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

Melisse, B.

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Chapter 9 Economic Evaluation of Web-based Guided Self-help Cognitive Behavioral Therapy- Enhanced for Binge- Eating Disorder Compared to a Waiting-List: a Randomized Controlled Trial

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Abstract

Introduction: The aim is to perform an economic evaluation alongside a randomized controlled trial comparing guided self-help Cognitive Behavioral Therapy- Enhanced (CBT-E) for binge-eating disorder (BED) to a waiting-list control condition.

Methods: BED patients (*N*=212) were randomly assigned to guided self-help CBT-E or to the three-month waiting-list. Measurements took place at baseline and at the end-of-treatment. The cost-effectiveness analysis was performed using number of binges during the last 28-days as outcome indicator according to the Eating Disorder Examination. A cost-utility analysis was performed using the EuroQol-5D.

Results: The difference in societal costs over the three-months of the intervention between both conditions was €641 [CI -86-1,393]. The incremental costs associated with one incremental binge prevented in the guided self-help condition was approximately €17 [CI -2-40]. From a societal perspective there was a 96% likelihood that guided self-help CBT-E led to a greater number of binges prevented, but at higher costs. Each additional QALY gained was associated with incremental costs of €33,000 [CI -4619-151,393]. With a 95% likelihood guided self-help CBT-E led to greater QALY gain at higher costs compared to waiting for treatment. Based on the NICE willingness-to-pay threshold of €35,000 per QALY, guided self-help CBT-E can be considered cost-effective with a likelihood of 95% from a societal perspective.

Discussion: Guided self-help CBT-E is likely a cost-effective treatment for BED in the short-term (three-months course of treatment). Comparison to treatment-as-usual is recommended for future research, as it enables an economic evaluation with a longer time horizon.

Public significance statement: Offering treatment remotely has several benefits for patients suffering from binge-eating disorder. Guided self-help CBT-E is an efficacious and likely

cost-effective treatment, reducing binge-eating and improving quality-of-life, albeit at higher societal costs.

Keywords: Randomized Controlled Trial; Binge-eating disorder; Guided self-help; Cognitive Behavioral Therapy-Enhanced; Cost-effectiveness; Cost-utility, Economic evaluation

Trial registration: The study protocol is registered with the Netherlands Trial Registry NTR (NTR 7994) since 6 September 2019.

Ethics: Study approval was given in August 2019 by the Medical Research Ethics Committees United (MEC-U) (reference number NL 6958.100.19) in Nieuwegein, the Netherlands.

Introduction

Binge-eating disorder (BED) is characterized by recurrent episodes of binge-eating accompanied by a sense of lack of control. Inadequate compensatory behavior such as self-induced vomiting and laxative misuse are absent. After binge-eating, patients experience feelings of shame, guilt, and disgust (APA, 2013). BED is associated with decreased quality-of-life, increased risk of excess weight, diabetes mellitus, and other non-communicable diseases. In addition, patients with BED experience poorer psychosocial functioning and poorer somatic health compared to individuals who merely suffer from excess weight (Melisse et al., 2020; Mond & Hay, 2007). The medical conditions associated with BED will potentially result in increased health care utilization and other societal costs including productivity losses (Aardoom et al., 2016; Agh et al., 2015; Striegel et al., 2012; van Hoeken & Hoek, 2020). Efficacious treatments are important in order to reduce the personal and societal burden of BED (Lynch et al., 2010). However, the exact reduction in quality-of-life of BED and costs of quality-of-life gain after treatment are unknown. When evaluating the economic impact of treatment for BED, such costs should also be considered.

Cognitive behavior therapy-enhanced (CBT-E) is an evidence-based treatment for eating disorders (Fairburn, 2008; Melisse et al., 2022). However, the BED international guidelines recommend guided self-help (ANZAED, 2014; NICE, 2017). Therefore, a promising web-based guided self-help version of CBT-E (guided self-help CBT-E) was developed (Melisse et al., 2023). Guided self-help CBT-E has several benefits for patients compared with in-person CBT-E, such as the removal of geographical barriers (Abrahamsson et al., 2018; Becker et al., 2010; Evans et al., 2011; Linardon et al., 2021). Furthermore, guided self-help CBT-E requires less therapist involvement, and is briefer than in-person CBT-E, and therefore associated with lower costs of offering treatment. For example, costs of offering guided self-help based on regular CBT vary between €630- €900, whereas costs for in-person CBT-E are

around €3,500 (Jenkins, 2021; König et al., 2018; van den Berg et al., 2020). In addition, a cost-effectiveness study of guided self-help for BED estimated the willingness-to-pay per binge-free day, representing the maximum amount that society is willing to pay for an additional unit of health outcome, between €118-177 (Jenkins, 2021).

Guided self-help CBT-E has been shown to be an efficacious treatment for BED (Melisse et al., 2023; Striegel-Moore et al., 2010). In order to distinguish the efficiency of the various eating disorder treatments (Streatfeild, 2021), it is important to evaluate the cost-effectiveness of guided self-help CBT-E. There is only limited economic evidence for the effect of BED treatments, for both in-person and guided self-help versions of CBT (König et al., 2018). In addition most economic evaluations face marked limitations: they do not involve BED (Striegel-Moore et al., 2008) and predominantly focus on younger patient populations, whereas BED affects patients of all ages (Ling et al., 2017; Streatfeild, 2021). Furthermore, most studies neglect costs outside of the health-care system (Streatfeild, 2021). Society's monetary valuation of health care benefits are represented by a willingness-to-pay (Steigenberger et al., 2022) for one quality-adjusted-life-year (QALY). One QALY is defined as one extra year lived in perfect health based on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (EuroQol-Group, 1990). One study showed that guided self-help for BED was likely to be cost-effective compared to treatment-as-usual, with an estimated willingness-to-pay per QALY gained of around €50,000 (König et al., 2018). No study has yet to provide an economic evaluation of web-based guided self-help CBT-E for BED compared to a waiting-list. Comparison to a waiting-list allows to examine if the costs and effects of guided self-help CBT-E are a reasonable investment compared to the costs of waiting for treatment.

The aim of present economic evaluation is to determine cost-effectiveness (costs per binge prevented) and cost-utility (costs per QALY gain) of web-based guided self-help CBT-

E for BED as compared to a waiting-list control condition. This will be measured alongside a randomized controlled trial (RCT) primarily examining the efficacy of guided self-help CBT-E. The economic evaluation will be performed from a societal perspective, covering all effects and costs of guided self-help CBT-E on the whole of society. It's expected that from a societal perspective guided self-help CBT-E will be more effective (binges prevented and increase in quality-of-life) compared to waiting for treatment, however, this will come at higher costs which are associated with the guided self-help CBT-E intervention.

2. Methods

2.1 Design

This economic evaluation of guided self-help CBT-E was performed using data obtained from a two-arm efficacy RCT among patients with BED or other specified feeding or eating disorder (OSFED)-BED. An extensive description of the study protocol (van den Berg et al., 2020) and efficacy results were published elsewhere (Melisse et al., 2023). The RCT had a balanced allocation (1:1) to either (i) guided self-help CBT-E (N = 106) or to (ii) a waiting-list with a delayed treatment control condition (N = 106). Participants (N=180) were recruited to take part in the efficacy study (Melisse et al., 2023). However, the first 51 participants were not administered the questionnaire on health care utilization and productivity losses (TiC-P; Hakkaart-van Roijen et al., 2002). Therefore, their data could not be used for the economic evaluation. Hence, an additional 83 participants were recruited (N= 212). The economic evaluation will focus on the three-month phase before the wait-listed participants received guided self-help CBT-E. The study protocol is registered with the Netherlands Trial Registry (NTR 7994), and was approved by the Medical Research Ethics Committees United (NL6958.100.19). The economic evaluation was performed and reported in line with the CHEERS guidelines (Husereau et al., 2013) and the ISPOR guideline for economic evaluation alongside RCTs (Ramsey et al., 2015).

2.2 Procedure

Potentially eligible patients referred to Novarum center for eating disorders (part of Arkin Mental Health Care) were invited to participate in the study. After the patients signed the informed consent, a baseline assessment was administered to assess for exclusion criteria, and to measure the severity of BED. Patients who met all inclusion criteria and no exclusion criteria were randomly allocated to the guided self-help CBT-E or waiting-list control condition. Randomization was performed in Castor EDC (CASTOR & EDC) by a 4,6,8 block design, and stratified for body mass index (BMI: kg/m^2) below 29.9 or above 30. Participants were informed about their study allocation. All treatment appointments were confirmed by email and those randomized to guided self-help CBT-E were informed on how to use the digital treatment environment. The time horizon was three months: assessments took place at baseline (week 0) and at three months post-randomization by interview and self-report questionnaires. Interviews were held by phone, and self-report measures were administered on the web, both of which were processed in Castor EDC (https://www.castoredc.com), which is ISO 27001/27002/9001 and NEN7510 certified. Non-responders were repeatedly contacted by phone. Participants received a €10 gift card after completion of the post-treatment assessments.

2.3 Participants and recruitment

Eligible patients were >18 years old, diagnosed with BED or OSFED-BED (APA, 2013) and had a BMI between 19.5 and 40. They also had internet access, a desktop or laptop computer and had sufficient proficiency in Dutch. Exclusion criteria were acute psychosis, clinical depression and/or suicidal ideation, as assessed by the Dutch version of the semi-

structured interview SCID-5-CV (APA, 2013; First et al., 2016), eating disorders other than BED/OSFED-BED, having received eating disorder treatment in the past six months, pregnancy or use of medication that might influence eating behavior. Inclusion period was September 2019-December 2020.

2.4. Intervention

All 17 therapists successfully completed a web-based CBT-E training provided by the Centre for Research on Eating Disorders at Oxford, United Kingdom (Fairburn, 2008), before they attended a two-day workshop provided by authors BM and MdeJ. Weekly 45-minutes supervision sessions with BM were offered to ensure protocol adherence. Therapists self-rated their level of adherence after each session on a scale ranging from 0-5 ("not at all" to "excellent"), and 94.7% of all sessions obtained the maximum score of adherence.

Guided self-help CBT-E is a three-month program and is a translated, digitalized version of part two of the self-help book *Overcoming Binge Eating* (Fairburn, 2013). Further details regarding the intervention are described elsewhere (Melisse et al., 2023; van den Berg et al., 2020). The intervention started in the same week as the baseline assessment. Before they commenced treatment, patients were instructed to read the psycho-educational section of the Dutch version of *Overcoming Binge Eating* (Fairburn, 2013). The intervention included psychoeducation, daily assignments and two self-evaluations each week. Feedback on the assignments was given by the therapists during 13 weekly telephone sessions of 20 minutes. In the telephone sessions, completed assignments were discussed, as well as upcoming assignments and compliance to treatment. The sessions were scripted in accordance with the treatment manual as developed by EvdB and BM, and offered by therapists.

Patients in the waiting-list group commenced treatment with a three month delay. They were instructed to read the psycho-educational section of *Overcoming Binge Eating* (Fairburn, 2013), and were called once for a 10-minute conversation in which questions about the recommended reading, BED, and other important areas of life were answered.

2.5 Outcomes

2.5.1 Effect measures

The primary outcome measure for the cost-effectiveness analysis was the number of binge eating episodes during the last 28 days. This was measured by the Eating Disorder Examination (EDE) (Cooper & Fairburn, 1987; Jansen, 2000), a semi-structured interview, with good psychometric properties (Cooper & Fairburn, 1987; Jansen, 2000; Rosen et al., 1990).

The outcome measure for the cost-utility analysis was the number of QALYs gained between randomization and post-treatment. To calculate QALYs, quality-of-life was measured using the Dutch three-level variant of the five-dimensional EuroQol instrument (EQ-5D-3L) (EuroQol-Group, 1990), which has good psychometric properties (Janssen et al., 2013; Rabin & Charro, 2001). The EQ-5D-3L determines health related quality-of-life based on five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. For each dimension one of three levels is chosen: “no problems”, “some problems” and “extreme problems” (Dolan, 1997). The Dutch tariff (Lamers, 2005) was used to translate the EQ-5D-3L score to health utilities: utility weights were assigned which reflected the patient’s health state between 0 (death) and 1 (perfect health). One QALY corresponds to one year living in perfect health; for the calculation of QALYs gained or lost for each individual, the studies’ time horizon of three months was taken into account.

2.5.2 Resource use and valuation

The costs of offering the intervention were based on Dutch standard prices in Euros (Zorginsituut, 2016). The costs of delivery of guided self-help CBT-E were based on (i) direct contacts between patients and therapists, and (ii) indirect contacts, which involved consultations between therapists concerning the patients. All contacts within Arkin were derived from the patients' electronic health records from Arkin Mental Health Care. Other care received by the patients included all types of healthcare such as inpatient mental health care, outpatient mental health care (other than within Arkin), other healthcare such as physiotherapy and alternative medicine, and the use of medication. Healthcare contact data that could not be derived from the patients' electronic health records were collected by the first section of the Questionnaire on healthcare Consumption and productivity loss in patients with a Psychiatric disorder (TiC-P) at pre- and post-treatment (Bouwmans et al., 2013; Hakkaart-van Roijen et al., 2002; van Hakkaart Roijen et al., 2011). The TiC-P has a four-week recall period, and in line with Hakkaart-van Rooijen et al. (2007), TiC-P data were extrapolated to the three-months intervention period. All healthcare resource utilization was valued based on Dutch standard unit cost prices in Euros (Zorginsituut, 2016). The number of health care contacts were multiplied by Dutch standard unit costs, medication costs were calculated by multiplying the reported drug dose with its unit cost price (Drost, 2014; Medicijnkosten, 2020; Zorginsituut, 2016).

Non-health care related costs such as productivity losses, decreased functioning professionally, and reduced efficiency of paid and unpaid work (presenteeism) were measured by the second section of the TiC-P (Bouwmans et al., 2013; Hakkaart-van Roijen et al., 2002; van Hakkaart Roijen et al., 2011). The four-week recall period was extrapolated to the three-months intervention period. Hours of productivity loss were multiplied by the average hourly

labor costs (women: €31.60, men: €37.90 in 2014) (Hakkaart-van Roijen et al., 2002; Zwaap et al., 2015). The friction-cost method estimates the indirect costs of presenteeism and absenteeism and takes the possibility to replace long-term absentees into account. The friction-cost method was used to value productivity losses (Koopmanschap, 1995). A maximum friction-cost period of 85 days was applied based on the amount of open and filled vacancies as derived by the Dutch authority of statistics (Hakkaart-van Roijen et al., 2015). An elasticity factor of 0.8 was applied to correct for the fact that reduction of labor-time causes less than a proportional decrease in productivity (Koopmanschap, 1995). Future costs after randomization were not calculated since follow-up data could not be used as both groups received the same treatment when follow-up measures were conducted. Cumulative inflation correction up until the index year 2021 was applied, and Organisation for Economic Co-operation and Development standard purchasing power parities for the study's index year 2021 (105% for the Netherlands) were applied to all costs (OECD, 2022).

2.6 Sample size

Sample size was based on the expected effect on the primary outcome measure (reduction of binges; Melisse et al., 2023). In order to detect an effect size of Cohen's d = 0.47 (Cohen, 1977; Hilbert et al., 2019) with sufficient power (β = 0.8), the required sample size was at least N = 144 (n = 72 per arm), and N = 180 (n = 90 per arm) to correct for expected drop-out. Sample size was calculated using *R* package 'pwr' (Champely, 2020).

2.7 Statistical analyses

Main analyses were performed according to an intention-to-treat (ITT) approach, with missing observations multiple imputed (10 times). Imputations were performed with the

multiple imputation by chained equations package in *R* (Van Buuren, 2011), using random forests as the prediction method; 10 iterations were sufficient to achieve convergence. Results from the analyses obtained from the 10 imputed datasets were combined using Rubin's rules (Rubin, 2004). The societal perspective of this economic evaluation was considered the base case scenario, including all costs (costs of guided self-help CBT-E, medication, all other health care costs and of productivity gains/ losses) for each patient. This analysis was repeated from a health care perspective only, in which productivity costs were excluded. Units of health care and productivity losses were multiplied with their associated costs for all patients. Differences in costs and effects between guided self-help CBT-E and the waiting-list condition were calculated as the difference in cumulative costs (in Euros) and effects over the three months of the intervention.

Incremental cost-effectiveness ratio (ICER) was calculated as: ICER = (Costs Guided self-help CBT-E – Costs waiting-list) / (Effects Guided self-help CBT-E – Effects waiting-list), where effects were QALYs gained or binges prevented. First, we applied multiple imputation to account for missing data. Next, we constructed (multilevel) regression models for costs and effects separately. In these models, costs or effects were the dependent variable, a random intercept to account for the nesting of multiple (in this case, 2) measurements within participants was included in the model, as was a Time (baseline or three months after) X Condition (guided self-help CBT-E or waiting list) interaction term. For the corrected model, we also included baseline costs and effects in the model. From this regression model, we were interested in the regression coefficient for the Time X Condition interaction term. Based on the estimate and standard error of this coefficient, a distribution of the incremental costs and incremental effects was created. using resampling (10,000 samples) (main analysis).

As an alternative approach, 10,000 non-parametric bootstrapped samples were extracted from the imputed datasets (bootstrapped analysis), of which for each incremental

costs, incremental effects, and ICER were calculated. The resulting costs, effects and ICERs were used for further calculations and plotted on a cost-effectiveness plane to present the differences between costs and effects of both conditions, of which the waiting-list control condition is positioned in the origin of the cost-effectiveness plane. In addition, cost-effectiveness acceptability curves (CEACs) were plotted based on the distribution of the ICERs over the cost-effectiveness planes (Van Hout et al., 1994) using the net benefit regression approach (base case). CEACs show the probability that the cost-effectiveness of guided self-help CBT-E is greater than a waiting-list by a willingness-to-pay for each additional unit of effect (QALYs or binges). Willingness-to-pay for each additional unit of effect generally ranges between €20,000-80,000 per QALY (Zwaap et al., 2015) in the Netherlands, and €22-110 per binge free day in the United-Kingdom and United-States (Jenkins, 2021; Lynch et al., 2010).

In a sensitivity analysis, baseline measures of the dependent variables in the model were also included in the linear mixed models of the main costs analyses. We also conducted a health care perspective scenario analysis, in which only health care related costs were taken into account. As a final sensitivity analysis, we assessed the impact of missing data to our results by performing the analyses using a dataset without imputed values (i.e. comprising of only the observed data). Analysis were performed in *R* version 4.2.1, lme4 package in *R* (Bates et al., 2015) and SPSS version 28.

Results

Participants

For the current study, 230 potential participants were recruited, of which 212 were randomized; *n* = 18 didn't meet in- or met exclusion criteria; *n* = 208 were diagnosed with BED, *n* = 4 had a history of bariatric surgery, had smaller binges and were therefore

diagnosed with OSFED-BED. Like in the efficacy study, as only a small proportion (17.5%;37/212) of participants had a BMI<30, no subgroup analyses based on stratification of 30>BMI≥30 were performed. **Fig. 1** shows participant enrollment and flow through the study; Table 1 summarizes participant characteristics at baseline.

Drop-out from treatment (i.e., non-adherence) was 15.1% (*n*=16/106) in the guided self-help CBT-E and, 3.7% (*n*= 4/106) in the waiting-list. Non-response for the measurements (i.e., non-adherence to complete the assessments) at three months was 15.1% (*n*= 16/106) in the experimental condition and, 2.8% (*n*= 3/106) in the waiting-list. Therefore, the overall study's measurement non-response was 8.9%.

Figure 1 Flowchart of patients in study

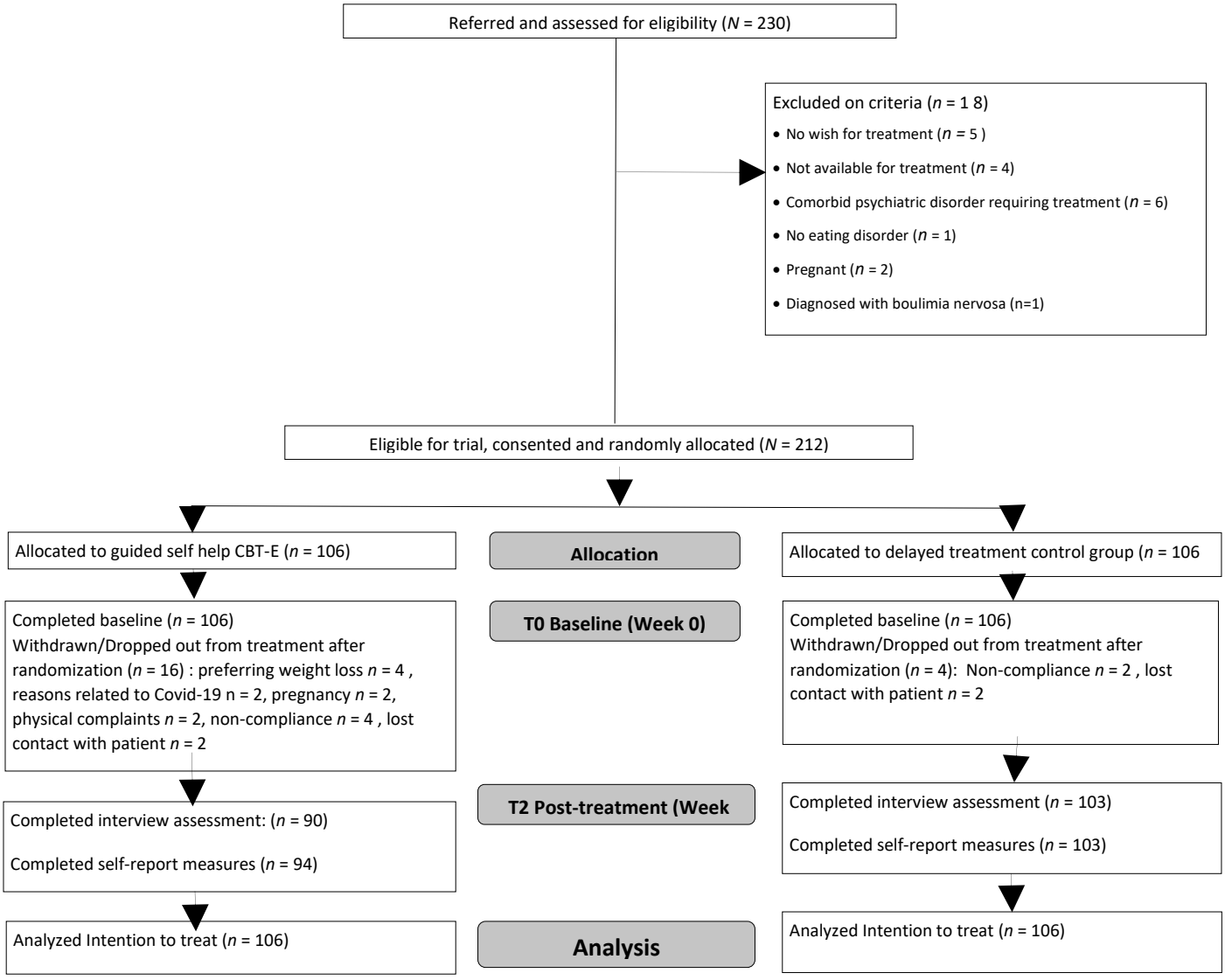


Table 1 Patient characteristics at baseline.

	Total sample *N* = 212	Experimental condition *n* = 106	Waiting-list condition *n* = 106
Age, mean (SD)	38.7 (13.3)	38.0 (13.4)	39.4 (13.2)
Baseline BMI, mean (SD)	33.4 (5.7)	33.4 (6.3)	33.5 (5.0)
Gender, *n* (%)			
Female	190 (91.1%)	95 (89.6%)	95 (89.6%)
Male	22 (9.9%)	11 (10.4%	11 (10.4%)
Highest level of education, *n* (%)			
Lower vocational education	4 (1.9%)	2 (1.9%)	2 (1.9%)
Lower general secondary education	16 (7.5%)	6 (5.7%)	10 (9.4%)
Senior general secondary education/ university preparatory education	23 (10.8%)	13 (12.3%)	10 (9.4%)
Secondary vocational education	59 (27.8%)	28 (26.4%)	31 (29.2%)
Higher professional education	70 (33.0%)	37 (34.9%)	33 (31.1%)
University	38 (17.9%)	18 (17.0%)	20 (18.9%)
Unknown	2 (0.9%)	1 (0.9%)	1 (0.9%)
Profession, *n* (%)			
Student	22 (10.4%)	13 (12.3%)	9 (8.5%)
Employed	139 (65.5%)	63 (59.4%)	76 (71.7%)
Volunteer job	4 (1.9%)	3 (2.8%)	12 (0.9%)
Unemployed	15 (7.1%)	5 (4.7%)	10 (9.4%)
Other	31 (14.5%)	21 (19.8%)	10 (9.4%)
Unknown	1 (0.5%)	1 (0.9%)	0 (0.0%)
Civil status, *n* (%)			
Single	123 (58.0%)	59 (55.7%)	64 (60.4%)
Registered partnership	18 (8.5%)	10 (9.4%)	8 (7.5%)
Married	56 (26.4%)	30 (28.3%)	26 (24.5%)
Divorced	14 (6.6%)	6 (5.7%)	8 (7.5%)
Unknown	1 (0.5%)	1 (0.9%)	0 (0.0%)
Duration of eating disorder (years), mean (SD)	22.6 (14.6)	21.9 (14.7)	23.3 (14.6)
Eating disorder treatment in the past, *n* (%)			
Yes	34 (16.0%)	14 (13.2%)	20 (18.9%)
No	177 (84.0%)	91 (85.8%)	86 (81.1%)
Comorbid diagnosis, *n* (%)			
No	91 (42.9%)	45 (42.5%)	46 (43.4%)
I don't know	30 (14.2%)	14 (18.0%)	14 (13.2%)
Mood disorder	32 (15.01%)	14 (13.2%)	18 (17.0%)
Anxiety disorder	7 (3.3%)	4 (3.8%)	3 (2.8%)
Attention deficit (hyperactive) disorder	14 (6.6%)	7 (6.6%)	7 (6.6%)
Post traumatic stress disorder	8 (3.8%)	4 (3.8%)	4 (3.8%)
Personality disorder	10 (4.7%)	6 (5.7%)	2 (2.5%)
Autism	7 (3.3%)	6 (7.5%)	1 (0.9%)

Obsessive compulsive disorder	1 (0.5%)	1 (0.9%)	
Other	18 (8.5%)	8 (7.5%)	10 (9.4%)
Use of psychopharmacology, *n* (%)			
Yes	53 (25.5%)	25 (23.6%)	28 (26.4%)
No	158 (74.5%)	80 (75.5%)	78 (73.6%)
Eating disorder pathology (EDE), *M* (SD)			
Global score	3.1 (1.0)	3.1 (0.9)	3.1 (0.9)
Objective binge episodes[1]	59.5 (51.0)	47.1 (43.7)	53.3 (47.4)
Quality of Life (EQ 5D NL), *M* (SD)	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)
Health care costs in euros[2], *M* (SD)		712 (1391)	578 (808)
Costs of absenteeism[2], *M* (SD)	1767 (2647)	2017 (3065)	1516 (2229)
Costs of presenteeism[2], *M* (SD)	1062 (2420)	1218 (2777)	905 (2063)

[1] Number of binges during the last four weeks extrapolated over the last three months before randomization
[2] Presenteeism and absenteeism over the last three months before randomization
BMI body mass index, *EDE* eating disorder examination, *EQ 5D NL* Dutch three-level variant of the five-dimensional EuroQol instrument

Costs

Table 2 shows the costs and effects during the three months trial (from pre- to post-treatment). The only difference in costs between both conditions, was found for outpatient mental health care costs (p=.009). Mean overall costs were higher in the guided self-help CBT-E condition; the difference in societal costs (p=.095) was €641 [95% confidence interval (CI) -86-1393]. The differential health care costs (p<.001) was € 893 [CI 671-1123].

Table 2. Costs and effects between baseline and three months after per cost category

	Guided self-help CBT-E (*n*=106)			Waiting-list control condition (*n*=106)		
Cumulative costs in €	Mean	SD	Reported by *n*	Mean	SD	Reported by *n*
Outpatient mental health care within Novarum	1,313.01	339.15	106	284.39	198.20	94
Other outpatient mental health care	144.38	805.19	22	81.15	221.54	21
Inpatient health care	0.14	4.44	0	42.54	214.02	6
Other healthcare	171.11	306.13	63	132.47	219.22	63
Medication	84.95	272.11	52	97.28	319.05	58
Productivity	1,161.92	2,670.98	42	1,098.21	2.072.54	45
Societal costs	2,875,.51	2,945.72	106	1,736.06	2.161.78	106
Overall health care costs	1,713.59	1,136.97	106	637.85	541.46	106
Effects[1]						
Binges last three months	16.96	33.80	106	42.78	46.14	106
QALYs	0.02	0.06	106	-0.00	0.05	106

Note base case model, based on the imputed dataset
[1]Effects extrapolated over the last three months
QALY quality-adjusted-life-year

Effects

Based on the linear mixed models in which the effect outcomes were evaluated between baseline and three months post-baseline, a significant Time x Group interaction for QALYs (*B*=0.020, SE=0.008, *p*=0.009) as well as for number of binges (*B*=-38.212, SE=7.454, *p*<0.0005) was found in the uncorrected model. In the baseline-corrected model, the Time x Group interaction term for QALYs was also significant (*B*=0.020, SE=0.007, *p*= 0.006), as was the Time x Group interaction term for the number of binges (*B*=-38.512, SE=6.899, *p*<0.0005). See also Table 2 for descriptives of costs and effects. These effects indicated that the decline in number of binges was stronger in the guided self-help CBT-E condition than in the wait-list condition, as well as the increase in number of QALYs.

Cost- effectiveness and cost- utility

The results of the cost-effectiveness and cost-utility analyses are presented in Table 3, Figure 2 presents the cost-effectiveness planes and the CEACs. The cost-effectiveness analysis over the three months trial showed that from a societal perspective, the incremental costs associated with one incremental binge prevented in the guided self-help CBT-E condition (ICER) was approximately €17 [CI -2-40]; this was €23 [CI 15-39] from a health care perspective. Figure 2 (north-east quadrant) shows that from a societal perspective there was a 96% likelihood that guided self-help CBT-E led to a greater number of binges prevented at additional societal costs compared to the control condition. There was a 4% likelihood that guided self-help CBT-E led to a greater number of binges prevented at lower societal costs compared to the wait list (south-east quadrant). From a healthcare perspective there was a >99% likelihood that guided self-help led to a greater number of binges prevented than the control condition, at higher health care costs (north-east quadrant).

The cost-utility analyses from a societal perspective (Table 3, Figure 2) indicated an ICER of €32,515 [CI -4619-151,393]. There was a 95% likelihood that guided self-help CBT-E led to a larger gain in QALYs at higher societal costs than the control condition (north-east quadrant) (Figure 2). Based on the NICE willingness-to-pay threshold of €35,000 per QALY (NICE, 2023), guided self-help CBT-E would be slightly preferrable over wait list in terms of cost-effectiveness. Figure 2 (north-east quadrant) shows that from a health care perspective there was a >99% likelihood that guided self-help led to a larger gain in QALYs at higher costs than the wait list control condition.

Sensitivity analyses

The robustness of the results was attested since the results of the sensitivity analyses were similar to those of the primary analyses, as can be observed from Table 3.

Table 3 Incremental costs, effects, and ICER after three months of to guided self-help CBT-E (*n*=106) or waiting list (*n*=106)

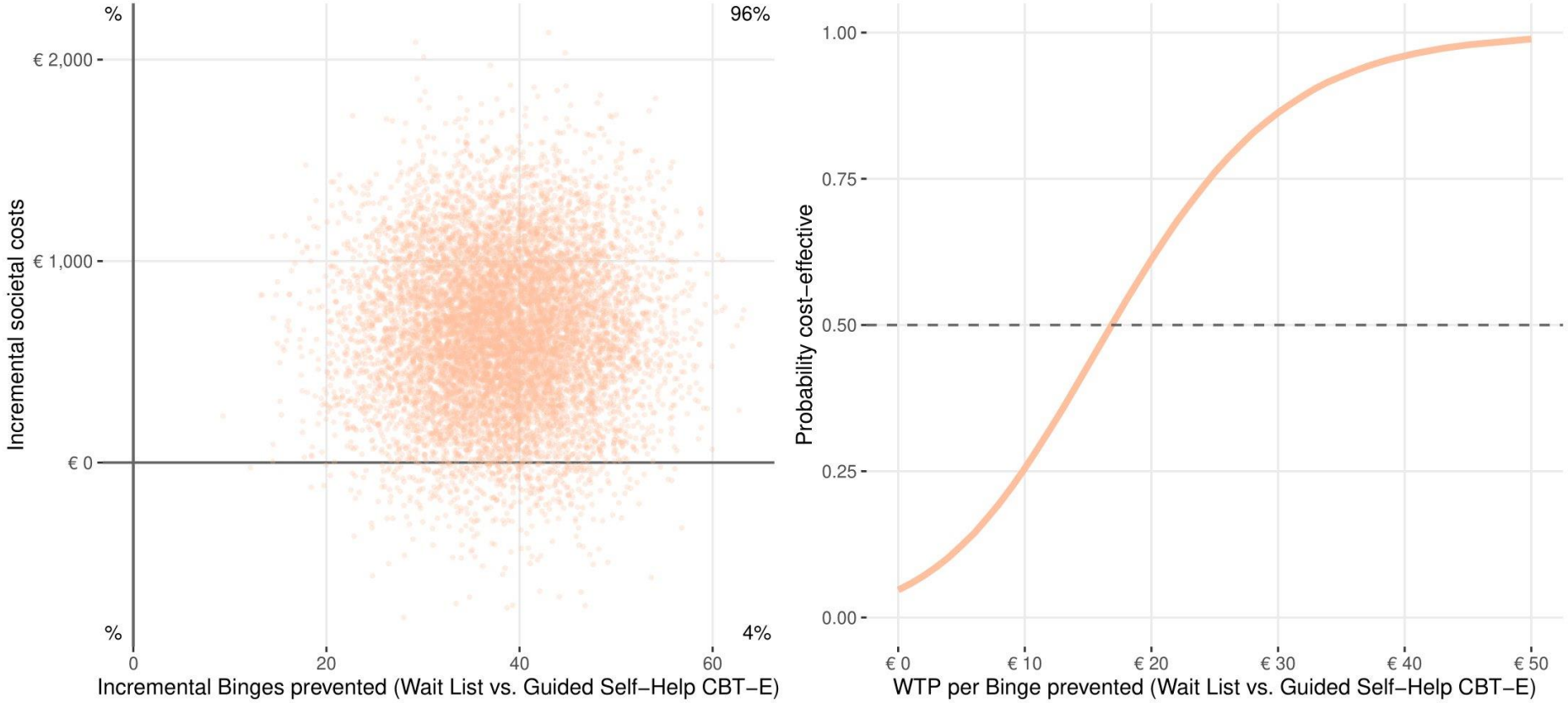
Outcome[1]		societal mean [95% C.I.]	societal bootstrapped mean [CI	societal baseline corrected mean [CI	societal complete cases mean [CI	healthcare mean [CI]
	Incremental costs[1]	641 [-86-1,393]	637 [-79-1,332]	641 [-39-1,345]	783 [55-1,573]	893 [671-1,123]
QALY						
	QALY [2]	0.02 [0.00-0.04]	0.02 [0.00-0.03]	0.02 [0.00-0.03]	0.02 [0.01-0.04]	0.02 [0.01-0.04]
	ICER[3]	32,515 [-4,619-151,393]	31982 [-3,885-159,278]	32,523 [-1,938-131,782]	3,2952 [2,306-92,691]	45,206 [23,981-186,654]
Binges						
	Binges	38.2 [23.4-52.8-]	38.1 [26.0-51.0]	38.2 [24.5-51.7]	42.1 [29.2-54.9]	38.2 [23.4-52.8]
	ICER[3]	17 [-2-42]	17 [-2-40]	17 [-1-40]	19 [1-40]	23 [15-39]

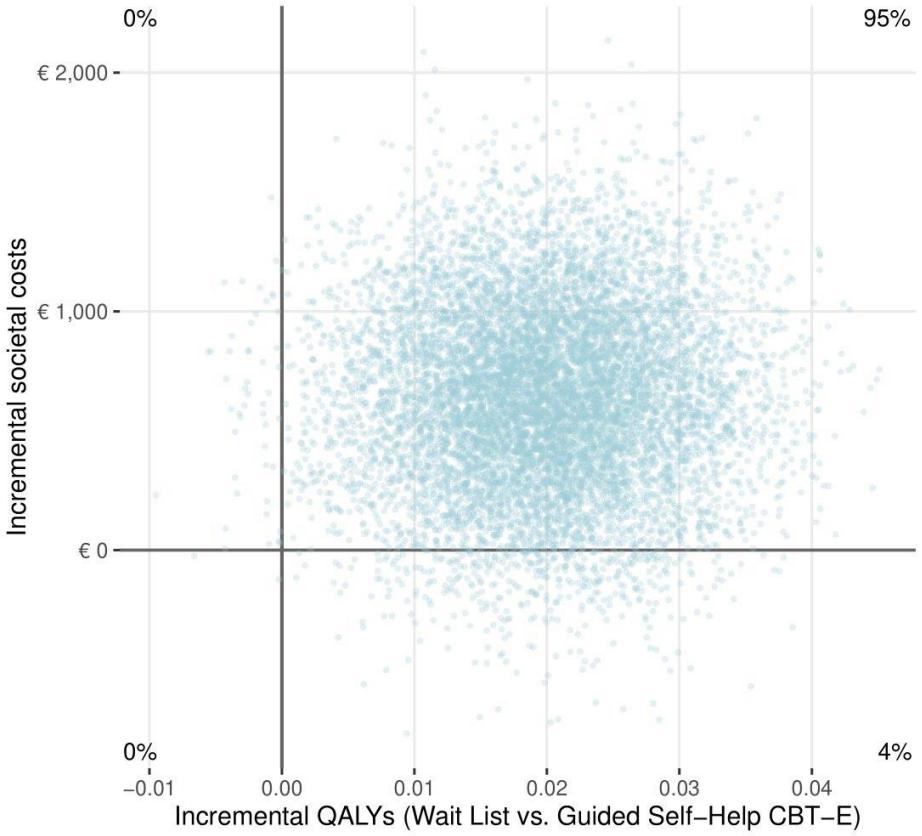
Note based on the imputed dataset
[1] Differences reported in Euro's

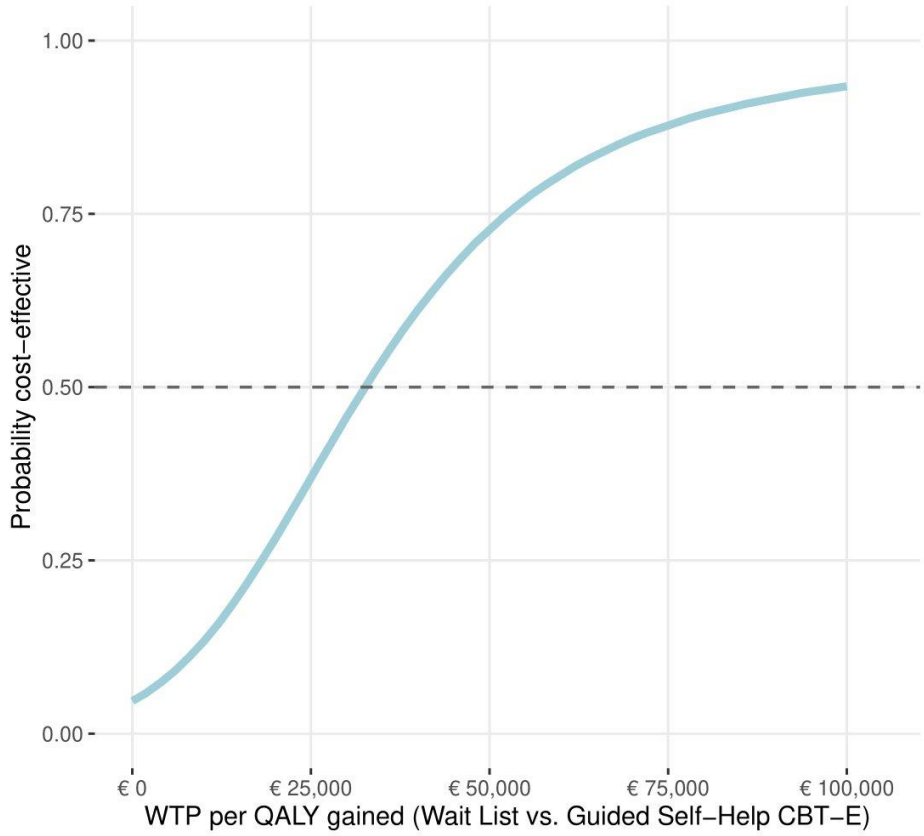
[2] QALYs were measured by the Dutch three-level variant of the five-dimensional EuroQol instrument [3] Incremental cost-effectiveness ratios were calculated as: ICER = (Costs Guided self-help CBT-E – Costs waiting-list) / (Effects Guided self-help CBT-E – Effects waiting-list)

ICER incremental cost-effectiveness ratio, *QALY* quality-adjusted life year

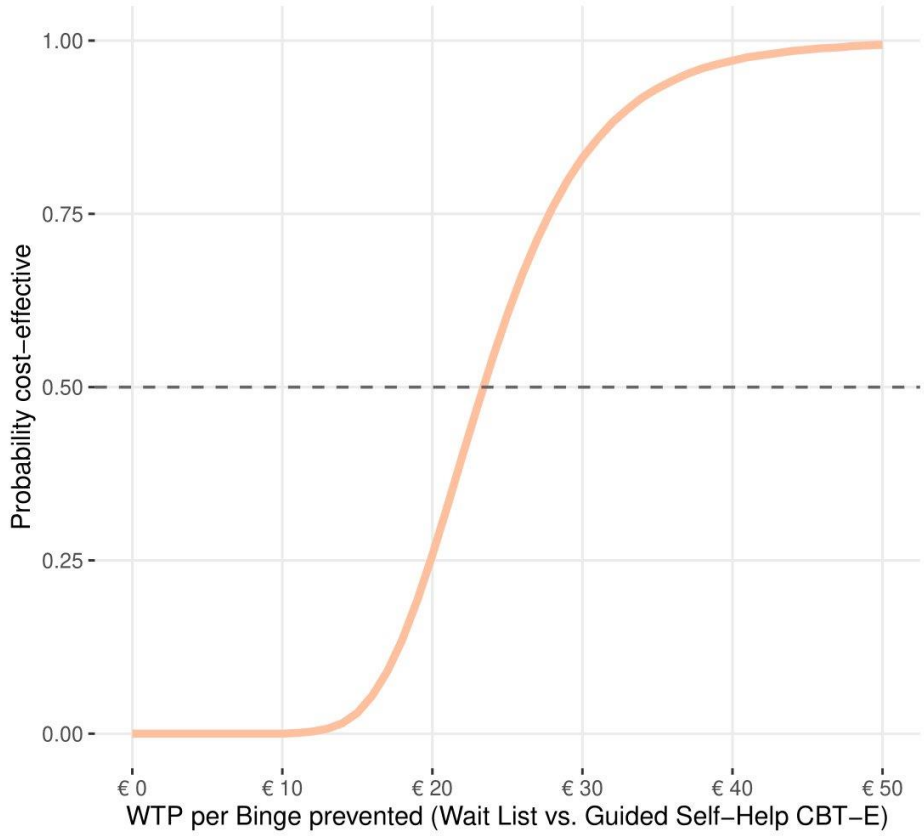
Figure 2 Cost-effectiveness and cost-utility planes and acceptability curves from a societal and health care perspective

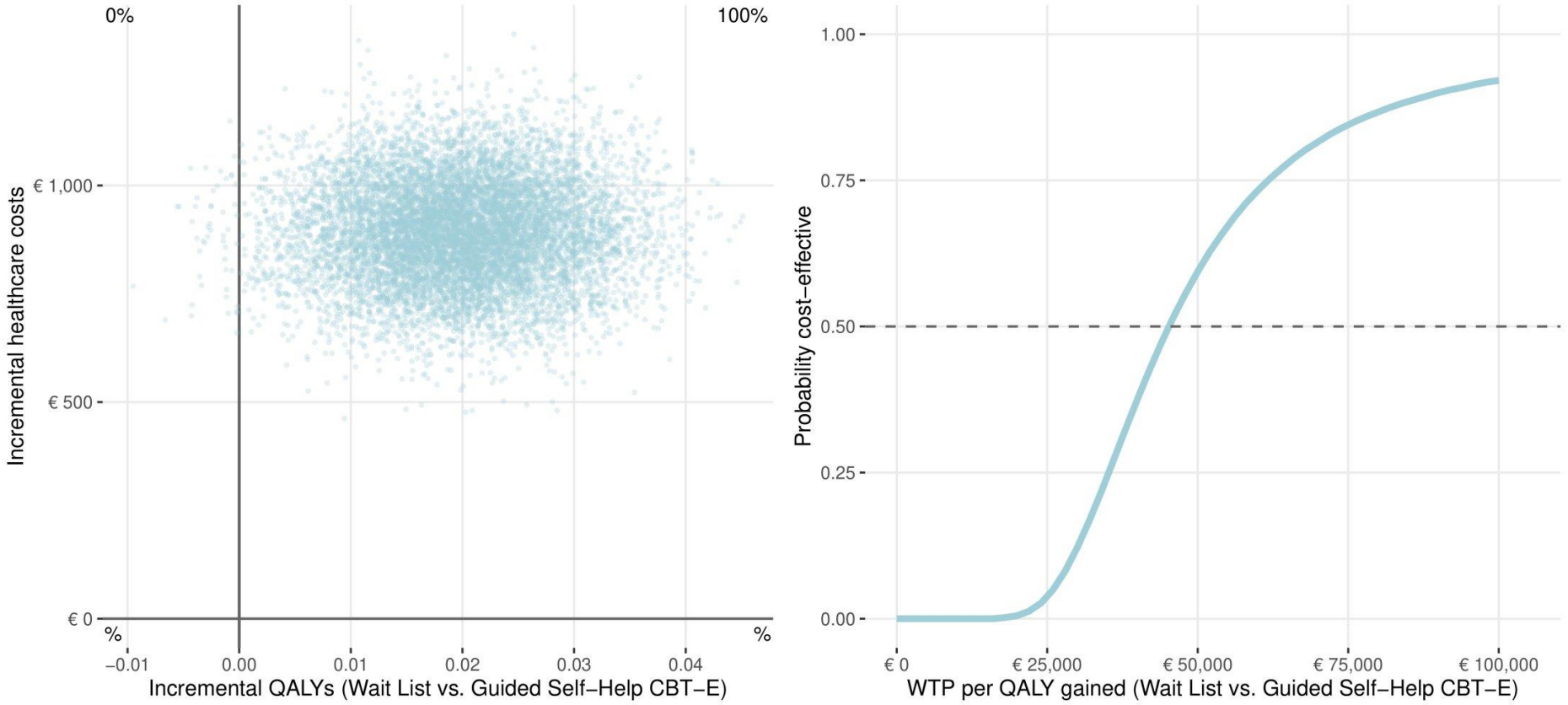



0%
95%
€ 2,000
€ 1,000
€ 0
0%
4%
Incremental societal costs
−0.01
0.00
0.01
0.02
0.03
0.04
Incremental QALYs (Wait List vs. Guided Self−Help CBT−E)


1.00
0.75
0.50
0.25
0.00
Probability cost−effective
€ 0
€ 25,000
€ 50,000
€ 75,000
€ 100,000
WTP per QALY gained (Wait List vs. Guided Self−Help CBT−E)

%
100%
€ 1,000
€ 500
€ 0
%
%
0
20
40
60
Incremental healthcare costs
Incremental Binges prevented (Wait List vs. Guided Self−Help CBT−E)


1.00
0.75
0.50
0.25
0.00
Probability cost−effective
€ 0
€ 10
€ 20
€ 30
€ 40
€ 50
WTP per Binge prevented (Wait List vs. Guided Self−Help CBT−E)



WTP willingness-to-pay

The four graphs on the left are cost-effectiveness planes. The horizontal axis indicated differences in binges prevented and QALY gains between guided self-help CBT-E and waiting for treatment over the three months course of treatment. The vertical axis represented the differences in costs. The chart area is divided into quadrants, each with a specific interpretation. All incremental cost-effectiveness ratios fell into the upper

right (“north-east”) quadrant. This indicated that guided self-help CBT-E generated a greater number of binges prevented and greater QALY gain at additional costs. The two plots on the right were cost-effectiveness acceptability curves. These curves show the probability that guided self-help CBT-E is cost-effective compared to waiting for treatment as a function of the willingness-to-pay for one additional unit of effect, represented as one additional binge prevented or one QALY gained. The probability 0.50 on the vertical axis indicated the point of indifference. Above the point of indifference point, guided self-help CBT-E has a greater likelihood to be preferred over waiting for treatment with regard to cost-effectiveness (with an equal likelihood to the probability on the vertical axis). As the exact willingness-to-pay per effect unit is generally unknown, willingness-to-pay is presented as a series of increments on the horizontal axis.

Discussion

Main findings

This study examined cost-effectiveness and cost-utility of guided self-help CBT-E versus a waiting-list for BED over a period of three months using data from the initial phase of an RCT. Key findings were that guided self-help CBT-E led to greater QALY gain, and a greater number of binge eating episodes were prevented compared to waiting for treatment. There was a >96% likelihood that guided self-help CBT-E led to more binges prevented, but at higher costs. Based on 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), guided self-help CBT-E would be preferable by the Dutch society in terms of cost-effectiveness compared to a waiting-list during the first three months and can be seen as a reasonable investment for the Dutch health care system. In addition, willingness-to-pay per QALY gain was lower in 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). There were no differences in costs between the two conditions, except for outpatient mental healthcare costs (associated with the intervention provided to the experimental group). The results remained stable in the sensitivity analyses, supporting the robustness of the findings.

Our study is among the first economic evaluations of guided self-help treatments for full-syndrome BED. Previously, two studies evaluated cost-effectiveness of guided self-help interventions for binge eating (König et al., 2018; Lynch et al., 2010) with smaller sample sizes ($N \leq 150$) than the present study. However, strength of these studies was that they represented a longer timeline than current study as guided self-help was compared to treatment-as-usual. One study analyzed cost-effectiveness of a guided self-help intervention based on the book *Overcoming binge eating* accompanied by eight in-person sessions among

patients with subsyndromal BED. This intervention was compared to treatment-as-usual, which consisted of advising patients on other treatment options. The intervention appeared cost-effective, however that study used a non-standardized measure to examine quality-of-life (Lynch et al., 2010). Another study compared CBT to guided self-help CBT among patients with BED and subsyndromal BED. The results of this study were inconclusive since guided self-help CBT led to greater QALY gain, whereas CBT led to greater reduction in binge eating at end-of-treatment (König et al., 2018). However, 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

The most significant limitation is the time horizon of three months. Since patients randomized to the waiting-list also received guided self-help CBT-E during follow-up, comparison of cost-effectiveness and cost-utility was not possible after three months. This precluded an evaluation of the long-term effectiveness as well as the costs of guided self-help CBT-E as compared to no treatment. A different study design, with a comparison to a treatment-as-usual control condition (e.g., in-person CBT-E), would have enabled an economic evaluation with a longer time horizon, which is recommended for future research. In addition, 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).

Therapists' protocol adherence was only measured by self-report, whereas adherence assessment by an independent rater would yield more valid information (Lopez-Alcalde et al., 2022). An alternative could be the adherence checklist for CBT-E which has recently become available (Bailey-Straebler et al., 2022). Last, although 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 over the last three months 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 the assessment and extrapolated over three months between the assessments. Furthermore, recall bias probably led to underestimation of the number of binges (Berg, Peterson, et al., 2012), therefore extrapolation might also have affected the measurement of binges.

This study has several strengths. This is the first study to perform an economic evaluation selectively including patients with full syndrome BED. Furthermore, the sample size was larger than in previously conducted studies, providing adequate statistical power to find differences between the two compared groups of patients. Study dropout of <10% was low and multiple imputation was performed to handle missing data. Patients were an accurate representation of patients with BED in the Netherlands. The EDE interview (Cooper & Fairburn, 1987; Jansen, 2000), is considered the gold-standard to measure binges, as especially patients with BED show a marked discrepancy between self-reported and investigator-based number of binges (Berg, Stiles-Shields, et al., 2012; Melisse et al., 2021).

Conclusions

Guided self-help is an internationally recommend treatment for BED, but was previously not available in the Netherlands. This study provides evidence for its efficacy and cost-effectiveness, which may contribute to future decision making in clinical practice (ANZAED, 2014; NICE, 2017). In addition, the current study findings may stimulate consideration into alternatives to the traditional mode of in-person delivery of CBT-E. Future studies should compare efficacy and cost-effectiveness of guided self-help CBT-E to in-person CBT-E. This will enable comparisons over a longer timeline and further enhance decision making on where the scarce resources should be allocated, and where they offer best

value for money (Konnopka et al., 2009; Stuhldreher et al., 2012). In conclusion, guided self-help CBT-E appeared the preferred treatment in terms of cost-effectiveness compared to a waiting-list for patients with BED. However, long-term data are necessary to establish the long-term efficiency and cost-effectiveness of this treatment mode.

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