Transdiagnostic treatment for eating disorders

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Chapter 7

Summary and general discussion

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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".

References

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5)*. Washington, DC: American Psychiatric Association.

Arcelus, J., Mitchell, A. J., Wales, J., & Nielsen, S. (2011). Mortality rates in patients with anorexia nervosa and other eating disorders. A meta-analysis of 36 studies. *Archives of General Psychiatry, 68*(7), 724-731. https://doi.org/10.1001/archgenpsychiatry.2011.74

Blackburn, I.-M., James, I. A., Milne, D. L., Baker, C., Standart, S., Garland, A.*, et al.* (2001). The revised cognitive therapy scale (CTS-R): Psychometric properties. *Behavioural and Cognitive Psychotherapy, 29*(4), 431-446. https://doi.org/10.1017/S1352465801004040

Cockerham, E., Stopa, L., Bell, L., & Gregg, A. (2009). Implicit self-esteem in bulimia nervosa. *Journal of Behavior Therapy and Experimental Psychiatry, 40*(2), 265-273. https://doi.org/10.1016/j.jbtep.2008.12.003

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*(1), 155-159. https://doi.org/10.1037//0033-2909.112.1.155

Collin, P., Karatzias, T., Power, K., Howard, R., Grierson, D., & Yellowlees, A. (2016). Multidimensional self-esteem and magnitude of change in the treatment of anorexia nervosa. *Psychiatry Research, 237*, 175-181. https://doi.org/10.1016/j.psychres.2016.01.046

Cowdrey, N. D., & Waller, G. (2015). Are we really delivering evidence-based treatments for eating disorders? How eating-disordered patients describe their experience of cognitive behavioral therapy. *Behaviour Research and Therapy, 75*, 72-77. https://doi.org/10.1016/j.brat.2015.10.009

De Houwer, J., Teige-Mocigemba, S., Spruyt, A., & Moors, A. (2009). Implicit measures: A normative analysis and review. *Psychological Bulletin, 135*(3), 347-368. https://doi.org/10.1037/a0014211

de Jong, M., Korrelboom, K., van der Meer, I., Deen, M., Hoek, H. W., & Spinhoven, P. (2016). Effectiveness of enhanced cognitive behavioral therapy (CBT-E) for eating disorders: study protocol for a randomized controlled trial. *Trials, 17*(1), 573. https://doi.org/10.1186/s13063-016-1716-3

DeRubeis, R. J. (2019). The history, current status, and possible future of precision mental health. *Behaviour Research and Therapy, 123*, 103506. https://doi.org/10.1016/j.brat.2019.103506

Fairburn, C. G. (2008). *Cognitive Behavior Therapy and Eating Disorders*. New York, NY: Guilford Press.

Fairburn, C. G., Bailey-Straebler, S., Basden, S., Doll, H. A., Jones, R., Murphy, R.*, et al.* (2015). A transdiagnostic comparison of enhanced cognitive behaviour therapy (CBT-E) and interpersonal psychotherapy in the treatment of eating disorders. *Behaviour Research and Therapy, 70*, 64-71. https://doi.org/10.1016/j.brat.2015.04.010

Fairburn, C. G., Cooper, Z., Doll, H. A., O'Connor, M. E., Bohn, K., Hawker, D. M., *et al.* (2009). Transdiagnostic cognitive-behavioral therapy for patients with eating disorders: a two-site trial with 60-week follow-up. *American Journal of Psychiatry, 166*(3), 311-319. https://doi.org/10.1176/appi.ajp.2008.08040608

Fiedler, K., Messner, C., & Bluemke, M. (2006). Unresolved problems with the "I", the "A", and the "T": A logical and psychometric critique of the Implicit Association Test (IAT). *European Review of Social Psychology, 17*(1), 74-147. https://doi.org/10.1080/10463280600681248

Franck, E., De Raedt, R., Dereu, M., & Van den Abbeele, D. (2007). Implicit and explicit self-esteem in currently depressed individuals with and without suicidal ideation. *Journal of Behavior Therapy and Experimental Psychiatry, 38*(1), 75-85. https://doi.org/10.1016/j.jbtep.2006.05.003

Glashouwer, K. A., Vroling, M. S., de Jong, P. J., Lange, W.-G., & de Keijser, J. (2013). Low implicit self-esteem and dysfunctional automatic associations in social anxiety disorder. *Journal of Behavior Therapy and Experimental Psychiatry, 44*(2), 262-270. https://doi.org/10.1016/j.jbtep.2012.11.005 23298819

Graves, T. A., Tabri, N., Thompson-Brenner, H., Franko, D. L., Eddy, K. T., Bourion-Bedes, S., *et al.* (2017). A meta-analysis of the relation between therapeutic alliance and treatment outcome in eating disorders. *International Journal of Eating Disorders, 50*(4), 323-340. https://doi.org/10.1002/eat.22672

Haas, H. L., & Clopton, J. R. (2003). Comparing clinical and research treatments for eating disorders. *International Journal of Eating Disorders, 33*(4), 412-420. https://doi.org/10.1002/eat.10156

Halmi, K. A., Agras, W. S., Crow, S., Mitchell, J., Wilson, G. T., Bryson, S. W., *et al.* (2005). Predictors of treatment acceptance and completion in anorexia nervosa: implications for future study designs. *Archives of General Psychiatry, 62*(7), 776-781. https://doi.org/10.1001/archpsyc.62.7.776

Hay, P., Chinn, D., Forbes, D., Madden, S., Newton, R., Sugenor, L., *et al.* (2014). Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of eating disorders. *Australian & New Zealand Journal of Psychiatry, 48*(11), 977-1008. https://doi.org/10.1177/0004867414555814

Hilbert, A., Hoek, H. W., & Schmidt, R. (2017). Evidence-based clinical guidelines for eating disorders: international comparison. *Current Opinion in Psychiatry, 30*(6), 423-437. https://doi.org/10.1097/YCO.0000000000000360

Hooke, G. R., Sng, A. A. H., Cunningham, N. K., & Page, A. C. (2018). Methods of delivering progress feedback to optimise patient outcomes: The value of expected treatment trajectories. *Cognitive Therapy and Research, 42*(2), 204-211. https://doi.org/10.1007/s10608-017-9851-z

Jenkins, P. E., Hoste, R. R., Meyer, C., & Blissett, J. M. (2011). Eating disorders and quality of life: a review of the literature. *Clinical Psychology Review, 31*(1), 113-121. https://doi.org/10.1016/j.cpr.2010.08.003

Keel, P. K., Brown, T. A., Holm-Denoma, J., & Bodell, L. P. (2011). Comparison of DSM-IV versus proposed DSM-5 diagnostic criteria for eating disorders: reduction of eating disorder not otherwise specified and validity. *International Journal of Eating Disorders, 44*(6), 553-560. https://doi.org/10.1002/eat.20892

Korrelboom, C. W., van der Weele, K., Gjaltema, M., & Hoogstraten, C. (2009). Competitive memory training (COMET) for treating low self-esteem: A pilot study in a routine clinical setting. *The Behavior Therapist, 32*(1), 3-8.

Korrelboom, K., Maarsingh, M., & Huijbrechts, I. (2012). Competitive memory training (COMET) for treating low self-esteem in patients with depressive disorders: a randomized clinical trial. *Depression and Anxiety, 29*(2), 102-110. https://doi.org/10.1002/da.20921

Korrelboom, K., Marissen, M., & van Assendelft, T. (2011). Competitive memory training (COMET) for low self-esteem in patients with personality disorders: a randomized effectiveness study. *Behavioural and Cognitive Psychotherapy, 39*(1), 1-19. https://doi.org/10.1017/S1352465810000469

La Mela, C., Maglietta, M., Lucarelli, S., Mori, S., & Sassaroli, S. (2013). Pretreatment outcome indicators in an eating disorder outpatient group: the effects of self-esteem, personality disorders and dissociation. *Comprehensive Psychiatry, 54*(7), 933-942. https://doi.org/10.1016/j.comppsych.2013.03.024

Lilienfeld, S. O., Ritschel, L. A., Lynn, S. J., Brown, A. P., Cautin, R. L., & Latzman, R. D. (2013). The research-practice gap: bridging the schism between eating disorder researchers and practitioners. *International Journal of Eating Disorders, 46*(5), 386-394. https://doi.org/10.1002/eat.22090

Linardon, J., de la Piedad Garcia, X., & Brennan, L. (2017). Predictors, Moderators, and Mediators of Treatment Outcome Following Manualised Cognitive-Behavioural Therapy for Eating Disorders: A Systematic Review. *European Eating Disorders Review, 25*(1), 3-12. https://doi.org/10.1002/erv.2492

Linardon, J., Kothe, E. J., & Fuller-Tyszkiewicz, M. (2019). Efficacy of psychotherapy for bulimia nervosa and binge-eating disorder on self-esteem improvement: Meta-analysis. *European Eating Disorders Review, 27*(2), 109-123. https://doi.org/10.1002/erv.2662

Lutz, W., Rubel, J. A., Schwartz, B., Schilling, V., & Deisenhofer, A. K. (2019). Towards integrating personalized feedback research into clinical practice: Development of the Trier Treatment Navigator (TTN). *Behaviour Research and Therapy, 120*, 103438. https://doi.org/10.1016/j.brat.2019.103438

Machado, P. P., Goncalves, S., & Hoek, H. W. (2013). DSM-5 reduces the proportion of EDNOS cases: evidence from community samples. *International Journal of Eating Disorders, 46*(1), 60-65. https://doi.org/10.1002/eat.22040

Masheb, R. M., & Grilo, C. M. (2008). Examination of predictors and moderators for self-help treatments of binge-eating disorder. *Journal of Consulting and Clinical Psychology, 76*(5), 900-904. https://doi.org/10.1037/a0012917

McAlpine, D. E., Schroder, K., Pankratz, V. S., & Maurer, M. (2004). Survey of regional health care providers on selection of treatment for bulimia nervosa. *International Journal of Eating Disorders, 35*(1), 27-32. https://doi.org/doi: 10.1002/eat.10217

Mulkens, S., de Vos, C., de Graaff, A., & Waller, G. (2018). To deliver or not to deliver cognitive behavioral therapy for eating disorders: Replication and extension of our understanding of why therapists fail to do what they should do. *Behaviour Research and Therapy, 106*, 57-63. https://doi.org/10.1016/j.brat.2018.05.004

Mussell, M. P., Crosby, R. D., Crow, S. J., Knopke, A. J., Peterson, C. B., Wonderlich, S. A., *et al.* (2000). Utilization of empirically supported psychotherapy treatments for individuals with eating disorders: A survey of psychologists. *International Journal of Eating Disorders, 27*(2), 230-237. https://doi.org/10.1002/(sici)1098-108x(200003)27:2<230::aid-eat11>3.0.co;2-0

National Institute for Health and Care Excellence (NICE). (2017). *Eating disorders: recognition and treatment. NICE guideline [NG69]*. London, UK: NICE.

Netwerk Kwaliteitsontwikkeling GGz. (2017). *Zorgstandaard Eetstoornissen*. Utrecht: Netwerk Kwaliteitsontwikkeling GGz.

Olij, R. J. B., Korrelboom, C. W., Huijbrechts, I. P. A. M., de Jong, M., Cloin, P. A., Maarsingh, M., *et al.* (2006). De module zelfbeeld in een groep: Werkwijze en eerste bevindingen. *Directieve Therapie, 26*(4), 307- 325.

Passos, I. C., Mwangi, B., & Kapczinski, F. (2016). Big data analytics and machine learning: 2015 and beyond. *Lancet Psychiatry, 3*(1), 13-15. https://doi.org/10.1016/S2215-0366(15)00549-0

Risch, A. K., Buba, A., Birk, U., Morina, N., Steffens, M. C., & Stangier, U. (2010). Implicit self-esteem in recurrently depressed patients. *Journal of Behavior Therapy and Experimental Psychiatry, 41*(3), 199-206. https://doi.org/10.1016/j.jbtep.2010.01.003 20132925

Ritter, V., Ertel, C., Beil, K., Steffens, M. C., & Stangier, U. (2013). In the presence of social threat: Implicit and explicit self-esteem in Social Anxiety Disorder. *Cognitive Therapy and Research, 37*(6), 1101-1109. https://doi.org/10.1007/s10608-013-9553-0

Sassaroli, S., Gallucci, M., & Ruggiero, G. M. (2008). Low perception of control as a cognitive factor of eating disorders. Its independent effects on measures of eating disorders and its interactive effects with perfectionism and self-esteem. *Journal of Behavior Therapy and Experimental Psychiatry, 39*(4), 467-488. https://doi.org/10.1016/j.jbtep.2007.11.005 18328461

Schoenwald, S. K., & Garland, A. F. (2013). A review of treatment adherence measurement methods. *Psychological Assessment, 25*(1), 146-156. https://doi.org/10.1037/a0029715

Shafran, R., Clark, D. M., Fairburn, C. G., Arntz, A., Barlow, D. H., Ehlers, A., *et al.* (2009). Mind the gap: Improving the dissemination of CBT. *Behaviour Research and Therapy, 47*(11), 902-909. https://doi.org/10.1016/j.brat.2009.07.003

Simmons, A. M., Milnes, S. M., & Anderson, D. A. (2008). Factors influencing the utilization of empirically supported treatments for eating disorders. *Eating Disorders, 16*(4), 342-354. https://doi.org/10.1080/10640260802116017

Smink, F. R., van Hoeken, D., & Hoek, H. W. (2013). Epidemiology, course, and outcome of eating disorders. *Current Opinion in Psychiatry, 26*(6), 543-548. https://doi.org/10.1097/YCO.0b013e328365a24f

Staring, A. B., van den Berg, D. P., Cath, D. C., Schoorl, M., Engelhard, I. M., & Korrelboom, C. W. (2016). Self-esteem treatment in anxiety: A randomized controlled crossover trial of Eye Movement Desensitization and Reprocessing (EMDR) versus competitive memory training (COMET) in patients with anxiety disorders. *Behaviour Research and Therapy, 82*, 11-20. https://doi.org/10.1016/j.brat.2016.04.002

Thompson-Brenner, H., Shingleton, R. M., Thompson, D. R., Satir, D. A., Richards, L. K., Pratt, E. M., *et al.* (2016). Focused vs. Broad enhanced cognitive behavioral therapy for bulimia nervosa with comorbid borderline personality: A randomized controlled trial. *International Journal of Eating Disorders, 49*(1), 36-49. https://doi.org/10.1002/eat.22468

Tobin, D. L., Banker, J. D., Weisberg, L., & Bowers, W. (2007). I know what you did last summer (and it was not CBT): a factor analytic model of international psychotherapeutic practice in the eating disorders. *International Journal of Eating Disorders, 40*(8), 754-757. https://doi.org/10.1002/eat.20426

Vall, E., & Wade, T. D. (2015). Predictors of treatment outcome in individuals with eating disorders: A systematic review and meta-analysis. *International Journal of Eating Disorders, 48*(7), 946-971. https://doi.org/10.1002/eat.22411

van den Berg, E., Schlochtermeier, D., Koenders, J., de Mooij, L., Goudriaan, A., Blankers, M., *et al.* (2020). Implementing cognitive behavioral therapy-enhanced in a routine inpatient and outpatient setting: Comparing effectiveness and treatment costs in two consecutive cohorts. *International Journal of Eating Disorders, 53*(3), 461-471. https://doi.org/10.1002/eat.23229

van der Gaag, M., van Oosterhout, B., Daalman, K., Sommer, I. E., & Korrelboom, K. (2012). Initial evaluation of the effects of competitive memory training (COMET) on depression in schizophrenia-spectrum patients with persistent auditory verbal hallucinations: a randomized controlled trial. *British Journal of Clinical Psychology, 51*(2), 158-171. https://doi.org/10.1111/j.2044-8260.2011.02025.x

von Ranson, K. M., & Robinson, K. E. (2006). Who is providing what type of psychotherapy to eating disorder clients? A survey. *International Journal of Eating Disorders, 39*(1), 27-34. https://doi.org/10.1002/eat.20201

Waller, G. (2009). Evidence-based treatment and therapist drift. *Behaviour Research and Therapy, 47*(2), 119-127. https://doi.org/10.1016/j.brat.2008.10.018

Waller, G. (2016a). Recent advances in psychological therapies for eating disorders. *F1000Research, 5*. https://doi.org/10.12688/f1000research.7618.1

Waller, G. (2016b). Treatment Protocols for Eating Disorders: Clinicians' Attitudes, Concerns, Adherence and Difficulties Delivering Evidence-Based Psychological Interventions. *Current Psychiatry Reports, 18*(4), 36. https://doi.org/10.1007/s11920-016-0679-0

Waller, G., Stringer, H., & Meyer, C. (2012). What cognitive behavioral techniques do therapists report using when delivering cognitive behavioral therapy for the eating disorders? *Journal of Consulting and Clinical Psychology, 80*(1), 171-175. https://doi.org/10.1037/a0026559

Whipple, J. L., Lambert, M. J., Vermeersch, D. A., Smart, D. W., Nielsen, S. L., & Hawkins, E. J. (2003). Improving the effects of psychotherapy: The use of early identification of treatment and problem-solving strategies in routine practice. *Journal of Counseling Psychology, 50*(1), 59-68. https://doi.org/10.1037/0022-0167.50.1.59

Wilson, G. T., Wilfley, D. E., Agras, W. S., & Bryson, S. W. (2010). Psychological treatments of binge eating disorder. *Archives of General Psychiatry, 67*(1), 94-101. https://doi.org/10.1001/archgenpsychiatry.2009.170

Wright, C., & Waller, G. (2020). The impact of teaching clinicians about implementing exposure therapy with patients with eating disorders: A nonrandomized controlled study. *International Journal of Eating Disorders, 53*(1), 107-112. https://doi.org/10.1002/eat.23171

Yager, J., Devlin, M. J., Halmi, K. A., Herzog, D. B., Mitchell III, J. E., Powers, P.*, et al.* (2014). Guideline watch (August 2012): Practice guideline for the treatment of patients with eating disorders, 3rd Edition. *Focus, 12*(4), 416-431. https://doi.org/10.1176/appi.focus.120404

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