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Binge-eating disorder in the Arabic world and the Netherlands, assessment, etiology, efficacy, effectiveness and economic evaluation of psychological interventions

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Chapter 10 General discussion

This dissertation aimed to investigate several gaps in the current state of knowledge about binge eating disorder (BED) in Saudi Arabia and in the Netherlands. Therefore, the several studies examined various aspects of eating disorders, mainly BED. BED is the most prevalent and most recently acknowledged eating disorder (APA, 2013; Kessler et al., 2013).

The objectives of part I and part II vary. Aim of **Part I** was two-fold: (1) to adapt and examine psychometric properties and to establish norms of the two most used assessment tools to examine body-shape dissatisfaction and eating disorder pathology: the Eating Disorder Examination- Questionnaire (EDE-Q) (chapter two) and the Body Shape Questionnaire (BSQ) (chapter three); (2) to investigate potential predisposing factors (chapter four and five) and correlates (chapter five) of eating disorder pathology. Main purpose of **Part II** was to examine the effectiveness and efficacy of two treatment modalities of CBT-E for BED. The first treatment modality, presented in chapter six, was in-person Cognitive Behavior Therapy- enhanced (CBT-E). The effectiveness of in-person CBT-E in clinical practice using ROM data was evaluated for patients with BED. Through a naturalistic design, outcome predictors of CBT-E were also examined. The second treatment modality, presented in chapter eight, was a newly developed eMental Health version of CBT-E offered with 12 brief guided telephone sessions (guided self-help CBT-E) among patients with BED. The efficacy of guided self-help CBT-E for BED was examined through a randomized controlled trial (RCT) and an economic evaluation was undertaken alongside the RCT (chapter nine).

Part I Assessment, etiology, and correlates of eating disorder pathology

Main findings

Chapter two and three examined the validity of the two most used self-report measures: the EDE-Q and BSQ. Psychometric characteristics of the Saudi version of the EDE-Q were satisfactory and the results supported the discriminant and convergent validity as compared to a golden standard, the eating disorder examination (EDE), a semi-structured diagnostic interview. The Receiver-operating-characteristic curve analysis showed that the EDE-Q could accurately discriminate between individuals at high and low risk for an eating disorder according to the EDE (area-under-the-curve value = .84). Severity level of eating disorder pathology was accurately determined by the EDE-Q global score. The optimal cut off of 2.93 on the global score yielded a sensitivity of .82 and specificity of .80. Furthermore, chapter two showed that the original four factor model of the EDE-Q was not supported.

Chapter three showed that the psychometric characteristics of the Saudi-Arabic BSQ were good. Both its full version (BSQ34) and the short version (BSQ8C) discriminated well between low and high levels of body-shape dissatisfaction (area-under-the-curve value = .93) according to the eating disorder examination- shape concern subscale. In addition, both Saudi-Arabic BSQs had high internal consistency and a unidimensional factor structure. When optimal specificity was called for, e.g., when screening for need of treatment, a cut-off of raw score > 123 ($T > 59.1$) would seem more appropriate. Sensitivity and specificity were balanced at .85 when a cut-off of raw score > 114 (T -score > 57.0) was applied. For the BSQ8C cut-off values for raw score > 28 and T -score > 56.4 were suggested. Cut-off values on the T score scale approximate quite well the generally recommend $T = 55$ to $T = 60$ for the transition from normal to clinical. The BSQ34 supplied more information on the type of concerns respondents had, which is worthwhile when the measure is used in clinical settings; the BSQ8C is recommended as a short screener.

In a systematic scoping review (chapter four), which included 81 studies and four websites that involved statistical data, such as GCC-stat, the number of Saudis who scored above a clinical cut-off on eating disorder measures were examined. In this review, 2- 55% scored above a clinical cut-off. Rates were higher among women (11.4- 54.8%) than among men (2- 47.3%) on eating disorder screening instruments. For chapter two of this dissertation, data regarding the prevalence of eating disorder pathology were collected in a Saudi community convenience sample. In this study ($N = 2690$), it was estimated that 28,8% ($n = 775$) of the sample screened positive on the EDE-Q. This was 28.5% ($n = 598$) for women and 29.7% ($n = 177$) for men, which was within the ranges of positive screens presented in chapter four. In chapter two, a subset ($N = 98$) was also subjected to the EDE interview. At first, participants with high scores on the EDE-Q were invited for an EDE interview. Later on, participants were randomly invited. On the EDE, 45% ($n = 44$) scored two standard deviations above average. The participants were consistent in presentation of the severity of their eating disorder pathology. However, they were not consistent in their symptom presentation between the EDE and EDE-Q. Therefore, data were insufficient to examine the exact prevalence of the various eating disorder symptoms. However, it was most likely that binge- eating was the most common eating disorder symptom. Around half of the Saudis included reported excess weight while BED was associated with high BMI. Furthermore, it is estimated that around 1/3 of individuals with excess weight suffered from BED (Van der Horst et al., 2019). The conclusion that BED was the most common eating disorder in Saudi Arabia was supported by the only study available that recently has been conducted: the Saudi National Health Survey among a large group of Saudis ($N = 4004$). That study reported a 12-months eating disorder prevalence of 3.2% and a life-time prevalence of 6.1%. BED was the most common eating disorder with a 12-months prevalence of 2.1% and a life-time prevalence of 2.6% (AlHadi et al., 2022). The review presented in chapter four established a gender difference, while our

data (reported on in chapter two and three) showed that there were no differences in eating disorder pathology between both genders, a finding in line with AlHadi., et al (2022).

This dissertation also investigated the prevalence of body-shape dissatisfaction in a Saudi convenience community sample, mainly existing of highly educated young women. On the Saudi-Arabic BSQ (see chapter three) it was found that among a total of $N = 867$ Saudis, 26.7% ($n = 231$) of them appeared at risk for body-shape dissatisfaction. However, the systematic review (chapter four) showed that on the Stunkard's body silhouettes test (Stunkard et al., 1983), around 66% of the Saudis displayed body-shape dissatisfaction (Madanat et al., 2011). The Stunkard's body silhouettes test was completed by a community sample of women who lived in urbanized areas. Chapter three did not find differences in body-shape dissatisfaction between women and men, while studies included in the review in chapter four found that women were more at risk for body-shape dissatisfaction than men (Al-Sendi et al., 2004; Ford et al., 1990). The substantial difference in body-shape dissatisfaction may be explained by the use of different measures. Another explanation could be that the Stunkard's body silhouettes test (Stunkard et al., 1983) is not valid for use in Arabic cultures (its validity has not been investigated). In addition, the studies included in the review did not use the culturally appropriate norms and the screeners used were not culturally adapted. This might have impacted the estimate rates and the gender differences that have been reported.

Lastly, chapter four and five of part I investigated potential predisposing factors for the development of eating disorder pathology. Both chapters confirmed that body shape-dissatisfaction was a correlate of eating disorder pathology. In addition, both studies concluded that higher BMI was associated with greater levels of body-shape dissatisfaction and eating disorder pathology. This is of great concern since currently Saudi Arabia has the highest prevalence of excess weight worldwide (Qamar Farshori et al., 2015; WHO, 2006). The review showed that Saudis with excess weight are known to be 2-3 times more likely to

develop eating disorder pathology than Saudis without excess weight, which was confirmed by the recently conducted Saudi national epidemiological survey (AlHadi et al., 2022). The high rates found of eating disorder pathology and body-shape dissatisfaction may be a reflection of the high rates of excess weight and maladaptive strategies for weight loss in Saudi Arabia. In addition, chapter five showed that high BMI is a covariate in the association between body-shape dissatisfaction and eating disorder pathology in Saudi Arabia.

The systematic review also examined other potential correlates of eating disorder pathology than BMI and body-shape dissatisfaction. It was found that eating disorder pathology in Saudi Arabia was associated with a western cultural orientation, high socioeconomic status and media use. In our cross-sectional study we found that unmarried Saudis reported more eating disorder pathology than married Saudis, which is in line with recent findings (AlHadi et al., 2022). In univariate analyses, it was found that socio-economic status was moderately associated with eating disorder pathology and a weak association was found between eating disorder pathology and media use. However, according to a multivariate regression analysis, only body-shape dissatisfaction and BMI were significantly associated with eating disorder pathology. Low self-esteem, western cultural orientation rather than Arab orientation, increased levels of stress, frequency of media use, and high socio-economic status were no longer associated with eating disorder pathology. Furthermore, the review suggested that cultural orientation was potentially associated with different types of symptomatology: western cultural orientation may be associated with bulimic symptoms and Arab cultural orientation may be associated with anorexic symptoms. This hypothesis was not confirmed in our cross-sectional study. Failure to reproduce the association between western cultural orientation and eating disorder pathology might be explained by the fact that only small associations were found in other studies (AlShebali et al., 2020; Thomas et al., 2018). Another explanation might be that eating disorder pathology was rather associated with

industrialization instead of westernization. Saudi Arabia also dealt with industrialization, while rapid industrialization is associated with increased risk for eating disorders (Ghubash et al., 2001; Nakai et al., 2018). The frequency of social media use was not associated with eating disorder pathology. Also other studies suggest that greater emotional investment, negative feedback seeking and social comparison were rather associated with eating disorder pathology instead of the frequency of media use (Fardouly et al., 2015; Holland & Tiggeman, 2016).

It can be concluded that eating disorder pathology is prevalent in Saudi Arabia, and BED appeared the most common eating disorder, a result also found for the western world. It can be concluded that young, highly educated women are at risk for the development of eating disorder pathology and body-shape dissatisfaction. Body-shape dissatisfaction and high BMI were associated with eating disorder pathology and the adapted EDE-Q and BSQ appeared reliable assessment tools.

Limitations and strengths

One of the major limitations that arose from the systematic review presented in chapter four was that many findings were based on non-validated assessment tools that were used in the included studies. For instance, several studies translated the EAT-40 or EAT-26 without adaptations, and used western norms (Eapen et al., 2006; Eladawi et al., 2018; Nasser, 1994). Use of non-validated assessment tools which were not adapted to the culture at hand is unfortunate, as it may lead to underestimation of symptom severity (Darcy et al., 2012), elevated rates of undiagnosed eating disorders, to a lack of knowledge and awareness about eating disorders (Griffiths et al., 2015) and may hamper timely proper treatment (Al Khadari 2016).

Another limitation of the systematic review was that several studies failed to provide essential information on the norms used, or how their statistical analysis was conducted (Musaiger & Al- Mannai, 2013). Furthermore, none of the studies on binge-eating behavior mentioned the frequency of binge-eating episodes, or whether the binges were of subjective or objective nature (Al Adawi et al., 2002; Latzer et al., 2009; Mousa, Al-Domi, et al., 2010; O'Hara et al., 2016). All the studies included in the systematic review relied on self-report measures, prone to socially desirable responding (Musaiger 2013). The resulting bias in self-report data may be even stronger present in the Saudi context, since the collectivistic culture of the Arab world made people hesitant to report individual desires (Raouf 2016). Consequently, the use of self-report measures made studies vulnerable to under- or overestimation of complaints (Mousa, Al-Domi, et al., 2010).

The studies presented in chapter two, three, and five also included several limitations: the samples were biased for age, gender and level of education. Therefore, all results should be interpreted with caution. A too large proportion of the samples consisted of highly educated young Saudi women. It is also likely that mainly more progressive men participated in the EDE interviews since Saudi Arabia dealt with strict gender separations in 2017 and 2018 and all the EDE interviews were conducted by women. This might have affected the study participation rate of men, as well as their willingness to confide in pathological eating behavior. At the same time, there were no effects of gender, age and level of education on eating disorder pathology and the EDE-Q and BSQ performed similarly among both genders and various age groups. In addition, chapter two describes our efforts to counteract the potential effect of selection bias. The percentile scores were separately presented for men and women and corrected for level of education by propensity weighting. Unmeasured factors also might have caused selection bias: participants might have had special interest in health care, mental health care or eating disorders, which motivated them to take part in the survey. In

addition, the psychometric properties of the Saudi EDE-Q and BSQ, and correlates of eating disorder pathology were investigated among community samples. Such studies among clinical samples were more reliable and show increased generalizability. Unfortunately, it appeared impossible to collect clinical data in order to examine the psychometric properties of the EDE-Q and BSQ and predisposing factors. There is a taboo on mental health and a stigma on psychotherapy (Latzer et al., 2009), therefore Saudis barely seek help and Saudi Arabia deals with a lack of specialists to treat body-shape dissatisfaction and eating disorders (Alkadari 2016).. In addition, the cross-sectional nature of the data described in chapters two, three and five also came with limitations. Only associations among eating disorder pathology and other variables could be investigated and it was not possible to address questions about causal relationships (e.g., “Is the rise of eating disorder pathology in Saudi Arabia due to body-shape dissatisfaction or is body-shape dissatisfaction a consequence of eating disorder pathology?”) Of the psychometric properties, we did not assess test-retest reliability, nor investigated whether the EDE-Q and BSQ were sensitive to change.

To evaluate the screening ability of the EDE-Q and BSQ we used a score above the community mean + 1 standard deviation on the EDE global score or the EDE shape concern subscale, respectively. The EDE is the gold standard to measure eating disorder pathology. It is yet not validated in Saudi Arabia. Moreover, some cultural adaptations were made to the EDE. Furthermore, due to the lack of a suitable alternative, the EDE appeared the best option due to it being assessor based and its detailed nature. In addition, the EDE measured pathology over the same period as the BSQ and EDE-Q and had the same rating scale and similar phrases and word use as the EDE-Q.

This thesis also includes several strengths. As Saudis are an understudied population, this dissertation was among one of the first studies examining eating disorder pathology in Saudi Arabia. In addition, it is the first study to examine eating disorder pathology with

validated and culturally adapted assessment tools. It is one of the few studies with large sample sizes, which provided ample statistical power to demonstrate significant associations. Sample sizes were large, despite all the challenges to collect data among Saudis, as they are perceived as a socially reclusive society. Compared to western societies, Saudis are quite sensitive to how they are perceived by others, and therefore, less inclined to participate in surveys where they are asked to express their personal values and beliefs (Al Darmaki 2003). Therefore, a lot of effort had to be put in data collection. In addition, Saudi Arabia dealt with stigma in relation to mental health problems, and a lack of knowledge about eating disorders (Alkhadari et al., 2016; Latzer et al., 2009). Therefore, study participation in this study was not self-evident for Saudis, as feelings of mistrust, lack of knowledge and awareness were barriers for study participation in other studies (Williams 2013, Schmotzer 2012, Honein-AbouHaidar 2016).

Other strengths were that chapter two and three were the first studies to be supplemented with interview data in order to understand the culture at hand (Gordon, 2001; AlHadi 2022). Though clinical samples were not available, analyses were repeated in a subsample at high risk for eating disorder pathology. Last, this dissertation evaluated the psychometric properties of the Saudi Arabic EDE-Q and BSQ and to provide preliminary normative data. In addition, this dissertation could be perceived as a first step to expanding knowledge regarding an understudied population investigating assessment, etiology and correlates of eating disorder pathology in Saudi Arabia.

Clinical implications

Results of the four studies included in part I indicated that eating disorder pathology and body-shape dissatisfaction are prevalent in Saudi Arabia. Since only body-shape dissatisfaction and a high BMI were found to be correlates of the severity of eating disorder

pathology it is recommended to offer preventative programs targeted to Saudis with excess weight and body- shape dissatisfaction. The proposed cut-offs of the EDE-Q and BSQ can be used to select Saudis for such programs aimed at avoiding the development of eating disorder pathology (Stice & Shaw, 2002). In addition, life style interventions counteracting the increase of the prevalence of excess weight in order to prevent associated health risks (Madanat et al., 2007), accompanied by psycho-education in order to prevent maladaptive weight-loss strategies, may be beneficial. In addition, Saudis with excess weight currently tend to seek bariatric surgery, without the recommended, screening for eating disorders taking place.

Screening for eating disorders and referral of Saudis at high risk for eating disorders might reduce delayed help seeking and prevent increased severity of eating disorder pathology. In addition, the Saudi-Arabic EDE-Q and BSQ could be used to measure reduction of eating disorder symptoms after eating disorder treatment. Furthermore, the availability of normalized standard scores (*T*-scores), will ease interpretation of test results and increase applicability of the BSQ (de Beurs et al., 2022). However, treatment is hampered by the lack of specialized therapists and treatment facilities (Qadan, 2009). More attention for eating disorder pathology is called for. Increased knowledge about eating disorders might decrease the current preference for self- or family help, and therefore counteract stigma associated with psychotherapy. Increased knowledge and awareness could be achieved by offering psycho-education at high-schools, including a parental program. Once college and high-school social workers are better educated in the recognition of eating disorders, they can refer their students to mental health care clinics. Furthermore, eating disorders should become a disorder of primary care in Saudi Arabia and therapists should be trained in treatment of eating disorders.

Future studies

This dissertation evaluated the psychometric properties and established norms for the Saudi-Arabic EDE-Q and BSQ. It is recommended to further examine the test- retest reliability of both measures in the Saudi context. Future studies should include data from clinical samples diagnosed with eating disorders. In order to increase generalizability such samples should be more balanced with regard to age, gender and level of education. Furthermore, the EDE, a detailed assessor-based interview, should be validated and become available in a Saudi- Arabic version to ease diagnosis of eating disorders. Concordance on eating disorder behaviors such as binge-eating and self-induced vomiting is only moderate at best (Berg 2012).

In order to investigate causal relationships between risk factors for eating disorder pathology, future studies should involve longitudinal designs. Such studies could potentially estimate whether high BMI and body-shape dissatisfaction caused eating disorder pathology or are a result of such pathology. In addition, the association between eating disorder pathology and social media use should focus on emotional involvement instead of solely establishing the frequency of social media use. When examining the association between westernization and eating disorder pathology a valid assessment tool should be used to measure eating disorder pathology. Moreover, it would be of interest to investigate the effect of recent transformations to modernize Saudi society, for example by releasing the obligation for women to wear an abaya, and whether this impacts body-shape dissatisfaction and eating disorder pathology. For instance, body-shape dissatisfaction could be compared between women who still wear an abaya and women who have decided not to wear the traditional abaya anymore. Last, since data from clinical samples are more reliable it is recommended to examine test- retest reliability of the EDE-Q and BSQ and associations or risk factors for eating disorder pathology among Saudis diagnosed with an eating disorder.

Part II Treatment

Main findings

Chapter six showed that in-person CBT-E is an effective treatment among adult patients diagnosed with BED outside the confines of a randomized controlled trial. At the end of treatment, 48% (42/113) showed abstinence from binges and 65% (74/113) had an EDE-Q score below clinical cut-off. Full recovery (abstinence from binges combined with an EDE-Q score below clinical cut-off) was achieved by 37% (54/113) and effect sizes of reduction in EDE-Q score were large. The results of this naturalistic study were comparable to other previously conducted naturalistic studies (Byrne et al., 2011; Dalle Grave et al., 2015; Knott et al., 2015; Wade et al., 2017). However, in chapter six larger effect sizes were found than in other studies that have been conducted. In addition, compared to trials conducted by Fairburn, chapter six found a somewhat lower effectiveness of in-person CBT-E (Fairburn et al., 2009; Fairburn et al., 2015). This diminished effectiveness of in-person CBT-E could not be explained by a low eating disorder severity at start, since severity at start was generally higher in the current thesis compared to other studies (Byrne et al., 2017; Poulsen et al., 2014; Wonderlich et al., 2014).

Consistent with the transdiagnostic nature of CBT-E, the naturalistic study displayed in chapter six showed that there were no differences in treatment outcomes among patients diagnosed with BED, BN, their respective OSFEDs and atypical AN. In addition, drop-out from treatment was only predicted by the diagnosis of BN. Furthermore, higher level of education predicted better treatment outcome at end of treatment and men had better treatment outcomes compared to women at 20 weeks follow-up. In line with several other studies which examined predictors of in-person CBT-E (Masheb & Grilo, 2008; Vall & Wade, 2015) or in-person CBT for BED (Lammers et al., 2015; Peterson et al., 2000), severity of the eating

disorder at start predicted a negative treatment outcome for all eating disorders at end of treatment and follow-up. However, the only exception was that eating disorder severity at start did not predict negative treatment outcomes at follow-up for BED patients. This indicated that 20 weeks after conclusion of in-person CBT-E, BED patients with a severe eating disorder did recover equally well as compared to patients with less severe eating disorders.

The naturalistic study conducted in chapter six also showed that there were no differences in treatment outcomes between the completers sample and the intention-to-treat sample. Therefore, patients might also recover with a less intense form of treatment (Berg et al., 2020; Moore et al., 2021; Waller et al., 2018), such as an online guided self-help. Therefore, in chapter eight a guided self-help version of CBT-E was compared in a randomized controlled trial (RCT) with a delayed treatment control design. Guided self-help CBT-E appeared superior to waiting for treatment. At end of treatment the experimental group showed greater rates of full recovery (as operationalized by an EDE score below clinical cut-off and abstinence from binges) than the delayed treatment control condition. In the guided self-help condition 40% (36/90) of the participants showed full recovery, abstinence from binge eating was reported by 48% (43/90) and eating disorder pathology score was below clinical cut-off for 63% (56/90) on interview data and 79% (71/90) on self-report data. Follow-up data revealed that there were no differences between groups after both conditions received treatment. The results based on self-report data were comparable to other studies who examined efficacy of in-person CBT-E (Dalle Grave et al., 2015; Fairburn et al., 2015; Poulsen et al., 2014; Wade et al., 2017) and guided self-help versions of CBT (Carter & Fairburn, 1998; Grilo et al., 2005; Hilbert et al., 2019). It should be noted that due to a lack of studies focusing specifically on BED populations, comparisons of present study results with in-person CBT-E are mostly made with transdiagnostic patient samples or BN patients.

However, chapter eight showed greater effect sizes compared to studies conducted by others. Comparisons with in-person CBT-E based on interview data were inconclusive: some studies showed that in-person CBT-E was superior to guided self-help CBT-E (Fairburn et al., 2015), some that in-person CBT-E was inferior (Wonderlich et al., 2014) and some showed equal outcomes (Poulsen et al., 2014; Thompson-Brenner et al., 2016).

Though chapter six and eight have different study designs, at Novarum center for eating disorders BED patients showed comparable rates of abstinence of binges after in-person CBT-E offered as treatment as usual and after online guided self-help CBT-E offered in an RCT. At end of treatment, 48% of the patients reported abstinence from binge eating. Furthermore, based on self-report data, around 80% of the BED patients who received guided self-help CBT-E reported scores under the clinical cut-off while this was 65% after conclusion of in-person CBT-E. Cautiously, guided self-help CBT-E seems as effective as in-person CBT-E.

The economic evaluation presented in chapter nine showed that guided self-help CBT-E led to a greater number of binges prevented, and greater QALY gain, but at higher costs, compared to waiting for treatment. Guided self-help CBT-E can be seen as a reasonable investment for the Dutch health care system as costs of one QALY gain are within the NICE willingness-to-pay threshold of €35,000 per QALY (NICE, 2023), and the Dutch willingness-to-pay threshold of €80,000 for severe diseases (Zwaap et al., 2015). In addition, costs per QALY gain were lower in the current study than in another study which found a willingness-to-pay of €50,000 for guided self-help CBT for BED (König et al., 2018). However, still, guided self-help CBT-E appeared an expensive treatment. This is most probably because the EQ-5D-3L was not specifically validated for BED. In addition, several questions have been raised whether the EQ-5D-3L should be used in economic evaluations of mental health care interventions. Due to a limited coverage of relevant domains of areas that are relevant to some

patients with mental health care problems (e.g. psychosis), the psychometric properties of the EQ-5D-3L showed mixed results (Brazier, 2014). However, the EQ-5D-3L appeared the most sufficient assessment tool, and therefore it is still likely that guided self-help CBT-E is cost-effective.

Chapter nine showed also that there were no differences in costs between the two conditions, except for outpatient mental healthcare costs. These outpatient mental health care costs were associated with the guided self-help CBT-E intervention provided to the experimental group. The results remained stable in the sensitivity analyses, supporting the robustness of the findings. Findings of current study are in line with the few studies available which indicated that guided self-help interventions for binge eating are cost-effective (König et al., 2018; Lynch et al., 2010).

Limitations and strengths

Part II has several limitations. A significant limitation of the effectiveness, efficacy and economic evaluation studies was the time horizon. Chapter eight and nine showed efficacy and cost-effectiveness over a three months time horizon. Since patients randomized to the waiting-list also received guided self-help CBT-E during follow-up, comparison of efficacy, cost-effectiveness and cost-utility was not possible after three months. This precluded evaluation of long-term effectiveness as well as the costs of guided self-help CBT-E as compared to no treatment. With regard to efficacy of guided self-help CBT-E only within group comparisons were meaningful during follow-up, though this was taken in consideration with the choice of statistical analyses. A different study design, with a comparison to a treatment-as-usual control condition (e.g., in-person CBT-E), would have enabled comparison of efficacy and an economic evaluation with a longer time horizon, which is recommended for

future research. In addition, effectiveness of in-person CBT-E in chapter six could only be examined until 20-weeks of follow-up. Longer term follow-up data were necessary in order to assess if long-term recovery was attained.

Another limitation of the designs was that chapter six was based on self-report data and the follow-up data of chapter eight and nine were only measured by self-report. Interview data are generally viewed as more reliable, especially when measuring binge eating behavior (Berg et al., 2012). Low concordance between interview and self-report data was also demonstrated in our data. In chapter eight, the frequency of objective binges at end of treatment showed a moderate relationship between interview and self-report data. This limits the comparison of the self-reported number of binges after conclusion of in-person CBT-E (chapter six) and number of binges as assessed by independent assessors after conclusion of guided self-help CBT-E (chapter eight). In both studies 48% of the BED patients showed abstinence from binges. However, around the globe there is high concordance of eating disorder severity as measured by self-report and interview data (Berg 2011, Berg 2012, (Melisse et al., 2021). Therefore, guided self-help CBT-E could be as effective as in-person CBT-E when outcomes are based on scores on the clinical cut-off of eating disorder measures. The use of self-report data was also a limitation of the economic evaluation. Though patient's electronic files were used to establish all mental health care costs of patients within Arkin foundation, other cost data were based on patients self-report which may have been affected by recall bias. However, in order to reduce the potential impact of recall bias, health care utilization and number of binges were only measured over the month before end of treatment and extrapolated over three months between the assessments.

The (absence of a) control group was also a limitation. Comparison of guided self-help CBT-E to waiting for treatment in chapter eight and nine had further limitations. Comparison to treatment-as-usual or another active comparator instead of a waiting-list would better

reflect what normally would happen in the absence of guided self-help CBT-E (Richards, 2020). In addition, it should be noted that treatment expectation may play a role when comparing active treatment to a waitlist condition (Constantino, 2018). Treatment expectation might affect symptomatology during the waiting period before treatment. However, the extend of this effect could not be established as treatment expectancy was not assessed. In addition, chapter six only measured eating disorder pathology at start and at end of CBT-E treatment. The lack of a control group in chapter six did not allow to compare effectiveness to waiting for treatment or another treatment.

Protocol adherence was not measured in chapter six. The studies reported on in Chapter eight and nine did included assessment of protocol adherence, but only by means of self-report of the therapists. Weekly supervision meetings were held to ensure protocol adherence, but the additional use of an adherence checklist, which recently became available for CBT-E (Bailey-Straebl et al., 2022), or adherence assessment by an independent rater would have yielded more valid information regarding treatment integrity (Lopez-Alcalde et al., 2022).

Last, all studies were biased for gender by an underrepresentation of men. Though 10% of the patients with AN or BN and around 35% of the patients with BED are men (Kessler et al., 2013), only 10% of the BED patients and less than 5% of the BN and atypical AN patients included in chapter 6-8 were men. However, no effect of gender was found on eating disorder pathology and the frequency of binges. The underrepresentation of males is common to most eating disorder studies and limits the generalizability of the findings (Shingleton et al., 2015).

Strength of all studies was that they were conducted in a relevant clinical context. Results could potentially be generalized to eating disorder clinics in the Netherlands, since treatments were conducted in a specialized eating disorder treatment center. However, it

should be noted that Novarum is known for its evidence-based approach, highly structured treatment provision, and trained therapists. All therapists received weekly supervision to ensure protocol adherence. Furthermore, therapists that offered treatment in the RCT received an additional weekly supervision session. All studies were adequately powered, had larger sample sizes than most previously conducted studies (de Zwaan et al., 2017; König et al., 2018; Lynch et al., 2010) and used advanced statistical techniques, such as multiple imputations to handle missing data. Internationally used valid self-report instruments (Bohn et al., 2008; Fairburn & Beglin, 2008) were administered. Furthermore, efficacy of guided self-help CBT-E at end of treatment was examined by standardized interview data (Cooper & Fairburn, 1987; Jansen, 2000). Moreover, the studies reported on in chapter eight and nine had some additional strengths compared to the study of chapter six. Guided self-help CBT-E was a manualized treatment. In addition, compared to in-person CBT-E, patients who received guided self-help CBT-E came to a greater extent from all over the Netherlands. Therefore, the sample can be deemed representative for patients seeking specialized eating disorder treatment in the Netherlands. A special mention deserves the Covid-19 pandemic. Fortunately, due to the treatment delivery mode (eMental Health) of guided self-help CBT-E, the social distancing measures of the pandemic had limited impact on the study's execution. Nevertheless, COVID-19 might have affected the outcome of the treatments negatively, as many patients reported that it was a challenge to combine therapy, work and home-schooling kids at the same time. This would suggest that guided self-help CBT-E might potentially demonstrate even better outcomes under less adverse circumstances. Last, this was the first study to examine efficacy of guided self-help CBT-E and the first to perform an economic evaluation of a guided self-help intervention which only included full-syndrome BED patients.

Clinical implications

In concordance with the Dutch guidelines (Zorgstandaard, 2021) CBT-E is an effective treatment when offered in clinical real world setting to patients with BED, BN, their respective OSFEDs and atypical AN. With regard to personalized medicine, especially men, highly educated patients and patients with severe BED benefit well from in-person CBT-E. Therefore, in-person CBT-E should be the treatment of choice for men and highly educated patients with BN, and atypical AN. Since the diagnosis of BN predicts treatment dropout, the motivational phase of the CBT-E underweight (Fairburn, 2008; van den Berg & Schlochtermeyer, 2017) could be considered when patients show low levels of motivation for treatment at start.

In concordance with the stepped care principle (Mitchell et al., 2011) and international guidelines (ANZAED, 2014; NICE, 2017) guided self-help CBT-E could be the first treatment of choice for patients with BED. When future studies confirm that guided self-help CBT-E appears non-inferior to in-person CBT-E, guided self-help CBT-E should be the first treatment of choice for patients diagnosed with BED. Preferably, the least resource-intensive treatment is delivered first (Mitchell et al., 2011). However, investigation of predictors of treatment outcomes of guided self-help CBT-E would enhance personalized medicine for BED (Kraemer, 2013) and enable information whether patients with severe BED should receive in-person CBT-E or guided self-help CBT-E. Furthermore, guided self-help treatment increased access to treatment (Abrahamsson et al., 2018; Mulken Sandra, 2021). Moreover, guided self-help CBT-E could potentially enhance access to treatment over the globe when adapted to various socio-cultural contexts and offered among other cultures. Guided self-help CBT-E could be a resolution in Saudi Arabia to deal with the great distances, the lack of specialized treatment centers and therapists and long waiting periods. Before and during the Covid-19 pandemic several studies have shown that outcomes of remotely offered

psychotherapy either as treatment as usual or eMental Health, including CBT-E, are on par with in-person offered psychotherapy (Abrahamsson et al., 2018; Backhaus et al., 2012; de Beurs, 2022; Nelson & Duncan, 2015; Raykos et al., 2021; Trainor et al., 2020; Wang, 2022). In addition, remotely offered CBT-E is accepted by clinicians and patients (Jenkins-Guarnieri et al., 2015; Raykos et al., 2021; Rees & Stone, 2005), especially in sparsely populated areas and among patients living in the periphery (Simpson, 2009). Furthermore, even when remotely offered treatment was not accepted by patients, treatment outcomes were positive (Linardon, 2022). However, informing the patient about guided self-help CBT-E will help patients to understand and engage in the process (Waller, 2020). Moreover, another benefit from guided self-help CBT-E is that patients are more likely to attribute the results of treatment to their own efforts rather than the help of therapists. This in turn will help them enhance their sense of self-efficacy, confidence and motivation to complete treatment (Vallejo et al., 2015). This proved that guided self-help CBT-E can have a positive effect on eating disorders around the globe. However, it should be noted that in case emergency interventions appear necessary, such as in the situation of expressions of suicidal ideations during remote sessions, emergency services should be contacted while the patient is on the line (Waller, 2020). In addition, guided self-help CBT-E is not recommended when patients engage in aggressive behavior, or have serious emotional problems (Murphy et al., 2020).

Future studies

Guided self-help CBT-E holds the promise of being a cost-effective alternative to traditional treatment. However, the majority of data were collected during the Covid-19 pandemic. Therefore, future work in non-pandemic circumstances should replicate the positive outcomes of guided self-help CBT-E before further implementation (Gorrell Sasha, 2022). In addition, future studies are necessary to estimate if the results could be replicated in

other specialized eating disorder centers. Furthermore, it is of interest to examine predictors of guided self-help CBT-E. Furthermore, it is yet unclear whether guided self-help CBT-E is definitely non-inferior to in-person CBT-E, as the results of the various studies conducted who compared guided self-help CBT to in-person CBT were inconclusive (Bailer et al., 2004; de Zwaan et al., 2017; Zerwas et al., 2017). Subsequently, a logical next step for future research is to compare the effectiveness of guided self-help CBT-E with in-person CBT-E in an RCT. Such an RCT could potentially confirm if the stepped care principle should be followed and if patients can recover with a less intense form of CBT-E (Moore et al., 2021, Waller et al., 2018). When non-inferior, guided self-help CBT-E has the potential to reduce waiting times for specialized treatment (Carter 2012). In addition, when moderators of treatment are known, the Dutch guidelines should then recommend guided self-help for BED instead of in-person CBT-E as a first line of treatment.

Future studies are also recommended to assess recovery beyond 24 weeks after end of treatment. This will enable comparisons of efficacy and cost-effectiveness over a longer timeline and further enhance decision making since the scarce resources can be allocated where they offer best value for money (Konnopka et al., 2009; Stuhldreher et al., 2012). More importantly, it is also recommended to examine the efficacy of guided self-help CBT-E through video call instead of by telephone as patients can see their appearance and body on the screen during treatment. This potentially is an intervention on its own as it enhances body and weight acceptance and tolerance, and consequently changes the evaluation of body and weight to some extent (Murphy et al., 2020). Future studies should not solely rely on self-report but collect interview data as they are deemed more reliable (Berg et al., 2012). However, such valid interview assessments are currently not available in Saudi Arabia. Therefore the Saudi- Arabic EDE-Q and BSQ can be used to evaluate progression of treatment in Saudi Arabia.

Examination whether guided self-help CBT-E reduces general psychopathology is also of interest. Once guided self-help CBT-E shows long-term effectiveness including general psychopathology, investigating its effect among other eating disorder populations, such as patients suffering from non-purging BN is recommended. Several studies already showed that guided self-help interventions based on regular CBT showed positive outcomes for patients with BN (Carrard et al., 2011; Zerwas et al., 2017). Last, knowledge of guided self-help CBT-E predictors or moderators around the globe, enhances decision making by offering in-person or guided self-help CBT-E or a different type of treatment (Kraemer, 2016).

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