetstoornis behandelpraktijk (TAU), werd tijdens de RCT die in hoofdstuk 6 beschreven staat de inhoud, duur en behandelintensiteit van deze behandelconditie gemonitord. Alle behandelingen in TAU bleken gebaseerd te zijn op CGT principes, echter in de meeste gevallen niet volgens een effectief gebleken behandelprotocol en met een grote variatie aan interventies, setting, behandel intensiteit, duur, hoeveelheid betrokken disciplines en behandeling van co morbiditeit. Deze resultaten liggen in het verlengde van de resultaten uit eerdere studies waarin werd aangetoond dat clinici vaak geen evidence-based behandelprotocollen gebruiken en de toepassing van essentiële CGT technieken in eetstoornis behandelingen minder is dan kan worden verwacht wanneer men een evidence-based behandelprotocol zou gebruiken. Ook wanneer patiënten rapporteren een CGT behandeling voor hun eetstoornis te hebben gevolgd (zoals aangeduid door hun therapeut), lijkt dit vaak niet te gaan om een effectief gebleken CGT variant. Clinici rapporteren dat ze vaak gebruik maken van een mix van technieken. Dit fenomeen wordt ook wel aangeduid als "therapist drift". Een veel voorkomende overtuiging onder behandelaren is dat de resultaten vanuit onderzoeksbevindingen niet toepasbaar zijn in hun dagelijkse behandelpraktijk, bijvoorbeeld vanuit de overtuiging dat patiënten die voor onderzoek geselecteerd worden niet representatief zijn voor de patiënten met de meer complexe problematiek die zij in hun praktijk zien. Vooralsnog was er weinig bekend over het verschil in effectiviteit tussen de meer individueel samengestelde behandelingen (in onze studie aangeduid als TAU) en de meer gestandaardiseerde behandelingen volgens een effectief gebleken behandelprotocol zoals CBT-E. Alhoewel we in onze studie na 80 weken geen verschillen vonden in effect tussen TAU en CBT-E ten aanzien van het verminderen van de eetpathologie, werden deze resultaten wel eerder bereikt met CBT-Ef die tevens de kortere en minder intensieve behandeling was. Deze bevinding vinden we ook in een recent gepubliceerd artikel waarin de effecten van een CBT-E implementatie studie worden beschreven (van den Berg et al., 2020). In deze studie bleek CBT-E voor volwassen eetstoornis patiënten met een BMI > 17.5 tot betere resultaten te leiden dan TAU vanuit een kosteneffectiviteitsperspectief.

Conclusies en aanbevelingen

We concluderen dat met een brede implementatie in de klinische praktijk van de gefocuste versie van CBT-E voor patiënten met een eetstoornis en een BMI > 17.5 de efficiëntie en toegankelijkheid van eetstoornis behandelingen in Nederland vergroot kan worden. Vanuit diverse studies weten we echter

dat de implementatie van een effectief gebleken behandelprotocol een grote uitdaging is. In dit kader wordt vaak gesproken over de kloof tussen onderzoek en praktijk hetgeen leidt tot suboptimale behandelingen. Ten aanzien van het ontstaan van deze kloof zijn diverse oorzaken bekend. Zo zijn clinici vaak niet op de hoogte van, en niet getraind in de effectief gebleken behandelprotocollen. En terwijl onderzoek aantoont dat de therapeutische relatie niet de drijvende kracht is achter veranderingen in gedrag bij eetstoornis therapieën, blijkt tevens uit onderzoek dat het niet toepassen van CGT voor eetstoornissen gerelateerd is aan de overtuiging van behandelaren dat de kwaliteit van de therapeutische relatie van groot belang is bij het bereiken van goede therapieresultaten. Verder noemde we al eerder dat veel clinici rapporteren dat de evidence-based behandelingen niet toepasbaar zijn in hun behandelpraktijk omdat zij veronderstellen dat er bij de patiënten die zij zien sprake is van meer complexe pathologie. Als gevolg besluiten behandelaren vaak een meer geïndividualiseerde mix van technieken toe te passen waarmee ze betere behandelresultaten verwachten. Echter, zoals beschreven, hebben we in dit proefschrift geen superieure effecten gevonden van de meer diverse, geïndividualiseerde, intensieve en langere TAU behandeling. Het tegengestelde blijkt waar. De meer gestandaardiseerde kortere en minder intensieve CBT-E behandeling bereikt betere resultaten op het gebied van zelfbeeld en de effecten op eetpathologie worden sneller bereikt. Daarnaast hebben we geen aanwijzingen gevonden dat meer zelfbeeldproblematiek, perfectionisme of interpersoonlijke problemen interfereren met lange termijn verbeteringen in CBT-Ef. Wat betekent dit voor de noodzaak om de tevens effectief gebleken zelfbeeld module (COMET) als aanvullende behandelinterventie toe te voegen aan een eetstoornis behandeling? Totdat er uitkomsten beschikbaar zijn van een studie waarin een directe vergelijking wordt gemaakt tussen CBT-Ef en CBT-Ef + COMET, kunnen we hier geen wetenschappelijk onderbouwde uitspraak in doen. We stellen voor nu voor om alleen COMET als aanvullende interventie aan te bieden wanneer tijdens de eetstoornis behandeling wordt vastgesteld dat er sprake is van een extreem laag zelfbeeld wat interfereert met een positief behandelverloop.

Op dit moment heeft onderzoek nog niet geleid tot antwoorden rondom welke patiënten het meest profiteren van CBT-Ef en voor welke patiënten deze behandeling minder geschikt is. Ontwikkelingen in het onderzoeksgebied van precision medicine hebben geresulteerd in meer multivariate benaderingen die in de toekomst kunnen helpen bij het beantwoorden van vragen rondom gepersonaliseerde behandeladviezen door informatie van multipele variabelen

te combineren. Dit is interessant voor de beantwoording van vragen als "welke behandeling werkt het best voor wie?" maar ook "welke interventie binnen een protocol is het meest veelbelovend"? Bij de beantwoording van dergelijke vragen kan machine learning en het gebruik van big data een belangrijke bijdrage leveren wat uiteindelijk kan leiden tot meer gepersonaliseerde behandelindicaties en een verdere verbetering van behandelresultaten.

Op dit moment is een belangrijke vraag hoe eetstoornis behandelaren aangemoedigd kunnen worden om meer evidence-based behandelmethoden toe te passen ook wanneer er sprake is van meer complexe problematiek bijvoorbeeld door de ernst van de eetstoornis of de aanwezigheid van comorbiditeit. Training, permanente supervisie en intervisie kan therapeuten helpen bij het leren toepassen van evidence-based behandelingen. Patiënten profiteren ervan wanneer supervisoren zich meer focussen op de implementatie van effectief gebleken protocollen. Daarnaast werkt een uitgewerkt behandelprotocol op papier faciliterend in het creëren van uniformiteit in training en supervisie. Verder zou elke training of opleiding een onderdeel moeten bevatten met een up tot date overzicht van de meest recente bevindingen uit wetenschappelijk onderzoek. Op deze manier wordt ook aan clinici meegegeven hoe essentieel onderzoek is en hoe uitkomsten uit onderzoek kunnen dienen als een bescherming tegen alomtegenwoordige vooroordelen. Uiteraard profiteert niet iedere patiënt van een evidence-based behandeling (waaronder CBT-E), ook niet wanneer het gedegen wordt toegepast door zeer ervaren behandelaren. Het is van groot belang om dit zo vroeg mogelijk in het therapie proces vast te stellen en niet te wachten tot het einde van de therapie om te bepalen of de therapie heeft aangeslagen. De vooruitgang in nieuwe technologieën en software heeft geleid tot de ontwikkeling van veelbelovende feedback systemen die clinici kunnen ondersteunen om op een meer systematische manier, gedurende het gehele behandelproces, behandeloverwegingen te maken (Hooke et al., 2018). Aanvullende klinische probleemoplossende middelen kunnen daarnaast suggesties geven over mogelijke aanpassingen in de behandeling (Whipple et al., 2003). Dergelijke innovaties geven clinici de mogelijkheid om in de toekomst op een meer empirisch ondersteunde manier behandeling te personaliseren.

Dankwoord

It always seems impossible until it's done (Nelson Mandela).

Het was een bijzonder en leerzaam proces met momenten waarin het behalen van de eindstreep onmogelijk leek. Vertrouwen, vallen en weer opstaan, doorzetten en leren, veel leren, hebben geholpen en geleid tot dit eindresultaat. Een eindresultaat waar ik trots op ben en wat ik nooit had kunnen volbrengen zonder de steun, liefde, hulp en lessen van veel waardevolle mensen om me heen. Ik heb dan ook uitgekeken naar dit moment; mijn dankwoord.

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Curriculum Vitae

Martie de Jong werd op 28 november 1975 geboren in Den Haag. Haar vwo-diploma behaalde zij in 1994 bij het Aloysius College te Den Haag. In 1999 rondde zij de studie klinische en gezondheidspsychologie af aan de Universiteit Leiden, waarna zij een aantal jaren als psycholoog in de verslavingszorg werkte. In 2002 begon zij aan de opleiding tot gezondheidszorgpsycholoog bij Parnassia Groep, waar zij ook startte in het eetstoornissenveld. In 2004 is zij bij Parnassia Groep gestart met de opleiding tot klinisch psycholoog waarbij ze ook aan de slag ging als onderzoeker. Haar onderzoeksactiviteiten als onderdeel van de opleiding tot klinisch psycholoog hebben haar geïnspireerd tot een PhD traject. Dit traject is ze gestart in 2010 bij het Instituut Psychologie aan de Universiteit Leiden. Vanaf 2009 heeft ze regelmatig les gegeven binnen de RINO en tussen 2015 en 2019 is ze verbonden geweest aan de RINO als jaargroepopleider van de opleiding tot klinisch psycholoog.

In 2014 is ze aangesteld als specialismeleider eet- en voedingsstoornissen voor Parnassia Groep. In deze rol is ze verantwoordelijk voor de kwaliteit van zorg, implementatie van effectief gebleken behandelmethoden, innovaties en daaraan gekoppeld wetenschappelijk onderzoek binnen het specialisme eetstoornissen. In 2013 behaalde zij haar registratie cognitief gedragstherapeut VGCT en in 2016 haar registratie als senior schematherapeut. Ze geeft vanaf 2015 cursussen en supervisie in de transdiagnostische behandelmethode voor eetstoornissen, cognitive behavior therapy – enhanced (CBT-E). Vanaf december 2020 is ze werkzaam als P-opleider voor Parnassia Groep regio Haaglanden.

Martie is getrouwd met Bram Schippers en samen hebben zij drie kinderen, Esmee (2004), Jesse (2007) en Lize (2011).