BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024693
Article Type:	Research
Date Submitted by the Author:	21-Jun-2018
Complete List of Authors:	Gentile, Andrew; Karolinska Institutet, Centre for Psychiatry Research, Department of Clinical Neuroscience La Lima, Christopher ; Karolinska Institutet, Centre for Psychiatry Research, Department of Clinical Neuroscience Flygare, Oskar; Karolinska Institutet Department of Clinical Neuroscience, Enander, Jesper; Karolinska Institutet Department of Clinical Neuroscience, Wilhelm, Sabine; Harvard Medical School, Department of Psychiatry Mataix-Cols, David; Karolinska Institutet, Department of Clinical Neuroscience Rück, Christian; Karolinska Institutet, Department of Clinical Neuroscience
Keywords:	Adult psychiatry < PSYCHIATRY, Anxiety disorders < PSYCHIATRY, Clinical trials < THERAPEUTICS, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, World Wide Web technology < BIOTECHNOLOGY & BIOINFORMATICS

Text word count: 3263
Abstract: 285
Tables: 2
Figures: 3

Internet-based, therapist guided, CBT for Body Dysmorphic Disorder with Global Inclusion: A Pilot Study

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ABSTRACT

Objectives: Cognitive–behavioural therapy (CBT) has been shown to be an effective treatment for body dysmorphic disorder (BDD) but access to treatment around the world is limited. One way to increase access is to administer CBT remotely via the internet. This study represents the first effort to remotely deliver a therapist-supported, internet-based CBT treatment to a globally recruited sample, and aims to assess whether this treatment can be delivered safely and effectively across international borders.

Design: Uncontrolled clinical trial.

Participants: Patients (N=32) in 9 different countries were recruited primarily through internet advertisements.

Intervention: BDD-NET is a 12-week treatment, consisting of 8 treatment modules previously shown to be effective in a Swedish version.

Setting: Therapists based at a single, secondary care centre in Sweden provided active guidance and feedback throughout the treatment via asynchronous electronic messages.

Main outcome measure: The clinician-administered Yale-Brown Obsessive Compulsive Scale for BDD (BDD-YBOCS). Symptom severity was assessed pretreatment, mid-treatment (6 week), post-treatment, and at the 3-month follow-up.

Results: There were significant improvements on BDD-YBOCS scores (F[3, 71.63] = 31.79, p < .001), that were maintained at 3-month follow-up. Mean differences from baseline in BDD-YBOCS scores were -8.12 (week 6), -12.63 (post-treatment), and -11.71 (3-month follow-up). Forty-seven percent and 50% of participants were considered treatment responders at post and 3-month follow-up, respectively. Additionally, remission rates were 28% at post-treatment and 44% at 3-month follow-up. The treatment was also deemed acceptable by patients.

Conclusions: The results suggest that BDD-NET can be safely and effectively delivered across international borders to a culturally diverse sample. Larger scale randomized controlled trials with more participants from non-western cultures are warranted to further validate the cross-cultural generalizability of this treatment.

Trial registration number: Clinicaltrials.gov registration ID: NCT03517384

Article Summary:

Strengths and limitations of this study

- This is the first study to investigate the feasibility and acceptability of a therapist-guided, internet-based CBT intervention, delivered from a single centre, to a globally recruited sample
- The absence of a control condition limits the ability to make inferences about what caused the changes observed

- Since most participants resided in western countries, it is unclear to what extent BDD-NET is generalizable to patients from non-western cultures

INTRODUCTION

Despite the enormous socio-economic costs and individual suffering caused by mental illness, there are far too few clinicians to meet the global need for mental health services. [1,2]. Moreover, outpatient health services are usually open during normal working hours, and this current service model disenfranchises individuals who may have difficulties taking time off work or accessing care if living in remote and underserved areas. Furthermore, issues like stigma, lack of awareness, cost of treatment, and the symptoms of psychiatric disorders themselves can also be barriers to accessing care [3]. As a result, most individuals with a mental disorder do not receive treatment [4].

This treatment gap is particularly wide for under-recognized disorders such as body dysmorphic disorder (BDD), where the affected individual is preoccupied with perceived flaws or defects in one's appearance that are not noticeable to others [5]. In fact, only 10-17% of those with the disorder report receiving an evidence-based psychotherapy like cognitive behavioral therapy (CBT), despite its common prevalence and significant functional impairment for sufferers [3,6–10].

Internet-based CBT (ICBT) aims to increase accessibility and availability to specialised treatment and has been shown to be efficacious and cost effective for a range of disorders [11]. Recently, BDD-NET, a therapist-guided, internet-based CBT program for BDD, was developed to improve access to evidence-based care, and the treatment has been shown to be safe, efficacious, and highly acceptable by patients [12,13]. The treatment is delivered through a secure tailored online platform that contains the treatment content. Communication between therapist and patient is done through asynchronous messaging,

requiring only a fraction of therapist time compared to conventional CBT. Crucially, BDD-NET removes key barriers to treatment, while yielding outcomes equivalent to traditional face-to-face CBT [14].

ICBT represents a promising solution for economically and efficiently targeting mental health disparities around the world. However, this integration of CBT with information technology has yet to realize its true potential to reach underserved populations. Therefore, our aim was to conduct the first investigation evaluating whether a therapist-guided, internet-based CBT intervention could be delivered safely and effectively across international borders, to a globally recruited sample. In doing so, the current researchers hope to shed light on aspects of feasibility and ethical considerations that arise in this novel treatment context.

METHODS

Trial design

The aim of this investigation was to evaluate the feasibility and safety of a global treatment initiative using an English-language version of BDD-NET [12,13]. This uncontrolled pilot study was intended to assess different aspects of conducting the study remotely and across international borders; including recruitment, assessment, and treatment delivery. The central ethical review board in Sweden approved the protocol (CEPN Ö 7-2016), as well as institutional review boards (IRB) at Massachusetts General Hospital (approved 11/23/2015), and Hofstra University (1/14/2016). The study was registered at Clinicaltrials.gov (NCT03517384).

Procedure

Participants were recruited by clinician referral as well as using internet advertisements through Google AdWords, bddfoundation.org, and on internet forums. Individuals interested in participating in the study were directed to the study's website where they provided initial informed consent, and completed an online screening consisting of the Montgomery–Åsberg Depression Rating Scale (MADRS-S) [15,16], the Body Dysmorphic Disorder Questionnaire (BDDQ) [17], the Dysmporhic Concerns Questionnaire (DCQ) [18], the Alcohol Use Disorders Identification Test (AUDIT) [19] and the Drug User Disorders Identification Test (DUDIT) [20]. Following this initial screening, eligible individuals were invited for an assessment over VSee, a Health Insurance Portability and Accountability Act (HIPAA) compliant video-conferencing software. During the video-conference assessment, final screening and baseline measures were obtained, as well as verbal informed consent, identification documents, and emergency information. Measures administered at this time were the Body Dysmorphic Disorder modification of the Yale-Brown obsessive compulsive scale (BDD-YBOCS) [21], Columbia Suicide Severity Rating Scale (CSSR-S) [22], Brown Assessment of Beliefs Scale (BABS) [23], Clinical Global Impressions Scale of Severity (CGI-S) [24], and Global Adaptive Functioning (GAF) [5]. Additionally, the obsessive-compulsive and related disorders module of the Structured Clinical Interview for DSM 5 [25] and the Mini International Neuropsychiatric Interview (M.I.N.I. 7) [26] were also administered at this time as a means to establish a primary diagnosis of BDD. For full eligibility criteria and details on recruitment and patient flow, see appendix A. Eligible participants were then granted access to treatment via the online platform. In order to guarantee participant

confidentiality, we used a dedicated server with encrypted traffic and a strong authentication login function.

Participants

Thirty-two participants were included in the study. These individuals resided in 9 different countries and represented 12 different nationalities (Socio-demographic and clinical characteristics of participants are presented in Table 1). Inclusion criteria were that participants needed to be aged 18 years or older, meet DSM-5 criteria for a diagnosis of BDD with symptom severity measuring ≥ 20 on the BDD-YBOCS [21], be outpatient, be fluent in English, and have regular access to a computer with an internet connection. Patients who were able to navigate the online registration and screening process were considered to have sufficient computer skills to participate in the study.

Exclusion criteria were concurrent psychological treatment, having received CBT for BDD within 12 months preceding treatment, changes in psychotropic medications within 12 weeks before inclusion, not having access to a 24 hour psychiatric emergency center in their proximity, or if they could not provide an emergency contact person. Additional grounds for exclusion were current substance dependence, lifetime bipolar disorder or psychosis, MADRS-S score ≥ 35, personality disorder diagnosis, lifetime history of suicide attempts, or clinically significant current suicidal ideation (≥ 5 on item 9 of MADRS-S; C-SSRS (past month) - Most Severe Ideation score ≥ 4).

Patient and Public Involvement

Patients and the general public did not have direct involvement in the design of this study, recruitment, or the development of research questions or measures. Upon publication, patients will be sent a copy of the article which would not have been possible without their participation.

Primary Outcome

The primary outcome was the BDD-YBOCS, administered at baseline, mid-treatment (week 6), post-treatment (week 12), and 3 months after treatment completion. BDD-YBOCS is a semi-structured clinician-administered scale, considered to be the gold standard for measuring BDD symptom severity and has demonstrated good psychometric properties [27]. Scores range from 0-48 with higher scores indicating greater severity. Prior to subject enrollment, all evaluators were trained to a reliability criterion (intra-class correlation coefficient (ICC) of at least .85) with a gold standard rater on the BDD-YBOCS.

Secondary Outcomes

Participants with ≥ 30% reduction on the BDD-YBOCS were considered responders [27]. Participants no longer meeting full criteria for DSM-5 diagnostic criteria for body dysmorphic disorder were considered to be in remission.

Clinicians rated patient overall severity and symptom change on the clinical global impressions scale (CGI). The CGI-S ranges from 1 (normal, not ill at all) to 7 (among the most extremely ill of subjects). Similarly, the CGI-I ranges from 1 (very much improved) to 7 (very much worse) [24]. Secondary measures of symptoms included the Montgomery -

Åsberg Depression Rating Scale – self-report (MADRS-S) [15,16], Global Assessment of Functioning (GAF) [5] and Brown Assessment of Beliefs Scale (BABS) [23]. See appendix A for a complete list of secondary outcome measures.

Treatment activity, completion, and acceptability

Therapist time spent on the platform reviewing patient progress and responding to messages, number of messages sent and received, and number of completed modules were automatically recorded for each patient. Patients rated working alliance every two weeks throughout treatment using the WAI-SR [28]. At post-treatment, patients rated treatment satisfaction on the client satisfaction inventory (CSI) [29]. Patient credibility and expectancy was also recorded every two weeks throughout treatment using the Credibility/Expectancy Questionnaire [30,31].

Adverse events monitoring

Each week patients were asked if they experienced any adverse events or side effects that could be attributed to treatment (e.g., sleep disturbances, increased anxiety, or depression symptoms). If so, they were asked to describe them in the form of free text [32].

For a full list of outcome measures used, as well as a detailed timetable for their administration, see protocol in appendix A.

Intervention

BDD-NET, a 12 week internet-delivered cognitive behavioral therapy intervention for BDD, was evaluated in Sweden in a pilot study (n=23) and then in a randomized controlled trial

(n=94), and showed sustained effects at 2-year follow-up [12,13]. It was translated to English for the current study in order to reach an international sample (For a full description of the treatment content, see [12,13]. Therapists were doctoral level psychology students supervised by licensed psychologists and psychiatrists based at Karolinska Institutet. Throughout treatment, patients had unlimited access to their therapist from Monday through Friday via asynchronous electronic text messages. The therapist's primary role was to offer clarification and emotional support, and to help participants design and practice EX/RP exercises that targeted their treatment goals.

Safety Procedures

Before the start of treatment, researchers verified the 24 hour emergency psychiatric centers in each participant's local area. Symptom levels and adverse events were evaluated weekly via the platform and considered along with patients' message content in order to continuously assess risk. Any increase in suicidal ideation (e.g. MADRS-S item 9 ≥ 4) was automatically flagged by the system and prompted the therapist for further assessment (see appendix A for details on this procedure).

Statistical Analyses

All statistical analyses are reported according to "intention to treat" principles unless otherwise stated. Linear mixed models were used to assess continuous outcomes, with time as a fixed effect and random intercepts for each participant [33], and reported using maximum likelihood estimation with 95% confidence intervals around estimated means. We calculated Cohen's *d* by dividing the estimated change by the standard deviation of that

measure at pre-treatment. For non-continuous outcomes, ordinal logistic regression was used with a fixed effect of time, reported as proportional odds ratios with 95% confidence intervals. To examine whether data could be deemed to be missing at random, we compared completers (i.e., those with BDD-YBOCS data at follow-up) with non-completers on baseline measurements from Table 1, using t-tests or chi-square tests where appropriate. Analyses were performed in R (version 3.4.4) and in SPSS version 25.

RESULTS

In total, 32 participants initiated treatment, 25 participants (78%) completed mid-treatment assessments, 21 (66%) post-treatment, and 25 participants (78%) follow-up assessments, respectively (see Figure 1 for patient flow throughout the study). There were no statistically significant differences between completers and non-completers on baseline demographic and clinical variables (p's 0.29 - 0.91), except that non-completers, on average, had undergone more previous plastic surgeries (p = 0.03).

Primary Outcome

From baseline to week 6, participants made significant improvements on the BDD-YBOCS (Estimate = -8.12, 95% CI = -10.93 to -5.32, d = 1.66, p < .001). Further improvements were seen at post-treatment (Estimate = -12.63, 95% CI = -15.61 to -9.65, d = 2.57, p < .001) and were maintained at the 3-month follow-up (Estimate = -11.71, 95% CI = -14.52 to -8.91, d = 2.39, p < .001). The effect of time in a linear mixed effects model was significant (F[3, 71.63] = 31.79, p < .001). These outcomes were similar to those of the previous BDD-NET trials (see figure 2).

Secondary Outcomes

At post treatment, 15 participants (47%, 95% CI = 24% - 70%) were considered treatment responders, with 16 (50%, 95% CI = 29% - 71%) participants considered responders at 3-month follow-up. At post treatment, 9 participants (28%, 95% CI = 7% - 49%) no longer met criteria for BDD, which increased to 14 (44%, 95% CI = 23% - 65%) at the 3-month follow-up.

Participants showed statistically significant improvements on the CGI-S at post- (pOR = 0.17, 95% CI = .06 - .47, $p < .001$) and at 3-month follow-up (pOR = 0.22, 95% CI = .07 - .60, $p = .004$). The majority of participants who participated in post- and follow-up assessments were much improved or very much improved on the CGI-I after treatment (see figure 3).

Additionally, participants showed significant improvement in depressive symptoms measured using the MADRS-S ($F[13, 243.83] = 5.85$, $p < .001$), global functioning using the GAF ($F[2, 46.89) = 10.46$, $p < .001$), and insight using the BABS ($F[2, 47.36] = 10.11$, $p < 0.001$). See table 2 for estimated means and change on primary and secondary outcome measures.

Treatment activity, completion and acceptability

Therapists spent an average of 15.2 minutes supporting patients (SD = 12.1 minutes) per participant per week, and sent or received an average of 3.7 (SD = 2.7) messages per week. In total, 18 (56%) participants completed the core treatment content (modules 1-5). Eight participants (25%) completed all 8 modules. The mean number of modules completed was 5.1 (SD = 2.47). The following results on acceptability measures reflect patient responses at

post-treatment which could not be acquired from the entire sample, and therefore, are not intention to treat analyses. The mean WAI-SR score after treatment was 49.7 (SD = 10.7) out of a possible 60, indicating a strong therapeutic bond. Additionally, 95% of participants who gave feedback at post-treatment (20/21) reported that they felt well supported or very well supported by their therapist. Furthermore, despite the fact that some participants were not native English speakers, 95% of participants found the language used in treatment to be easy or very easy to understand. On average, participants were satisfied with the treatment and found it to be credible. Treatment satisfaction on the CSI was moderate to high at post-treatment, with a mean score of 129.4 (SD = 32.6) out of a possible 175. Participants rated treatment credibility as moderate on the CEQ at post-treatment (mean = 33.1, SD = 9.8).

Adverse Events

During the course of treatment, (8/32) 25% of participants reported at least one mild adverse event which did not pose any acute health risk. This included increased depressive symptoms (21.9%), a temporary increase in anxiety (15.6%), sleep disturbance or nightmares (9.4%), and feelings of shame (6.3%). Two adverse events needed further action due to increased suicidal ideation. One participant was admitted to high-intensive psychiatric care and ended participation in the study. In this case, researchers facilitated the connection to services in the participant's local area. Another participant who reported a high frequency of suicidal ideation remained in the study and was monitored by a local psychiatrist who had previously treated the patient.

DISCUSSION

Here we report the results of the first fully remote, global psychological treatment of BDD. We found that BDD-NET was associated with a large reduction of BDD symtoms at post-treatment and follow-up. Participant-rated reductions in body dysmorphic symptoms and depressive symptoms were 46% and 34%, respectively. Remission rates were 28% at post-treatment and 44% at follow-up. Additionally, patients at post-treatment (n= 21) reported a strong therapeutic bond with mean Working Alliance Inventory scores at 49.8 (sd = 10.4) out of a possible 60. The safety procedures tested in this study worked well. These results indicate that delivering BDD-NET across international borders is feasible, safe, and acceptable to clients. Furthermore, as required therapist time was minimal as compared to face to face CBT, our findings highlight international ICBT treatment as a promising solution to the global mental health epidemic in general.

Comparison to previous results

Current results are in line with previous evaluations of BDD-NET as well as face-to-face CBT for BDD. [12–14]. These findings suggest that delivering BDD-NET across borders in a new language, to a more culturally diverse patient population, has little to no impact on treatment effects. That said, while our sample comprises 12 different nationalities, only 25% came from non-western cultures. Post-hoc analyses did not identify nationality as a statistically significant predictor of BDD-YBOCS score, but larger samples recruiting more heavily from non-western countries are needed to detect differences between nationalities and to determine if adaptations should be made to the core treatment content.

Limitations

While the amount of missing data (35% at post-treatment and 21% at follow-up) is higher than previous investigations of BDD-NET (4% at post-treatment and 9% at follow-up in BDD-NET pilot), it is similar to estimates from recent meta-analyses of both face-to-face and Internet CBT [34,35]. Furthermore, our sensitivity analysis showed that participants with incomplete data at post-treatment did not differ from participants with complete post-treatment data on most baseline measures. However, participants with missing data did report more cosmetic surgeries. This could potentially be related to poorer insight or higher overall severity, which in turn could have impacted their commitment to treatment. Also, since there was no active comparison group, one cannot conclusively say that treatment caused the improvements that were observed. However, this was not the primary aim of the current study since the specific treatment effects of BDD-NET have already been established in comparison with online supportive therapy [13].

Challenges for clinical trials with global inclusion

Legal considerations

Trials are currently regulated by ethical review boards at universities and health care providers. These typically oversee research at their specific site. While multi-center trials may be international, this is to our knowledge the first one-site therapist-guided ICBT treatment study with global inclusion. Legislation on ethical vetting is by default national and there are presently no clear guidelines on how trials with international participation of study subjects should be regulated. Internet treatment may also be subject to regulations

that govern communications as well as clinical practice. Any legal ambiguity could potentially put some patients at risk when receiving treatment. Therefore, it is essential that international treatment programs protect patients' privacy and safety in this new context.

Risk management

Another challenge for studies with global inclusion is to ensure adequate care for at-risk patients while also reaching those in need of treatment. While high-risk patients may make clinicians uncomfortable due to liability concerns, many patients seek out ICBT because it is their only viable treatment option. Our procedure for monitoring and responding to suicidality was effective in ensuring patient safety despite the distance between patients and clinicians. One strategy used in this study to manage higher risk patients was to partner with local mental health practitioners who could facilitate risk assessment and expedite a safety plan in their local area if necessary. Psychiatrists can function particularly well in this role, as pharmacological treatment (when indicated) could complement ICBT treatment with minimal redundancy or interference. It is our view that offering remotely delivered evidence-based treatment will always be safer for patients than not having access to treatment at all.

Cultural differences

International ICBT treatment also poses some novel challenges to cultural competence. Patients not only have different cultural backgrounds, but are currently residing in a different cultural context. Therefore cultural considerations in treatment may be magnified. Special care should be taken when establishing treatment goals and designing

exposure exercises that are culturally appropriate. While our results suggest that a competent therapist can adapt the treatment to the needs of patients from different cultural backgrounds, it should be noted that the participants in this trial were relatively homogeneous (mainly from industrialised nations, highly educated, good command of English language, availability of local psychiatric services). Therefore, it is not yet clear to what extent ICBT can be made available in other settings.

Conclusion

This is, to our knowledge, the first investigation of a fully remote, therapist-guided psychological treatment recruited on a global scale. We found large reductions in core BDD symptomatology, with 44% of patients in remission at follow-up. Participants accepted the treatment and rated their therapist as supportive in the majority of cases. Future trials should evaluate the specific effects of BDD-NET compared to a credible control condition and strive to include more participants from non-western cultures. In summary, we found that an internet-delivered treatment for BDD can be delivered fully remotely with intact treatment effects, and in a safe way, across countries.

Author Contributions: CR was he primary investigator for the study and drafted the design of the study with CL, JE and D-MC. AG and CL both independently served as project manager during different periods of time. The treatment manual was written by JE with notable influence from work by SW, and was translated to English by CL. CL also developed the study website, protocol, drafted the ethics submissions, and international regulations pertaining to treatment. AG was in charge of the recruitment, assessment, and treatment of participants, with significant contributions by CL and additional work by OF. Data analysis was primarily conducted by OF and AG. The manuscript was primarily written by AG, with significant contributions by OF, CR, JE, SW, D-MC, and CL.

Funding: This study was funded through the regional agreement on medical training and clinical research (ALF) between the Stockholm County Council and Karolinska Institutet. CR was supported by the Swedish Research Council (grant No: K2013-61X-22168-01-3).

Competing interests: All authors declare: No support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Data sharing statement: No additional data are available.

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Table 1

Socio-demographic and Clinical Characteristics of the Sample (N = 32)

Variable	
Gender, n (%)	
Men	8 (25)
Women	24 (75)
Age, mean (SD)	31.91 (7.44)
Highest education, n (%)	
Primary school	1 (3.1)
High school	6 (18.8)
Bachelor's degree	14 (43.8)
Master's degree	10 (31.2)
Doctorate degree	1 (3.1)
Occupational status, n (%)	
Working, full time	9 (28.1)
Working, part time	10 (31.2)
Student	7 (21.9)
Unemployed	5 (15.6)
Disability pension	1 (3.1)
Years with BDD, mean (SD)	16.22 (9.10)
Number of areas of concern, mean (SD)	12.16 (5.84)
Comorbid conditions, n (%)	
Major depressive disorder	10 (31.2)
Panic disorder	2 (6.2)
Social anxiety disorder	5 (15.6)
Generalized anxiety disorder	5 (15.6)
Current medication, n (%)	
SSRI	2 (6.2)
SNRI	3 (9.4)
Benzodiazepines	1 (3.1)
Stimulants	1 (3.1)
Previous psychological treatment, n (%)	25 (78.1)
CBT	8 (32.0)
PDT	2 (8.0)
Non-specific counseling	12 (48.0)
Religious counseling	1 (4.0)
Unknown	2 (8.0)
Plastic surgery	
Previous plastic surgery, n (%)	13 (40.6)
Number of surgeries, mean (SD)	1.38 (2.46)

Nationality, n (%)	
American	12 (37.5)
Swedish	7 (21.9)
Indian	1 (3.1)
Bulgarian	1 (3.1)
Finnish	1 (3.1)
English	4 (12.5)
Serbian	1 (3.1)
South Korean	1 (3.1)
Irish	1 (3.1)
Norwegian	1 (3.1)
Sri Lankan	1 (3.1)
Lithuanian	1 (3.1)
Dysmorphic concerns questionnaire, mean (SD)	15.63 (2.50)

Abbreviations: BDD, Body dysmorphic disorder; SSRI, Selective serotonin reuptake inhibitor; SNRI, Serotonin and norepinephrine reuptake inhibitor; CBT, Cognitive behavior therapy; PDT, Psychodynamic therapy

Table 2. Estimated means and change on primary and secondary outcomes

Outcome	Time	Estimated mean (SE)	Estimated change [95% CI]	d	p
BDD-YBOCS	Pre	28.72 (1.35)			
	Mid	20.6 (1.43)	-8.12 [-10.93 to -5.32]	-1.66	0.001
	Post	16.09 (1.52)	-12.63 [-15.61 to -9.65]	-2.57	0.001
	Follow-up	17.01 (1.43)	-11.71 [-14.52 to -8.91]	-2.39	0.001
MADRS-S	Pre	20.16 (1.59)			
	Week 1	19.54 (1.08)	-0.62 [-2.74 to 1.51]	-0.07	0.57
	Week 2	17.02 (1.09)	-3.14 [-5.28 to -1]	-0.38	0.004
	Week 3	17.24 (1.11)	-2.91 [-5.1 to -0.73]	-0.35	0.01
	Week 4	16.15 (1.16)	-4.01 [-6.29 to -1.72]	-0.48	0.001
	Week 5	16.8 (1.13)	-3.35 [-5.57 to -1.14]	-0.4	0.003
	Week 6	16.7 (1.23)	-3.46 [-5.86 to -1.06]	-0.42	0.005
	Week 7	14.76 (1.25)	-5.4 [-7.84 to -2.95]	-0.65	0.001
	Week 8	15.37 (1.28)	-4.78 [-7.29 to -2.28]	-0.58	0.001
	Week 9	14.88 (1.25)	-5.27 [-7.72 to -2.82]	-0.63	0.001
	Week 10	16.37 (1.21)	-3.78 [-6.14 to -1.42]	-0.46	0.002
	Week 11	13.5 (1.34)	-6.66 [-9.28 to -4.03]	-0.8	0.001
	Post	13.36 (1.17)	-6.8 [-9.08 to -4.51]	-0.82	0.001
	Follow-up	12.37 (1.3)	-7.78 [-10.34 to -5.23]	-0.94	0.001
BABS	Pre	14.75 (1.06)			
	Post	10.1 (1.18)	-4.65 [-6.96 to -2.34]	-0.98	0.001
	Follow-up	10.72 (1.1)	-4.03 [-6.19 to -1.87]	-0.85	0.001
GAF	Pre	57.34 (1.73)			
	Post	67.43 (2.2)	10.08 [5.76 to 14.4]	0.94	0.001
	Follow-up	61.55 (2.07)	4.21 [0.15 to 8.27]	0.39	0.048

Abbreviations: SE, standard error; CI, confidence interval; d, Cohen's d; p, p-value (estimated change); BDD-YBOCS, Body dysmorphic disorder modification of the Yale-Brown obsessive compulsive scale; MADRS-S, Montgomery-Åsberg depression rating scale – self-rated; BABS, Brown assessment of beliefs scale; GAF, Global adaptive functioning.

Figure legends

Figure 1. Participant flow through the study

Figure 2. Clinician-rated BDD-YBOCS, Comparison with previous BDD-NET trials

Figure 3. CGI improvement

Figure 1. Participant flow through the study

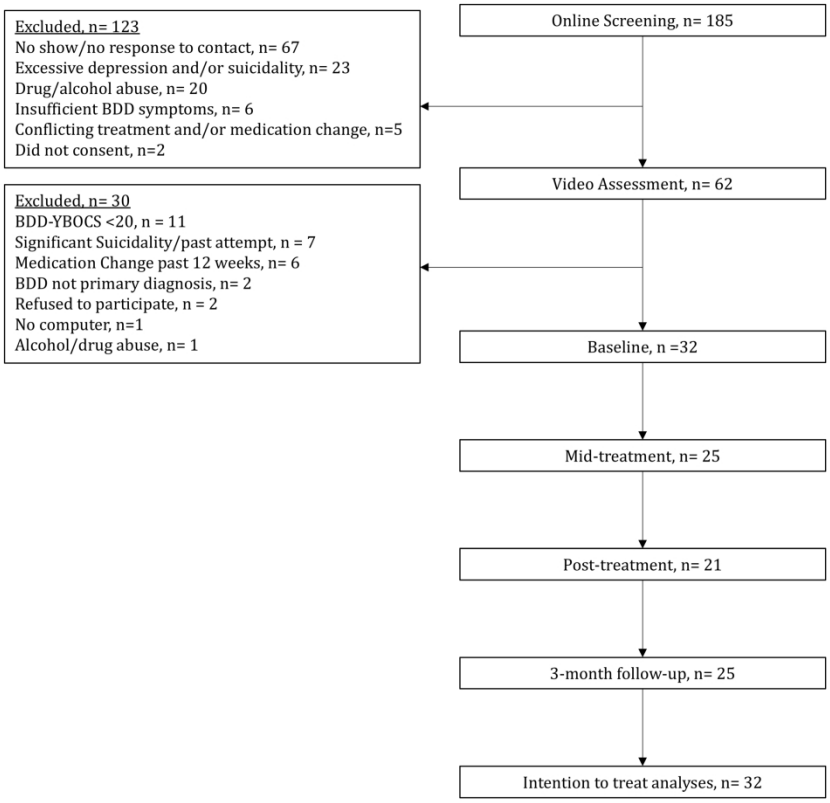

Figure 1

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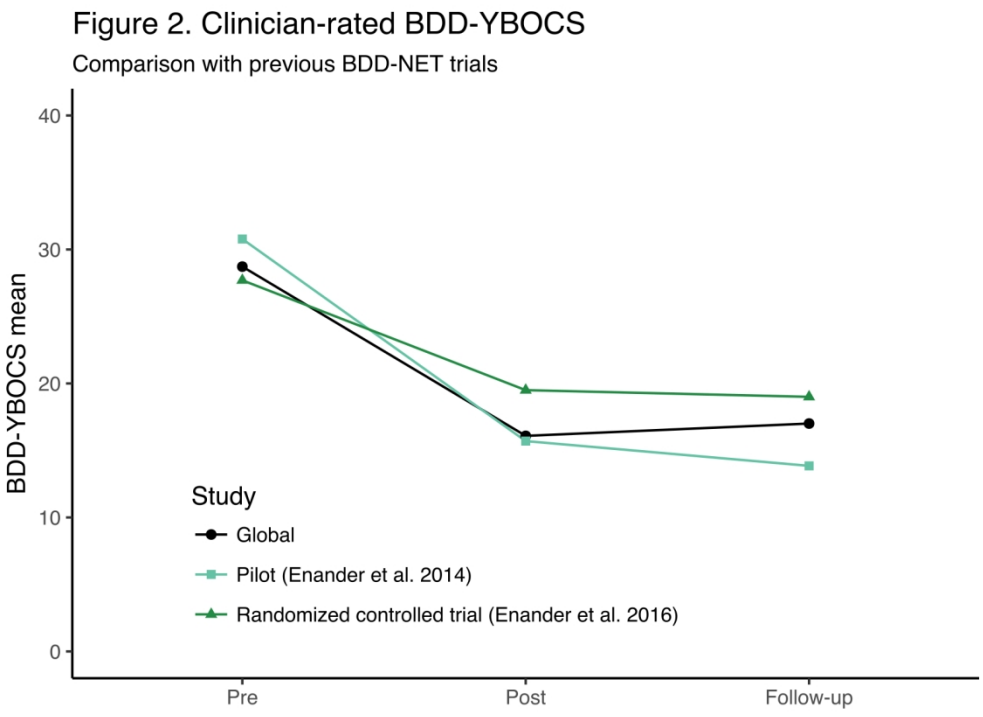

Figure 2. Clinician-rated BDD-YBOCS: Comparison with previous BDD-NET trials

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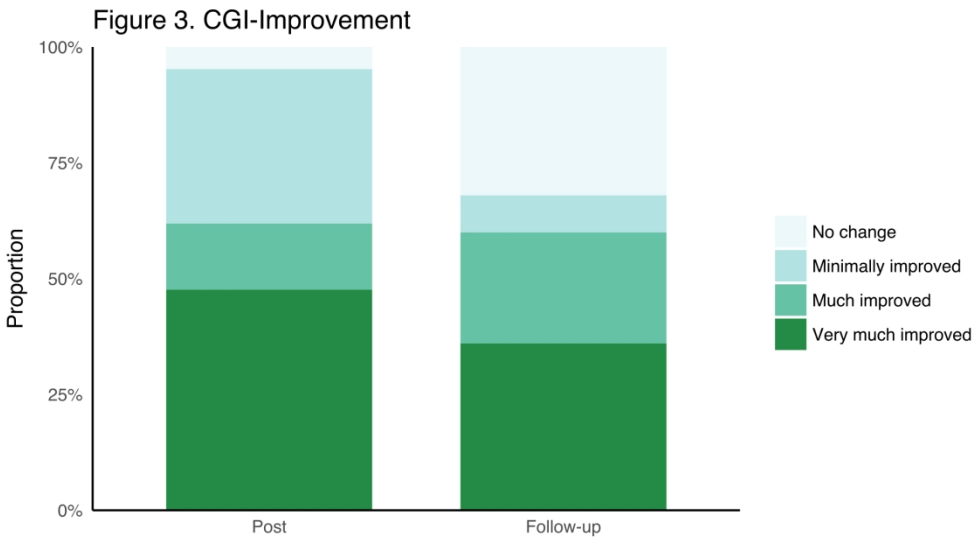

Figure 3. CGI Improvement

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Appendix A

Methods

Supplementary table 1. Overview of inclusion and exclusion criteria
Inclusion criteria
Fluent in English
Outpatient
≥ 18 years of age
BDDQ ≥ 4 at internet screening
DCQ ≥ 9 at internet screening
Primary diagnosis of BDD according to DSM-5
BDD-YBOCS ≥ 20
Verbal consent via video-conference and check yes to consent via treatment platform
Regular access to a computer with internet connection
Adequate skills to use the internet
Photo ID with name and age
Exclusion criteria
Psychotropic medication changes within 12 weeks prior to treatment
Completed CBT for BDD within 12 months prior to treatment
AUDIT ≥ 8 or DUDIT ≥ 8
Lifetime bipolar disorder or psychosis
MADRS-S ≥ 35
Clinically significant suicidal ideation or lifetime history or suicide attempts
Personality disorder that could jeopardize treatment participation (e.g. borderline personality disorder with self-harm)
Other current psychological treatment

No access to a 24 hour psychiatric emergency care center
No specific emergency contact person or emergency contact person phone number

Measures

Appearance Anxiety Inventory (AAI)

The AAI is a self-report, process measure that identifies cognitive processes and behaviors in the treatment of BDD. The maximum total score is 40, with higher scores indicating greater frequency of a process [1].

Brown Assessment of Beliefs Scale (BABS)

The BABS is a 7 item, clinician administered measure with excellent psychometric properties [2]. Scores can range from 0 to 24 with higher scores indicating poorer insight.

EuroQol – 5 Dimension Questionnaire (EQ-5D)

The EQ-5D is used as a non-disease specific assessment of quality of life and global functioning. It measures these constructs along 5 dimensions: Mobility, self-care, main activity, pain, and mood [3,4]. EQ-5D scores range between 0 (dead) and 1 (perfect health).

Sheehan Disability Scale (SDS)

The SDS has 3 items measuring functional impairment and disability regarding work/school, social life/leisure, and family life/home responsibilities on a likert scale between 0 (no interference) to 10 (extreme impairment). Two items measure days lost at work/school and days being underproductive at work/school. Items are on a likert scale of 0 (not at all) to 10 (very severe) [5,6].

Skin-Picking Scale – Revised (SPS-R)

The SPS-R is a self-report measure containing 8 items evaluating skin-picking severity. Scores range from 0 to 32 with higher scores indicating higher severity [7].

ICBT – EX/RP Adherence Scale

The ICBT – EX/RP Adherence Scale is modified from the Patient EX/RP Adherence Scale (PEAS) [8]. This measure assesses a patient's overall level of engagement in treatment with particular emphasis on quality and quantity of exposure and response prevention exercises. It looks at number of days, total hours, and quality of approach behaviors in EX/RP practice. In addition, it also looks other aspects of internet treatment adherence such as reading psychoeducational content and communicating with their therapist.

Results

Self-reported symptoms of BDD were significantly reduced over the course of treatment (F[13, 244.7] = 16.93, p <.001).

There were statistically significant reductions in delusionality on the BABS (F[2, 47.36] = 10.11, p < 0.001), as well as skin-picking using the SPS-R (F[2, 34.64] = 6.41, p = .004).

Changes in overall quality of life using the EQ-5D were not statistically significant (F[2, 36.28] = 1.35, p = .273). There were statistically significant improvements in functioning on the SDS (F[2, 35.07] = 12.78, p < .001).

Self-reported adherence to treatment (PEAS) increased over the course of treatment, from 16.83 (se = 1.88) at week 1, to 29.09 (se = 2.33) at post-treatmen

Supplementary table 2. Estimated means and change on secondary outcome measures

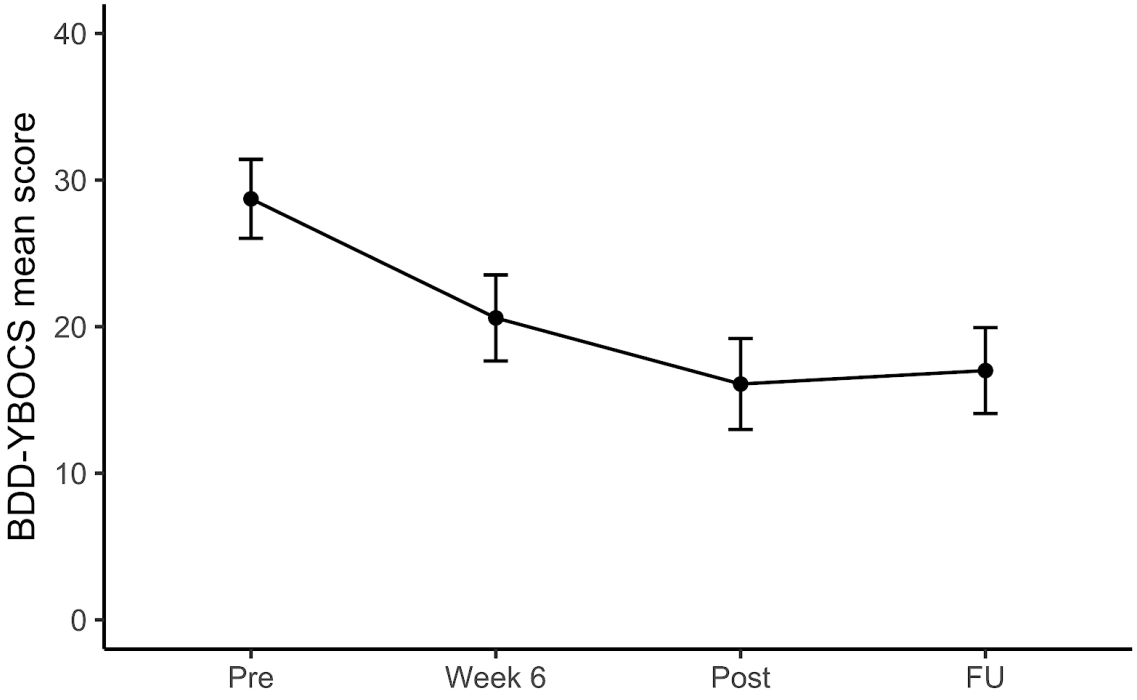
Outcome	Time	Estimated mean (SE)	Estimated change [95% CI]	d	p
AAI	Pre	26.66 (1.36)			
	Week 1	24.88 (1.11)	-1.78 [-3.95 to 0.39]	-0.26	0.109
	Week 2	22.25 (1.12)	-4.41 [-6.6 to -2.22]	-0.66	0.001
	Week 3	20.73 (1.14)	-5.93 [-8.16 to -3.69]	-0.88	0.001
	Week 4	19.09 (1.19)	-7.56 [-9.89 to -5.23]	-1.13	0.001
	Week 5	18.96 (1.15)	-7.69 [-9.95 to -5.43]	-1.14	0.001
	Week 6	18.52 (1.25)	-8.13 [-10.59 to -5.68]	-1.21	0.001
	Week 7	17.18 (1.28)	-9.48 [-11.98 to -6.97]	-1.41	0.001
	Week 8	17.47 (1.3)	-9.18 [-11.74 to -6.63]	-1.37	0.001
	Week 9	16.63 (1.28)	-10.03 [-12.53 to -7.53]	-1.49	0.001
	Week 10	16.86 (1.23)	-9.8 [-12.21 to -7.39]	-1.46	0.001
	Week 11	16.42 (1.37)	-10.23 [-12.91 to -7.56]	-1.52	0.001
	Post	14.38 (1.19)	-12.28 [-14.61 to -9.94]	-1.83	0.001
	Follow-up	13.45 (1.33)	-13.21 [-15.82 to -10.6]	-1.97	0.001
EQ-5D	Pre	0.75 (0.03)			
	Post	0.82 (0.04)	0.07 [-0.02 to 0.15]	0.33	0.126
	Follow-up	0.8 (0.05)	0.05 [-0.04 to 0.15]	0.25	0.302
SDS	Pre	14.56 (1.35)			
	Post	9.33 (1.43)	-5.17 [-7.93 to -2.41]	-0.6	0.001
	Follow-up	7.13 (1.6)	-7.43 [-10.57 to -4.29]	-0.86	0.001
SPS-R	Pre	6.38 (1)			
	Post	4.34 (0.74)	-2.03 [-3.49 to -0.58]	-0.33	0.01

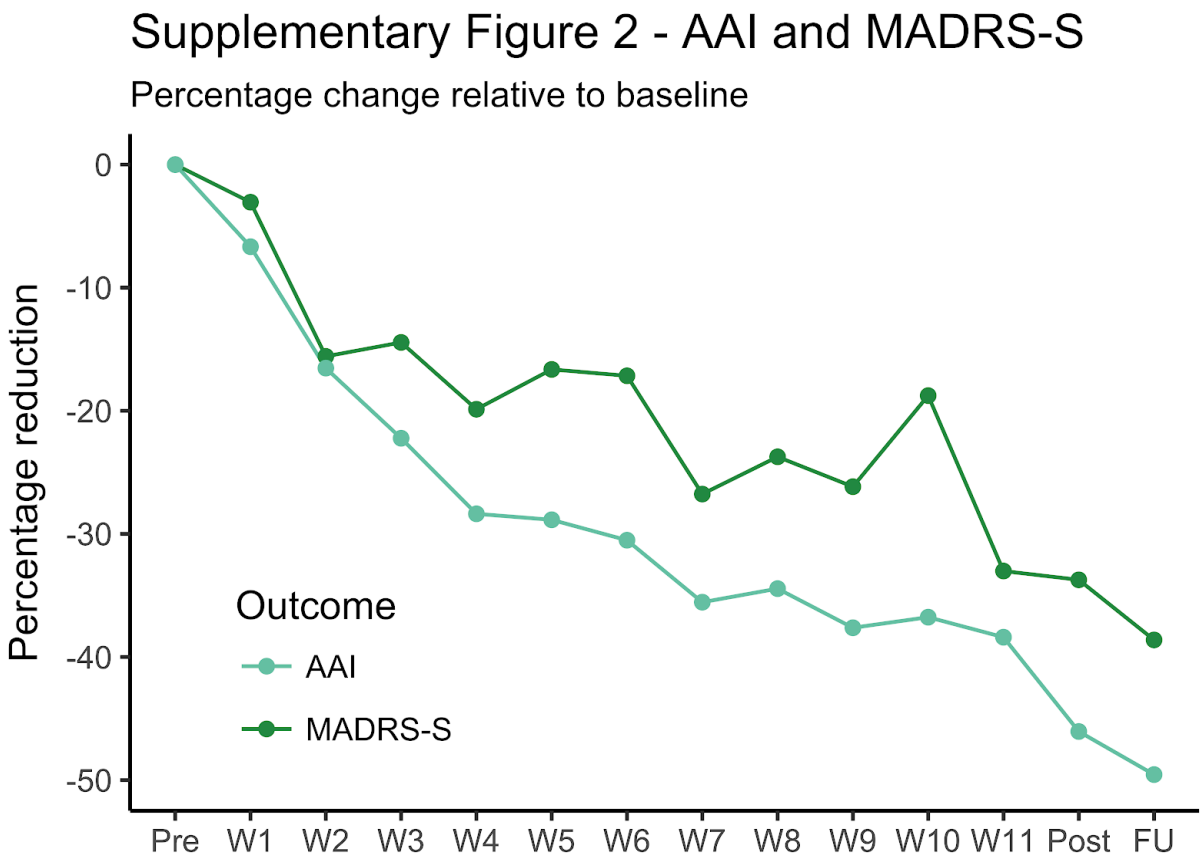
	Follow-up	3.66 (0.85)	-2.72 [-4.38 to -1.06]	-0.44	0.003
PEAS	Week 1	16.83 (1.88)	-12.26 [-15.95 to -8.57]	-1.22	0.001
	Week 2	18.49 (1.91)	-10.6 [-14.33 to -6.86]	-1.05	0.001
	Week 3	24.83 (1.96)	-4.26 [-8.1 to -0.41]	-0.42	0.031
	Week 4	23.82 (1.98)	-5.27 [-9.15 to -1.39]	-0.52	0.008
	Week 5	26.62 (2.08)	-2.47 [-6.54 to 1.59]	-0.25	0.235
	Week 6	28.54 (2.1)	-0.55 [-4.68 to 3.57]	-0.06	0.793
	Week 7	29.22 (2.05)	0.13 [-3.9 to 4.16]	0.01	0.949
	Week 8	28.47 (2.07)	-0.63 [-4.68 to 3.43]	-0.06	0.763
	Week 9	28.19 (2.06)	-0.9 [-4.94 to 3.14]	-0.09	0.664
	Week 10	32.18 (2.18)	3.09 [-1.18 to 7.36]	0.31	0.157
	Week 11	36.1 (4.04)	7 [-0.91 to 14.92]	0.7	0.084
	Post	29.09 (2.33)			
WAI-SR	Week 2	43 (1.33)	-4.64 [-7.25 to -2.04]	-0.48	0.001
	Week 4	45.28 (1.34)	-2.37 [-4.99 to 0.25]	-0.25	0.08
	Week 6	46.02 (1.37)	-1.62 [-4.31 to 1.07]	-0.17	0.24
	Week 8	46.19 (1.38)	-1.45 [-4.16 to 1.26]	-0.15	0.296
	Week 10	46.75 (1.4)	-0.9 [-3.65 to 1.85]	-0.09	0.524
	Week 12	46.88 (2.53)	-0.77 [-5.73 to 4.2]	-0.08	0.763
	Post	47.65 (2.05)			
CSI	Pre	110.77 (5.72)			
	Post	124.27 (4.85)	13.49 [3.99 to 23]	0.43	0.011

Abbreviations: SE, standard error; CI, confidence interval; d, Cohen's d; p, p-value (estimated change); AAI, Appearance anxiety inventory; EQ-5D, EuroQol – 5 dimension questionnaire; SDS, Sheehan disability scale; SPS-R, Skin-picking scale – revised; PEAS, ICBT – exposure and response prevention adherence scale; WAI-SR, Working alliance inventory – short revised; CSI, Client satisfaction inventory.

Supplementary Figure 1. BDD-YBOCS

Estimated means with 95% confidence intervals





Protocol

Therapist-Guided, Internet-Based Cognitive Behavioral Therapy for Body Dysmorphic Disorder – English Version (BDD-NET): A Feasibility Study

Principal Investigator: Christian Rück, MD, PhD, Department of Clinical Neuroscience

Version: XXXX

Date: XXXX

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1. Protocol Summary

PROTOCOL IDENTITY AND OBJECTIVES	
Protocol Title:	Therapist-Guided, Internet-Based Cognitive Behavioral Therapy for Body Dysmorphic Disorder – English Version (BDD-NET): A Feasibility Study
Trial Objectives:	Primary: Establish ICBT for BDD, English version (BDD-NET), as an acceptable, feasible, and potentially efficacious treatment.

METHODOLOGY	
Trial Design:	Uncontrolled clinical trial with within-subjects repeated measures design.
Treatment/Duration:	Internet-based cognitive behavioral therapy for 12 weeks.
Primary Endpoints:	Change from W0 to W12, 3 and 12-month follow-ups.
Efficacy Parameters:	Clinician-administered BDD-YBOCS[41]
Safety Parameters:	Designated emergency care centers, adverse events assessed weekly via the internet and also at post-treatment and 3-month follow-up using clinician assessments via video-conference or telephone.

POPULATION OF TRIAL SUBJECTS	
Description of Trial Subjects:	Adults, fulfill DSM-5 diagnostic criteria for BDD.
Number of Subjects:	30

TRIAL TIMETABLE	
First Subject In:	December 2015
Last Subject In:	January 2016
Last Subject Out:	April 2016

2. Administration Information

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PERSONNEL INFORMATION

Personnel	Background	Role	Affiliation
Christopher La Lima, MA	Clinical Psychology PhD student at Hofstra University	Co-Investigator, Project Manager	Karolinska Institutet (KI) and Hofstra University
Christian Rück, MD, PhD	Psychiatrist, associate professor, senior lecturer. Co-founder of Internetpsykiatrienheten, the world's largest implementation of ICBT in mental health. Research group leader in a group specializing in ICBT for OCD, BDD, and related disorders (www.rucklab.com)	Principal Investigator	KI
Jesper Enander, MSc	Doctoral candidate, psychologist, KI. Has written the ICBT program for BDD (BDD-NET).	Development and monitoring psychological treatment, IT platform	KI
Sabine Wilhelm, PhD	Chief of Psychology, Massachusetts General Hospital (MGH) Director, OCD and Related Disorders Program, MGH Professor, Harvard Medical School	Treatment development, recruitment, design	Harvard, MGH
David Mataix-Cols, PhD	Professor at KI. The most cited European researcher in OCD and related disorders (ISI Web of Science).	Supervising, study design	KI

3. Research field overview

WHAT IS BDD?

Body Dysmorphic Disorder (BDD) is a disabling illness characterized by excessive preoccupation with minor or imagined defect(s) in one's physical appearance, followed by

repetitive behaviors (e.g. mirror checking, camouflaging, mentally comparing one's appearance to another) and avoidance. This preoccupation leads to clinically significant distress and/or impairment[1]. BDD is associated with decreased social, emotional, and occupational functioning, as well as reduced quality of life[2, 3]. It is a chronic disorder linked to high rates of hospitalization[3, 4]. Individuals with BDD tend to have elevated rates of suicidal ideation and suicide attempts[5-7]. Furthermore, preliminary results suggest that they have a higher rate of completed suicide[6].

BDD is a prevalent disorder, affecting 0.7 % to 2.4 % of the general population across a variety of nationalities and geographic locations[7-12]. Specifically, it has a point prevalence of 2.4 % in the United States, exceeding schizophrenia and bipolar I disorder, and 2.1% among Swedish women[8, 9]. Additionally, BDD is a heritable disorder, with genetic factors accounting for approximately 44% of the variance in dysmorphic concerns[13].

While relatively common, many individuals with BDD are not receiving proper treatment. BDD is underdiagnosed in mental health care settings, and patients often do not express body image concerns to physicians due to feelings of shame[5, 14, 15]. Furthermore, individuals with BDD often have poor insight and seek non-psychiatric care, such as dermatological treatments and cosmetic surgery. Such treatments are rarely effective and can lead to a worsening of symptoms[16-18].

CBT FOR BDD

Evidence based treatments for BDD include cognitive behavioural therapy (CBT) and pharmacotherapy with serotonin reuptake inhibitors (SRIs)[19-22]. Veale et al. (2014) conducted the only RCT comparing CBT with an active comparison group to date. They reported superiority of CBT over anxiety management, including progressive muscle relaxation and breathing techniques. Wilhelm et al. (2013) developed a multimodal treatment manual for BDD that was tested in one open trial and one wait-list controlled trial. Both studies resulted in improved BDD symptoms at post-treatment and maintained gains at a 6-month follow-up[21, 23]. Wilhelm et al. (2014) additionally found that depression, insight, and disability significantly improved with this treatment. These studies show promising results that CBT is effective and can have a lasting effect on symptom reduction in the months following treatment. However, to date there are relatively few studies of CBT treatment for BDD, and they include relatively small samples, so larger studies are needed to better understand this area.

While studies of CBT for BDD suggest that this treatment is efficacious, few patients are in fact receiving it[24]. In an online survey, 17.4% of participants diagnosed or self-diagnosed with BDD had received empirically supported psychotherapy (i.e. CBT) for body dysmorphic concerns, and 34.4% had been treated with SSRIs[25]. In another internet survey, 19.8% of people with body dysmorphic concerns were participating in psychosocial treatment, and 18.6% were receiving psychotropic medications[24]. Participants in both studies reported that shame associated with talking openly about one's appearance concerns was a major factor in not seeking help. In addition to underreporting symptoms associated with shame, underdiagnosis of BDD in mental health settings, and patients seeking non-psychiatric treatments that are ineffective or potentially worsen symptoms, individuals face restricted access to CBT[5, 14, 15, 16-18, 25-27]. This includes cost of services, a lack of trained therapists, and not having a specialized healthcare provider

nearby[25-27]. Furthermore, scheduling difficulties and transportation to healthcare providers hinder help-seeking efforts[25]. Therefore, it is clear that improved access to CBT treatments is needed.

ICBT FOR BDD

In response to limited CBT availability and accessibility, internet-based CBT (ICBT) with therapist support has been developed. In ICBT, the patient, instead of going to a clinic, logs onto a secure website and works with written self-help materials and homework assignments, supported online by a clinician. It has the advantage of being more accessible and requiring less therapist time than face-to-face[28]. ICBT has been shown to be effective in treating a variety of psychiatric disorders, such as obsessive-compulsive disorder, social anxiety disorder, depression, and panic disorder[29-31]. When compared to face-to-face CBT, a recent meta-analysis suggests no difference in treatment outcomes between the two, although there might be disorder-specific differences[32]. Additionally, ICBT is cost-effective and has been employed as a part of healthcare systems in Sweden, Australia, and the Netherlands[30, 32-36].

Recently, members of our research group (Enander et al. 2014)[37] developed ICBT for BDD (BDD-NET), based on existing BDD CBT manuals[38, 39], and tested it with a Swedish-speaking sample in an uncontrolled clinical trial. Results indicated BDD-NET was effective, with 82% of participants responding to treatment and large effect sizes. Participants also showed improvement in the areas of depression, skin picking, global functioning, and body image-related quality of life. Treatment gains in this study were maintained at a 3-month follow-up, and ICBT for BDD was highly accepted by participants[37]. Additionally, therapist interaction time was lower than that of typical CBT. Enander et al. (2015)[40] then conducted an RCT comparing BDD-NET with an active control (supportive therapy). In this trial, BDD-NET was superior to supportive therapy and associated with significant improvements in symptom severity, depression, and quality of life (submitted manuscript). Furthermore, self-reported satisfaction with BDD-NET was high.

ICBT for BDD may be especially important to address restricted access to treatment, including therapist availability, costs of services, and proximity to a clinician with specialized training. In addition, patients with BDD who have difficulties seeking face-to-face care may be easier reached via the internet. To test the BDD ICBT protocol (BDD-NET) in an English-language adaptation may be a first step to greatly increasing the availability of evidence-based treatment in the United States, Great Britain, India, and other areas with English-speaking populations. The current study aims to do just that in a pilot trial.

4. Purpose and Objectives

GENERAL PURPOSE

We plan to establish ICBT for BDD, English version (BDD-NET), as an acceptable, feasible, and potentially efficacious treatment for English-speakers across national borders. To achieve these goals, we need to:

PRIMARY OBJECTIVES

O1: Gain evidence that BDD-NET with therapist support leads to decreased symptoms of BDD.
O2: Assess patient satisfaction with the BDD-NET treatment platform and online therapist guidance.

O3: Evaluate patient engagement and ability to utilize tools and services offered in BDD-NET.

RESEARCH QUESTIONS

Q1: Does BDD-NET lead to a decrease in BDD symptom severity, dysmorphic concerns, and appearance concerns in English-speaking patients diagnosed with BDD?
Q2: Does BDD-NET improve insight/delusionality in these patients?
Q3: Does BDD-NET reduce symptoms of depression in these patients?
Q4: Does BDD-NET improve global functioning, quality of life, and disability in these patients?
Q5: Are these patients satisfied with BDD-NET and do they report a good working alliance with BDD-NET therapists?
Q6: Do these patients see BDD-NET as a credible intervention?
Q7: Are these patients compliant with the BDD-NET treatment protocol and able to complete treatment behaviors with its given resources?
Q8: Does the completion of EX/RP exercises and/or other treatment behaviors in BDD-NET predict outcome?

5. Hypotheses

H1. English-speakers diagnosed with BDD will decrease their BDD symptom severity, dysmorphic concerns, and appearance concerns at the end of the BDD-NET program (week 12), and at 3 and 12 month follow-ups, as compared to pretreatment.
H2. These patients will improve in insight/delusionality at week 12, and 3 and 12 month follow-ups, as compared to pretreatment.
H3. These patients will reduce in depression symptoms at week 12, and 3 and 12 month follow-ups, as compared to pretreatment.
H4: These patients will improve in global functioning, quality of life, and disability at week 12, and 3 and 12 month follow-ups, as compared to pretreatment.
H5: These patients will report satisfaction with treatment at W2, W7, and W12, and good working alliance with therapists.
H6: These patients will report treatment credibility for BDD-NET throughout treatment.
H7: These patients will complete BDD-NET core treatment modules (1-5) within 12 weeks of treatment, including module homework questions, written worksheets, and monitoring completed EX/RP exercises, provided BDD-NET resources and online therapist guidance.
H8: Reported EX/RP behaviors throughout treatment will predict outcome, with more EX/RP practice leading to greater improvement.

6. Endpoints

PRIMARY ENDPOINT

H	Measure	Utility	Time Points by Week															
			S	0	1	2	3	4	5	6	7	8	9	10	11	12	Post (12)	3m	12m
H1	Clinician-rated Body Dysmorphic Disorder	BDD symptom severity		x						x							x	x	x

	Modification of Y-BOCS; BDD-YBOCS[41]																	

SECONDARY ENDPOINTS

H	Measure	Utility	Time Points by Week															
			S	0	1	2	3	4	5	6	7	8	9	10	11	12	Post (12)	3m	12m
	Structured Clinical Interview for DSM 5 – Research Version (SCID-5-RV) module G[42]	BDD Remission status, comorbid anxiety diagnoses (e.g. social phobia)		x													x	x	x
	Mini-International Neuropsychiatric Interview – version 7.0 (M.I.N.I. 7.0)[43]	Current major depressive episode, comorbid diagnoses		x													x	x	x
H1	Dysmorphic Concerns Questionnaire (DCQ)[44]	BDD screening/ dysmorphic concerns	x	x													x	x	x
H1	Appearance Anxiety Inventory (AAI)[45]	BDD symptoms	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
H2	Brown Assessment of Beliefs Scale (BABS)[46]	Conviction and insight regarding beliefs/ obsessions		x													x	x	x
H3	Montgomery-Åsberg Depression Rating Scale, self-report (MADRS-S)[47]	Depressive symptoms	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Columbia-Suicide Severity Rating Scale (C-SSRS)	Suicide severity, suicidal		x													x	x	x

	Lifetime Recent – Clinical Version[48]	ideations and behaviors																	
	Skin-Picking Scale – Revised (SPS-R)[49]	Skin-picking severity		x												x	x	x	
H4	Global Assessment of Functioning (GAF)[50]	Global functioning		x												x	x	x	
H4	Clinical Global Impressions Scale – Severity (CGI-S)[51]	Global severity		x												x	x	x	
H4	Clinical Global Impressions Scale – Improvement (CGI-I)[51]	Global Improvement														x	x	x	
H4	EuroQol – 5 Dimension Questionnaire (EQ-5D)[52]	Quality of life		x												x	x	x	
H4	Sheehan Disability Scale (SDS)[53]	Functional Impairment		x												x	x	x	
H5	Client Satisfaction Inventory (CSI)[54]	Client satisfaction				x				x						x			
H5	Working Alliance Inventory – Short Revised (WAI-SR)[55]	Therapeutic alliance				x		x		x		x		x		x	x		
H6	Credibility Scale (Credibility/Expectancy Questionnaire)[56]	Treatment Credibility and expectancy		x		x		x		x		x		x		x	x		
H7	Completion of core treatment modules (1-5)	Treatment compliance	Continually monitored throughout treatment																
H7	Early Termination Checklist (Appendix Figure 1)	Reasons for early discontinuation or withdrawal	Continually monitored throughout treatment																

H8	ICBT – EX/RP Adherence Scale (modified from the Patient EX/RP Adherence Scale (PEAS)[57])	EX/RP adherence and practice; treatment adherence				x	x	x	x	x	x	x	x	x	x	x	x	

7. Efficacy of Data Collection

CLINICIAN-ADMINISTERED INTERVIEWS AND MEASURES

Clinician-Rated Body Dysmorphic Disorder Modification of Y-BOCS (BDD-YBOCS)[41]. The BDD-YBOCS is a modification of the Yale-Brown Obsessive Compulsive Scale designed to rate BDD symptom severity. It is a 12-item, semi-structured, clinician-administered interview with a total score of 0-48. Higher scores indicate more severe BDD symptoms[41]. In a recent study examining the psychometric properties of the BDD-YBOCS, it was found to have excellent interrater intra-class correlation coefficients (ICC), [.77 to 1.00 (p's < .001)] on all items, good test-retest ICCs for individual items [.73 to .93 (p's < .001)], and strong internal consistency [Cronbach's α = .92][41].

Structured Clinical Interview for DSM 5 – Research Version (SCID-5-RV), module G[42]. The SCID-5-RV is a semi-structured, clinician-administered interview designed to diagnose disorders according to the DSM-5[42]. For the purposes of the present study, only module G (obsessive-compulsive and related disorders) will be utilized.

Mini-International Neuropsychiatric Interview – Version 7.0 (M.I.N.I. 7.0)[43]. The M.I.N.I. 7.0 is a reliable and valid, brief, structured diagnostic assessment administered by a clinician[43]. It covers a range of disorders, including Agoraphobia, Alcohol Dependence/Abuse, Anorexia Nervosa, Antisocial Personality Disorder, Bulimia Nervosa, Generalized Anxiety Disorder, (Hypo) Manic Episode / Bi-Polar Disorder, Major Depressive Episode, Obsessive Compulsive Disorder, Panic Disorder, Posttraumatic Stress Disorder, Psychotic Disorders, Social Phobia (Social Anxiety Disorder), Substance Dependence/Abuse, and Suicidality[43]. This instrument will be used to screen and assess comorbid disorders and co-occurring pathology.

Columbia-Suicide Severity Rating Scale (C-SSRS) Lifetime Recent – Clinical Version[48]. The C-SSRS was designed to assess the severity of suicidal thoughts and behaviors. The C-SSRS has good convergent, divergent, and predictive validity, as well as sensitivity and specificity[48]. The ideation and behavior subscales show strong convergent validity with established suicidal ideation and behavior scales. In this study, exclusion during the W0 screen is based on a Most Severe Ideation score ≥ 4 (Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts) in the past month, or any reported lifetime actual attempt, interrupted attempt, aborted attempt, or preparatory behavior for suicide[48].

Global Assessment of Functioning (GAF)[50]. The GAF is a clinician rating of 1 to 100 indicating a patient's overall level of functioning. A higher score indicates greater functioning[50].

Clinical Global Impressions Scale - Severity (CGI-S)[51]. The CGI-S is a clinician global rating of a patient's overall severity. It ranges from 1 (normal, not ill at all) to 7 (among the most extremely ill of subjects)[51].

Clinical Global Impressions Scale – Improvement (CGI-I)[51]. The CGI-I is a clinician global rating of a patient's overall symptom change. It ranges from 1 (very much improved) to 7 (very much worse)[51].

SELF-REPORT MEASURES

Body Dysmorphic Disorder Questionnaire (BDDQ)[58]. The BDDQ is a BDD screening tool with good sensitivity and specificity[15]. A BDDQ cut-off score of at least 4 (positive BDD-screening) will be used to screen eligible participants for this study[59].

Dysmorphic Concerns Questionnaire (DCQ)[44]. The DCQ is a 7-item questionnaire assessing dysmorphic concerns in which patients compare their degree of concern with that of others for each item. It has good internal consistency (Cronbach's $\alpha = .88$), and strong correlations with other measures of distress and work and social impairment[44]. A DCQ cut-off score of 9 will be used to determine a positive BDD screen following the initial internet screening, as it has been shown to correctly identify 96.4% of BDD patients and 90.6% of undergraduates[60].

Brown Assessment of Beliefs Scale (BABS)[46]. The BABS is a clinician-administered, 7-item scale designed to assess delusional beliefs and insight in a range of psychiatric disorders. Total scores range from 0 to 24, with higher scores indicating greater delusionality or lack of insight. This instrument has good internal consistency (Cronbach's $\alpha = .87$), test-retest reliability (individual item test-retest ICCs = .79-.98, median = .95), interrater reliability (ICC = .96), and sensitivity to change, and very good convergent validity[46]. There is evidence to suggest that a score of 4 on the first item (conviction) in addition to a total score of at least 18 out of 24 is an empirically supported criteria for classifying a patient's beliefs as delusional[46].

Appearance Anxiety Inventory (AAI)[45]. The AAI was designed to be a process measure that identifies cognitive processes and behaviors possibly mediating outcome in the treatment of BDD[45]. It consists of 10 self-report items, each scored on a 5-point Likert scale ranging from 0 (not at all) to 4 (all the time). The maximum total score is 40, with higher scores indicating greater frequency of a process[45]. It has good internal consistency (Cronbach's $\alpha = .86$), test-retest reliability (ICC = .87, $p < .001$), convergent validity for the measurement of appearance anxiety, and sensitivity to change[45].

Skin-Picking Scale – Revised (SPS-R)[49]. The SPS-R is a self-report measure containing 8 items evaluating skin-picking disorder severity. It has acceptable internal consistency for the total score (Cronbach's $\alpha = .83$), as well as the symptom severity (Cronbach's $\alpha = .81$) and impairment (Cronbach's $\alpha = .79$) subscales[49]. Preliminary evidence supports convergent/concurrent and discriminant validity for the 2 subscales[49].

Montgomery - Åsberg Depression Rating Scale – self-report (MADRS-S)[47]. The MADRS-S contains 9 items evaluating depressive symptoms. It has satisfactory test-retest reliability and internal consistency (ICC = .78, Cronbach's alpha = .84), and good sensitivity to change[61]. It correlates well with the Beck Depression Inventory (BDI) [$r = .87$ ($p < .0001$)][62]. Holländare, Andersson, and Engström (2010) found a high correlation between total scores on the MADRS-S paper and internet versions [$r = .84$ ($p < .001$)][63]. Additionally, their results indicated no significant main effect for administration format between paper and internet versions. The MADRS-S was found to have good discriminative validity with the physician-rated Montgomery - Åsberg Depression Rating Scale (MADRS) in detecting a score of at least 35 (severe) during a current depressive episode[61].

Client Satisfaction Inventory (CSI)[54]. The CSI contains 25 items evaluating overall satisfaction with treatment. Total scores on this measure range from 0 % to 100 % satisfied. It is reliable, with very good internal consistency (Cronbach's $\alpha = .93$), and a standard error of measurement less than 5 % of the full range of scores[52]. Additionally, there is evidence to support good content and construct validity (μ item-total $r = .57$)[54].

Working Alliance Inventory – Short Revised (WAI-SR)[55]. The WAI-SR measures 3 aspects of therapeutic alliance: agreement on the tasks of therapy, agreement on the goals of therapy, and development of an affective bond. The WAI-SR correlates well with the original Working Alliance Inventory total score (r = .94-.95), as well as other alliance measures[55].

Credibility/Expectancy Questionnaire[56]. The Credibility/Expectancy Questionnaire is divided into 2 subscales that assess beliefs about the credibility of a treatment and thoughts/feelings of treatment expectancy. It was found to have a high internal consistency across 3 studies (expectancy factor standardized α = .79-.90; credibility factor Cronbach's α = .81-.86; whole scale standardized α = .84-.85). Additionally, it had good test-rest reliability over the course of 1 week (expectancy: .82, credibility: .75)[56].

EuroQol – 5 Dimension Questionnaire (EQ-5D)[52]. The EQ-5D is used as a non-disease specific assessment of quality of life and global functioning. It measures these constructs along 5 dimensions: Mobility, self-care, main activity, pain, and mood, and has shown some evidence for construct validity and good test-retest reliability[52, 64].

Sheehan Disability Scale (SDS)[53]. The SDS is a 4-item questionnaire measuring functional impairment and disability. Items 1-3 assess the domains of disability regarding work, social life and leisure, and family life and home responsibilities. They are on a likert scale of 0 (not at all) to 10 (very severe). Item 4 measures overall impairment and is on a likert scale of 1 (no symptoms) to 5 (symptoms radically change or prevent normal work or social life). In a study conducted by Leon, Olfson, Portera, Farber, and Sheehan (1997), this instrument was found to have high internal consistency (Cronbach's α = .89) and good construct validity, with over 80 % of patients with psychiatric disorders having an elevated SDS score[53].

ICBT – EX/RP Adherence Scale (modified from the Patient EX/RP Adherence Scale (PEAS)[57]). The ICBT EX/RP Adherence Scale is loosely based on the Patient EX/RP Adherence Scale (PEAS)[57]. It is a questionnaire designed for this study measuring number of days in which EX/RP was practiced, total hours EX/RP was conducted, quality of approach behaviors (1, (Didn't do exposure, 0% approach/100% avoidance) to 7 (Most, > 90%)) and ritual prevention (0, (0% response prevention) to 7 (Most > 90%)) during planned EX/RP practice, and quality of approach behaviors and ritual prevention outside of planned EX/RP practice in the past week. It also assesses number of days and total hours in which other ICBT treatment behaviors were completed in the past week (E.g. messaging therapist and reading psychoeducational materials).

BEHAVIORAL OUTCOME DATA

Completion of core treatment modules (1-5). Modules 1-5 contain the core components of treatment (psychoeducation, EX/RP hierarchy formation, cognitive restructuring, and EX/RP practice). Patients will be granted access to subsequent modules after completion of the previous one unless otherwise clinically indicated. In order to consider a module completed, subjects must provide written text relevant to symptoms, concerns, and treatment, according to module prompts, for all module homework assignments and written worksheets, as well as monitor their SUDS levels related to EX/RP practice.

Treatment termination (as measured by the Early Termination Checklist). The Early Termination Checklist is to be completed by the therapist of each subject immediately following early discontinuation for any reason. It provides the reason(s) for ending treatment prematurely, whether related to early termination or voluntary withdrawal.

8. Project description

DESIGN

A pilot study with within-subjects repeated measures design. Analysis of primary (BDD-YBOCS[41]) and secondary outcome measures between baseline and post treatment will be conducted to determine if the treatment significantly reduced symptoms associated with BDD. In a comparable study using a Swedish-language version of BDD-NET, Enander et al. (2014) [N = 23] found effect sizes of $d = 2.01$ ($p < .01$) at post-treatment and $d = 2.04$ ($p < .01$) at a 3-month follow-up, with 82% of completers being responders (≥ 30% decrease on the BDD-YBOCS)[37]. Furthermore, Enander et al. (2015) [N = 94] had effect sizes of .95 ($p < .001$) and .87 ($p < .001$) at post-treatment and 3-month follow-up, respectively, in an RCT comparing BDD-NET to supportive therapy[40]. Given 80% power, 30 participants are needed to be able to detect an effect size of $d = 0.66$. Clinical assessments of treatment effects and feedback from participants will be utilized to improve upon the BDD-NET treatment protocol.

SELECTION, WITHDRAWAL, AND DISCONTINUATION OF SUBJECTS

INCLUSION CRITERIA

Criteria	Method of Ascertainment
1. Fluent in English	Video-conference inclusion evaluation. If English is not subject's native language, he/she will be asked to read through 1 page of non-CBT treatment text and follow prompts; assessment based on the judgment of the evaluator
2. Outpatient	Self-report
3. At least 18 years of age	Self-report
4. Positive screening for BDD on BDDQ[58]	BDDQ score ≥ 4 at initial internet screening[59]
5. Positive screen for BDD on DCQ[44]	DCQ score ≥ 9 at initial internet screening[44]
6. Primary Diagnosis of BDD according to DSM-5[1]	SCID-5 module G[42]
7. A score of at least 20 on the BDD-YBOCS at baseline[41]	BDD-YBOCS[41]
8. Signed Informed Consent	Verbal consent via video-conference and check yes to consent on secure webpage
9. Regular access to a computer with internet capabilities	BDD-NET Accessibility and Confidentiality Interview
10. Adequate skills to use the internet	Self-report, completion of initial internet screening
11. Photo ID with name and age	Shown via video-conference at inclusion evaluation

EXCLUSION CRITERIA

Criteria	Method of Ascertainment
1. Psychotropic medication changes within 12 weeks prior to treatment	Self-report
2. Completed CBT for BDD within 12 months prior to treatment (defined as at least 12 sessions of EX/RP)	Self-report
3. Current substance dependence	Alcohol Use Disorders Identification Test (AUDIT) score ≥ 8[65], Drug User Disorders Identification Test (DUDIT) score ≥ 8[66], Mini-International Neuropsychiatric Interview – version 7.0 (M.I.N.I. 7.0)[43]
4. Lifetime bipolar disorder or psychosis	Self-report and M.I.N.I. 7.0[43]
5. Severe Depression	MADRS-S[47] score ≥ 35
6. Clinically significant suicidal ideation or lifetime history of suicide attempts	Video-conference inclusion evaluation; ≥ 5 on item 9 of MADRS-S[47]; C-SSRS Lifetime Recent – Clinical Version: Recent (past month) - Most Severe Ideation score ≥ 4, or any lifetime actual attempt, interrupted attempt, aborted attempt, or preparatory behavior for suicide[48].
7. Personality disorder that could jeopardize treatment participation (e.g. borderline personality disorder with self-harm)	PD diagnosis based on self-report and video-conference inclusion evaluation.
8. Other current psychological treatment	Self-report
9. No access to a 24 hour psychiatric emergency care center	Self-report; Co-investigator will confirm access based on subject's location and contact with emergency care center
10. No specified emergency contact person or emergency contact person phone number	BDD-NET Safety Interview

CRITERIA FOR WITHDRAWAL

1. Consent withdrawal by patient.
2. High suicide risk determined by the investigators.
3. Attempt at suicide during treatment.
4. Worsening of BDD symptoms better addressed by treatment incompatible with this protocol, as determined by the investigators' clinical judgment.
5. Psychiatric hospitalization during treatment.

OTHER REASONS FOR PREMATURE DISCONTINUATION OF TREATMENT

1. Adverse event or circumstances justifying the discontinuation of treatment as determined by the investigators.

2. Protocol deviation that jeopardizes the patient's safety.
3. Patient lost to follow-up: In the event that a patient is non-responsive following treatment, the investigators are to make efforts to contact him/her, establish a reason for discontinuation of treatment, and suggest the subject participate in an end-of-study video-conference interview. If these attempts to contact the participant fail, the investigators declare him/her "lost to post-treatment assessment." The previous contact attempts should be documented in the patient's medical file.

SUBJECT LOG

- The investigators must record the reason and date of premature discontinuation of treatment both in Take Care (electronic medical records system) and on the Early Termination Checklist (Appendix Figure 1). If the investigator gives more than one reason, he/she must indicate the main reason. Specifically if a subject withdraws, his/her therapist will ask him/her the reason for withdrawal.
- In the case of treatment discontinuation, participants will be asked to participate in all remaining scheduled assessments, including all measures for weekly internet self-reports and video-conference interviews at W12, 3 month follow-up, and 12 month follow-up. If subject is unable to complete the remaining video-conference assessments, he/she will be asked to complete the same assessment measures via phone.

PROCEDURES

A flow diagram of procedures can be found in Figure 2 of the appendix.

INITIAL INTERNET SCREENING

Participants can be referred by a clinician or self-referred. Participants interested in partaking in the study first do an Internet-administered screening on an encrypted webpage using the BDDQ[58], MADRS-S[47], Alcohol Use Disorders Identification Test (AUDIT)[65], Drug User Disorders Identification Test (DUDIT)[66], DCQ[44], and AAI[45], and filling out general demographic information. Before partaking in the screening, the participant is given written information about the study (objectives, requirements for participation, etc.). Participants will be excluded from the study at this point if they: *a)* score an 8 or higher on the AUDIT, which was found to have sensitivity of 92 % and specificity of 94 % for hazardous and harmful alcohol use[65], *b)* score an 8 or higher on the DUDIT[66], which was found to correspond to impairing drug issues with 90 % sensitivity and 85 % specificity[63], *c)* score at least 5 on item 9 of the MADRS-S[47], *d)* score less than 9 on the DCQ, as 9 was determined to be an optimal cut-off when screening for BDD[44], or *e)* score less than 4 on the BDDQ, as 4 was determined to be an appropriate cut-off for a positive screening of BDD[59].

VIDEO-CONFERENCE INCLUSION/BASELINE ASSESSMENT

If the participant fulfils selection criteria, he/she is interviewed by a psychiatrist/psychologist/supervised Masters level clinician at Karolinska Institutet via video-conference. The aims of this visit are to *a)* discuss informed consent and obtain verbal consent *b)* verify diagnosis of BDD, *c)* assess symptom severity and global functioning, *d)* confirm subject's identity, *e)* evaluate English language competency, *f)* establish a safety plan while in treatment, *g)* assess subject's access to a computer, *h)* obtain subject's treatment history, and *i)* inform patient of treatment protocol. This interview includes the Protocol # XXXX BDD-NET

Informed Consent form (Appendix Figure 3), BDD-YBOCS[41], SCID-5-RV module G[42], M.I.N.I. 7.0[43], BABS[46], C-SSRS Lifetime Recent-Clinical version[48], GAF[50], clinician-rated CGI-S[51], BDD-NET Safety Interview (Appendix Figure 4), and BDD-NET Accessibility and Confidentiality Interview (Appendix Figure 5). Subjects will be evaluated for English language competency via real time conversation during the inclusion evaluation. They will also be asked if English is their native language. If it is not, they will be prompted to read through 1 page of a non-CBT treatment text and to follow prompts to further assess English language proficiency. Additionally, subjects will be asked to hold up a government-issued form of photo identification to confirm name, age, gender, and country of citizenship or residency. During this interview, subjects will be asked about their treatment history related to BDD and mental health concerns.

VIDEO-CONFERENCE INCLUSION/BASELINE ASSESSMENT FOLLOW-UP

Following the video-conference inclusion/baseline assessment, the interviewer will complete an inclusion criteria checklist and review it with a consulting psychiatrist. If the participant meets all criteria for enrolment, he/she will have a follow-up video-conference with a psychiatrist/psychologist/supervised Masters level clinician at Karolinska Institutet in order to *a)* review informed consent and *b)* orient patient to the platform. Participants entered into the study are presented with the informed consent via a secure webpage in order to check yes to consent. Through this webpage, they are then administered baseline assessment measures, including the MADRS-S[47], AAI[45], SPS-R[49], EQ-5D[52], SDS[53], and Credibility/Expectancy Questionnaire[56] prior to beginning treatment.

WEEKLY ASSESSMENTS

Weekly assessments (weeks 1-12) are done in the secure internet platform with the MADRS-S[47], AAI[45], and a form asking about involvement with concomitant medications and/or therapies. Additionally, subjects will be administered the WAI-SR[55] and the Credibility/Expectancy Questionnaire[56] during weeks 2, 4, 6, 8, 10, 12, and post-treatment; the CSI[54] at the beginning of W2 and W7 (mid-treatment), and post-treatment; and the ICBT – EX/RP Adherence Scale weeks 2-12 and post-treatment through the secure platform.

MID-TREATMENT ASSESSMENT

Subjects will be administered the BDD-YBOCS at W6 via video-conference by a psychiatrist/psychologist/Master's level clinician to assess BDD symptom severity.

POST-TREATMENT ASSESSMENT

At post-treatment, a psychiatrist/psychologist/Master's level clinician will administer the same instruments used at the video-conference screening, as well as the CGI-I[51]. Post treatment assessment will also be made via a secure webpage with the MADRS-S[47], DCQ[44], AAI[45], SPS-R[49], WAI-SR[55], ICBT – EX/RP Adherence Scale, and CSI[56]. Additionally, subjects will be asked to complete a treatment feedback form via the internet. If subjects are unable to follow-through with a video-conference evaluation (e.g. no computer access), they will be asked to complete a phone interview containing the same assessment measures.

3-MONTH FOLLOW-UP

A psychiatrist/psychologist/Master's level clinician will administer the BDD-YBOCS[41], SCID-5-RV module G[42], M.I.N.I. 7.0[43], BABS[46], C-SSRS Lifetime Recent-Clinical version[48], GAF[50],

clinician-rated CGI-S[51], and clinician-rated CGI-I[51]. Participants will complete self-ratings via the secure webpage, including the MADRS-S[47], DCQ[44], AAI[45], SPS-R[49], EQ-5D[52], and SDS[53]. If subjects are unable to follow-through with video-conference evaluation (e.g. no computer access), they will be asked to complete a phone interview containing the same assessment measures.

12-MONTH FOLLOW-UP

A psychiatrist/psychologist will administer the same instruments used at video-conference 3-month follow-up. Participants will also complete the same self-ratings as the in the 3-month follow-up via the secure webpage. If subjects are unable to follow-through with video-conference evaluation (e.g. no computer access), they will be asked to complete a phone interview containing the same assessment measures.

MEASURES TO MINIMIZE BIAS

- Prior to subject enrollment, all evaluators will be trained to a reliability criterion (intra-class correlation coefficient (ICC) of at least .85) with a gold-standard rater on the BDD-YBOCS. All video-conferencing inclusion evaluations and post-treatment and 3-month follow-up BDD-YBOCS assessments will be recorded. 10% of videos from each of these assessment points for enrolled subjects will be randomly selected using simple randomization through a true random number service (www.random.org) to be evaluated by a gold-standard rater. If at any point throughout the trial an evaluator's BDD-YBOCS ratings fall below an ICC of .85 with a gold-standard rater, he/she will be retrained to meet this criterion.
- Inclusion evaluators will complete an inclusion criteria checklist for each potential subject and review it with a consulting psychiatrist/psychologist to determine patient suitability for the study prior to enrollment.

TREATMENT

Treatment will utilize an English-language version of the BDD-NET platform employed by Enander, et al. (2015)[40], which uses a hospital server with encrypted traffic and an authentication login function to guarantee participant confidentiality. Treatment starts within seven days after inclusion and is 12 weeks long. BDD-NET incorporates the established CBT techniques of psychoeducation, self-monitoring, cognitive restructuring, exposure with response prevention (EX/RP), and a relapse prevention program. Information in the internet treatment platform is provided in text and divided into 8 modules, with the first 5 containing the core treatment components. Worksheets accompany modules to apply concepts, gather patient information related to symptoms, and monitor EX/RP exercises. Modules 1-4 focus on psychoeducation, functional behavior analyses, cognitive restructuring of meta-cognitions, and individual EX/RP hierarchy formation. Modules 5-8 focus on daily in-vivo EX/RP exercises, monitoring of subjective units of distress (SUDS) levels, and a relapse prevention program. Throughout treatment participants are assigned a psychologist with whom they can communicate through a secure online messaging system. The role of the psychologist is to support patient efforts, trouble-shoot skills applications, and give feedback on written material. Psychologists also use clinical judgement based on each patient's needs and homework completion of each module to grant participants access to subsequent modules[40]. A screen shot of an ICBT platform format can be found in Appendix Figure 6.

CONTINUATION OF TREATMENT

- Patients will not be receiving therapist support beyond W12, but are recommended to continue EX/RP in accordance with the CBT model for BDD.
- Patients will have unlimited access to the BDD-NET platform, including access to all 8 modules, written communications with therapist from W0-W12, and worksheets, but not including ongoing platform communication with a therapist, for 12 months following treatment.
- Referrals will be given to subjects who request them only if the BDD-NET research team is adequately able to provide such recommendations given the location and needs of the patient.

TRIAL TIMETABLE

Goal	Date
Ethical Approval	Jan 2016
Inclusion of First Subject	Feb 2016
Inclusion of Last Subject	Feb 2016
Treatment Completion of Last Subject, first manuscript	May 2016
Last 3-month Follow-up, second manuscript	September 2016
Last 12-month Follow-up, 1-year follow-up manuscript	June 2017

SAFETY

CLINICAL SAFETY ASSESSMENTS

- C-SSRS[48] administration via video-conference will be obtained prior to inclusion to ensure included subjects are at low risk for suicide. It will also be administered at post-treatment and 3 and 12-month follow-up assessments.
- The MADRS-S[47] will be administered via the internet weekly to monitor mood symptoms and suicidal ideations during treatment.
- All platform communications will be monitored by each subject's assigned therapist within 36 hours on weekdays and utilized in clinician risk assessment.
- The AAI[45] will be administered weekly via internet to monitor fluctuations in appearance anxiety.
- Suicidal ideation or risk, as indicated by clinician interview, internet self-report, or platform communication, will be quickly responded to according to a modified version of the Psychiatry Southwest, Stockholm's County Council suicide process (located in Figure 7 of Appendix). This protocol includes criteria for making decisions related to risk and action steps for responding to situations in which sufficient risk is indicated. The main forms of clinician response to further evaluate risk and intervene are reaching out to patients via the secure internet platform, calling, referring subjects to their designated emergency unit, coping skills coaching, developing safety plans, and coordinating services with designated emergency units. Therapists will utilize a safety checklist and structured steps for conducting and responding to risk assessments (Appendix Figure 8). Incidents of risk or suicidal behavior will be documented in patients' medical files, reviewed, and countersigned by a consulting psychiatrist.

PROCEDURES FOR MINIMIZING RISK

- *Informed Consent:* Prior to treatment, subjects will be fully informed of the study procedures, amount of time required of them, and possible benefits and risks of participating in this study. Additionally, they will be advised of the voluntary nature of their participation, their right to refuse participation, and their right to terminate participation at any time. Verbal informed consent will be obtained via video-conference, and subjects will check a box indicating consent in the secure online platform. At request, patients will be sent a paper copy of their informed consent to their mailing address. Subjects will be given the name and telephone number of the Co-Investigator.
- *Confidentiality:* Patients will be notified in the informed consent that all information they provide and all study findings will be kept confidential, with limited access to research staff. All staff involved will be informed of measures to protect patient confidentiality. All communications and handling of protected health information (PHI) will be compliant with standards set forth by the United States Federal Health Information Portability and Accountability Act (HIPAA). This act establishes a number of rules related to ethical healthcare practices and health insurance coverage, including steps for the handling of PHI. Subjects access the secure treatment platform through their internet browsers, and platform data is stored on a KI server running MySQL. This server is owned by Stockholm County Council, and protected by the Swedish data act and Swedish health care laws, as well as the Helsinki declaration. Methods of HIPAA compliance for 4 major areas of privacy are described below.
    1. *Treatment platform access:* Subjects will be given personalized usernames and passwords to access the secure treatment platform.
    2. *Transfer of data in the platform:* Internet communications between subject and therapist will be done via a secure messaging system on a confidential platform. Information entered into the platform through subjects' internet browsers will be sent to the MySQL database at the Stockholm County Council. Data will be transmitted using Secure Socket Layers (SSL) (128 bit encryption), in line with HIPAA security requirements.
    3. *Data storage:* Platform information will be stored behind a Stockholm County Council firewall. Medical records will be stored in the Stockholm County Council TakeCare electronic medical records system. Additionally, certain patient PHI will be kept in a research database on a secure KI server with password encryption.
    4. *Data auditing:* Time points in which data are accessed and parties accessing are tracked by the MySQL system. Only study personnel will have access to patient PHI.
- Video-conferences will be completed using software that is secure and compliant with standards set forth by HIPAA. Video-conference software will be provided by VSee. VSee agreed to sign a Business Associate Agreement stating that their members and employees will not have access to patient videos, will not save patient videos, can provide audit trails of parties viewing videos if asked, and will notify covered entities at KI in the event of a confidentiality breach. Videos between evaluator and patient will not operate through a VSee server, but will require a relay server, likely in patients' home countries, to connect with their computers. If relay servers were to be breached, videos would remain inaccessible, but usernames may not. Therefore, to fully protect PHI and pertinent information, subjects will be assigned a random username composed of digits

and letters that they can log into VSee with. Subjects can download a free version of VSee software and will be covered under KI's Business Associate Agreement with VSee for video-communication with designated parties at KI. Subjects will be advised that they are not covered for VSee communications with outside parties under the VSee-KI Business Associate Agreement. The VSee package used in this study is FIPS-140 level 2 compliant and utilizes 256-bit AES encryption. It also abides by the criteria established in the HIPAA Privacy and Security Rules, as well as the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009.

- Careful pre-treatment assessment to identify and exclude participants who are at high risk for suicide or adverse treatment effects.
    1. Steps for minimizing risk for participants excluded prior to enrollment:
        - Following completion of the initial internet screening, participants will be presented with a form that notifies them when and how they will be contacted by phone if they are eligible for inclusion at this point. This form also includes contact information for the research team and outlines steps for participants to take if they are experiencing acute mental health concerns or do not receive a call within 14 days indicating they are eligible at this point of the study (e.g. visiting an emergency care unit, consulting with mental health specialists). In order to proceed, participants will have to check a box stating that they understand the appropriate steps to take following the initial internet screening.
        - Participants excluded during or after the W0 evaluation or W0 follow-up video-conference will be offered mental health recommendations during these video-conferences as appropriate. Specific types of specialists will be suggested to fit mental health needs. E.g. CBT therapist, licensed psychologist, outpatient care provider with experience treating depression/alcohol abuse/substance abuse, psychiatric consultation, psychiatric evaluation at a local emergency care center. Consultation with emergency care centers and crisis counseling will be offered on the spot if the patient is in imminent risk during the W0 and W0 follow-up video-conferences.
- Monitoring any deterioration of symptoms, adverse treatment effects, and suicidal ideations, and terminating treatment when in the patient's best interest.
    1. Deterioration of anxiety and mood symptoms and suicidal ideations are measured weekly via internet self-report forms. Patients will be contacted via platform or phone call if their MADRS-S[47] item 9 score reaches 4 or higher, or if suicidal ideation or intent is otherwise indicated (e.g. via platform). Deterioration of symptoms will be monitored using the MADRS-S[47] total score and AAI[45] total score. Subjects will be contacted in the event that their MADRS-S[47] and AAI[45] scores increase by 20% of the respective total score ranges. For the MADRS-S[47], deterioration is measured by a 5-point increase, and for the AAI[45], an 8-point increase.
- Offering treatment recommendations and referrals following discontinuation of treatment or treatment withdrawal when a suitable mental health care provider can be located.

- When a subject is withdrawn for reasons related to self-injury or suicidal behaviors, the BDD-NET team will provide ongoing consultation with a designated emergency unit while he/she is stabilized. Additionally, referral options will be offered when feasible.
- Following up completion of the BDD-NET protocol with referrals when patients are interested and a suitable mental health care provider can be located.
- Staff being informed of the modified Psychiatry Southwest, Stockholm County Council's suicide process, and implementing it when suicidal ideation and/or elevated risk of suicide are present.

ADVERSE EVENTS

WHAT IS AN ADVERSE EVENT (AE)?

- Unwanted events caused by treatment (adverse treatment reactions), adverse reactions caused by the correct treatment (side effects), and adverse reactions caused by inappropriate treatment (malpractice effects), will all be considered in the assessment of adverse events.

SERIOUS ADVERSE EVENTS (SAEs)

AEs can be categorized by the investigators as either serious or non-serious. An AE is considered a SAE if it:

- Requires psychiatric hospitalization
- Results in attempt at suicide
- Results in significant deterioration of symptoms or large increase in impairment in daily routines or social or occupational functioning.

PROCEDURES FOR IDENTIFYING AND RESPONDING TO ADVERSE EVENTS

- *Assessment:* AEs will be clinician-evaluated at post-treatment and 3-month follow-up using a checklist by video-conference. AEs will also be assessed weekly using an online adverse events questionnaire. AEs will also be assessed at post-treatment and at 3-month follow-up via video-conference with a clinician.
- *Reporting:* All SAEs or situations in which sufficient risk of a SAE is indicated, as determined by the investigators, will be reported immediately to the Karolinksa Institutet IRB.
- *Responding:* AEs detected by an online weekly adverse events questionnaire will be followed up immediately with a call. In the event that treatment is likely leading to a significant deterioration of symptoms or increased risk of suicide, patients will be withdrawn from treatment. Investigators will offer mental health referrals to patients withdrawn from treatment due to AEs when suitable, appropriate, and feasible. When appropriate, investigators and clinicians will refer patients to emergency care centers and work with them to inform acute treatment.
- *Following up:* Follow-up information regarding the outcome of SAEs and actions taken will be reported to the KI IRB as soon as it's available. The investigators must ensure that actions taken in response to AEs are appropriate to the nature of the event, and that actions continue to be taken until resolution.
- *Documenting:* All AEs will be recorded in KIs TakeCare medical records system. Follow-up information describing the outcome of the SAEs and actions taken will also be recorded in patients' medical records.

QUALITY CONTROL & ETHICS

- The Karolinska Trial Alliance will monitor the study regularly.
- The study will follow Good Clinical Practice (GCP).
- It will be subject to approval of the Regional Ethics Board in Stockholm.
- It will be registered on the ClinicalTrials.gov trial registry.

9. Patient Benefit/Significance for the Health Service

Access to CBT therapists in the United States and elsewhere is limited, and individuals with BDD face substantial barriers to treatment. There is a lack of trained professionals available, face-to-face CBT comes with geographic, financial, and scheduling limitations, and people commonly have difficulty reporting BDD symptoms associated with shame. As a result, too few people with BDD symptoms are left receiving treatments that are not evidence-based, and too often ineffective or harmful. ICBT could start to address these issues, dramatically increasing patient access to evidence-based treatment for BDD. For the individual who cannot afford face to face CBT, does not have a specialized therapist close to home, or has long work hours, BDD-NET can provide a more time flexible option that can be utilized from home. For those who experience shame associated with their appearance and do not want to openly talk about their symptoms and concerns with a therapist face to face, BDD-NET provides another avenue for treatment.

Enander et al. (2014) has shown promising preliminary support for BDD-NET as an efficacious, acceptable, and feasible treatment in Sweden in an uncontrolled pilot study[37]. Enander et al. (2015) then showed BDD-NET to be superior to an active control group in an RCT[40]. If BDD-NET – English version proves to be effective, future directions for research include conducting a larger randomized controlled trial testing the efficacy of this intervention among English-speakers, globally or within certain English-speaking subpopulations and nationalities. Long term goals for this treatment are to either implement it as a part of healthcare systems and private clinics globally, or to continue to treat those with limited access to CBT through the Internet Psychiatry Unit (Internetpsykiatrienheten) at the Stockholm County Council.

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Appendix

Figure 1. Early Termination Checklist

Reason(s) for Early Treatment Termination (Check all that apply):

Specify details of early termination in comments below

Reason	Comments
Need for higher level of care (e.g. hospitalization)	
Current clinically significant suicidality and/or MADRS-S suicide item (Q9) score ≥ 5	
PI decision	
Lost to follow-up	
Experienced NSAE	
Experienced SAE	
Protocol Violation	
Life Circumstances	
Treatment No Longer Needed	
Patient Not Willing to Continue	
Time commitment too great	
Noncompliance with protocol	
Voluntary withdrawal due to not enough time/other priorities (subject report)	
Voluntary withdrawal due to treatment not right fit (subject report)	
Voluntary withdrawal due to problems with treatment itself (subject report)	Problems:
Voluntary withdrawal Other (subject report)	
Other	

Figure 2. Flow Diagram of Procedures

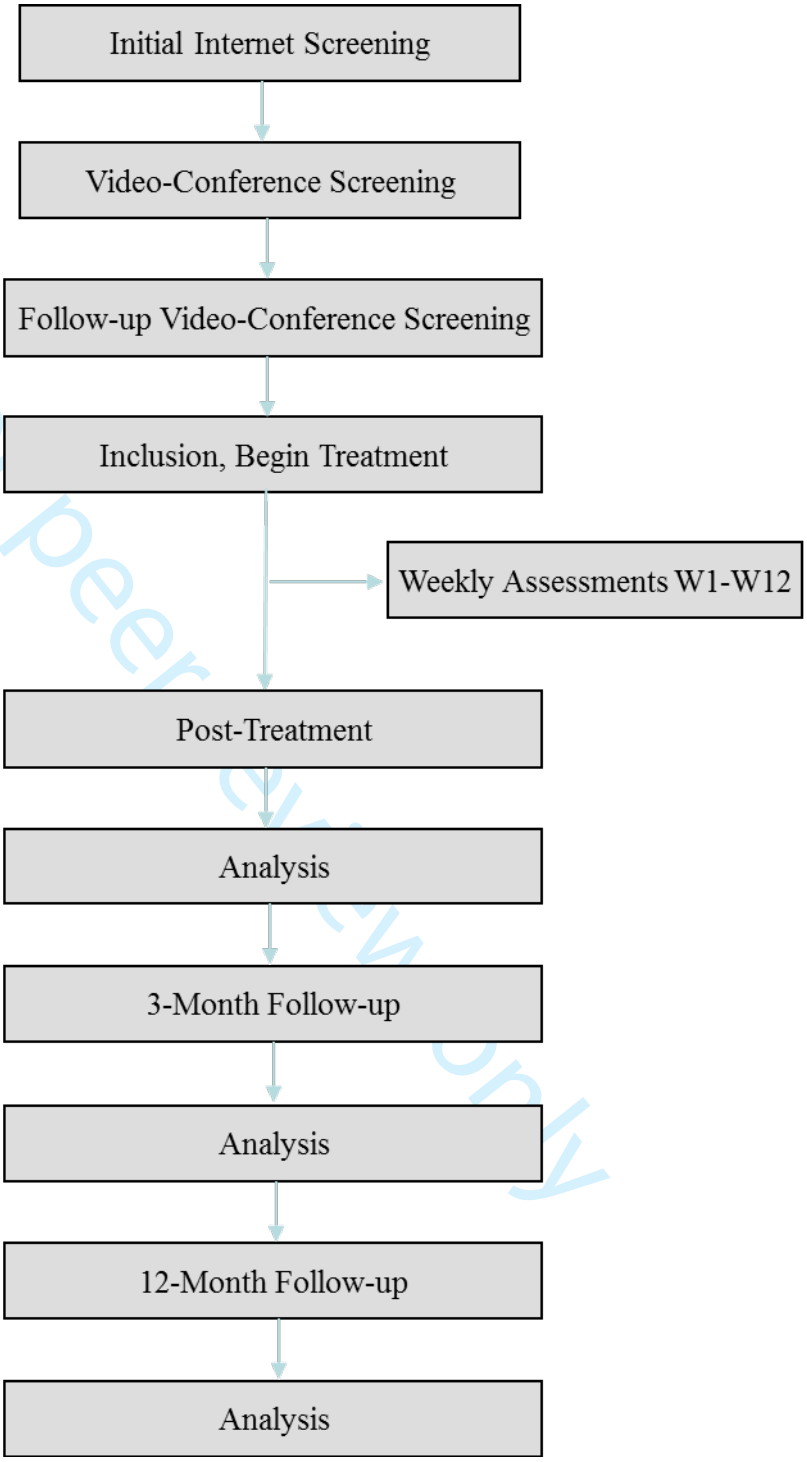


Figure 3. Informed Consent Form

Department of Clinical Neuroscience

Informed Consent Form

Therapist Guided, Internet-based Cognitive Behavioral Therapy for Body Dysmorphic Disorder – English Version (BDD-NET): A Feasibility Study

You have expressed interest in participating in this study at BDDstudy.com.

Objectives of this study
There is evidence to support that cognitive behavioral therapy (CBT) may be an effective treatment for people with body dysmorphic disorder (BDD). However, global access to specialized CBT therapists is very limited. Internet-based CBT (ICBT) has been developed, showing promising evidence as an effective treatment for BDD, but is currently only available in Sweden. Karolinska Institutet (Sweden) is conducting this study in order to investigate the efficacy and feasibility of CBT for BDD administered through a global internet platform.

Methods used and why they are used
In order to participate in the project, you must meet pre-determined criteria for body dysmorphic disorder and not suffer from other serious psychiatric problems, such as bipolar disorder. This is assessed by a diagnostic interview via video-conference where you will have to answer questions about body dysmorphic disorder and other psychiatric conditions. Video-conference assessments will generally take approximately 90 minutes. Minimum age for participation is 18 years. In order for us to be able to evaluate the results of treatment you will be given various questionnaires before, during, and after treatment. You will be contacted for video-conference evaluations once during treatment, immediately after completing treatment, and 3 and 12-months after completing treatment.

Internet treatment consists of a self-help program with therapist support via e-mail. ICBT has shown to be effective for treating a number of disorders, and the current treatment is based on proven CBT principles. The name of this treatment program is BDD-NET – English version. It is in English only and fully available through the internet.

Treatment is free of charge.

Participation
To be considered for this study, it is required that you have access to an internet connected computer, that you have the opportunity to work with the material for at least six hours per week, and that you are fully fluent in English, including reading, writing, and speaking. All participants will receive 12 weeks of treatment.

Participation is completely voluntary. You can choose not to participate and you can cancel participation at any time, for any reason, without having to disclose the reason, and without penalty. Your participation will not affect your ability to get other care. You will be able to take part in the results in the form of a scientific publication, but will not see your own results.

Duration of participation
Treatment lasts for twelve weeks. Video-conference interviews will be conducted before, during, and after the completion of treatment, as well as three and twelve months after treatment. The treatment will take about 6 hours per week.

Privacy and Confidentiality
All results of surveys, questionnaires, and interviews, as well as private or personal information provided to BDD-NET research personnel by participants in this study will be treated as confidential. The continued scientific processing of the information gathered from surveys, questionnaires, interviews, and communications with therapists will be done without identifying information of patients. The primary person held responsible for this is Associate Professor Christian Rück at Karolinska Institutet.

All information you provide is protected under Swedish secrecy and privacy regulations. Additionally, the current study has taken steps to by fully compliant with the United States federal Health Information Portability and Accountability Act (HIPAA) Privacy and Security Rules, as well as the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009. Protected Health Information (PHI) will be protected in accordance with these legislations for all forms of communication with study personnel, including all access, storage, transfer, and auditing of private and personal information.

HIPAA Privacy Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/index.html
HIPAA Security Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/securityrule/index.html
HITECH Act of 2009:
http://www.hhs.gov/ocr/privacy/hipaa/administrative/enforcementrule/hitechenforcementifr.html

This study will utilize secure video-conference technology to conduct assessments. Please note that information transmitted with this technology is only secure for communications with designated research personnel at Karolinksa Institutet. The use of this technology to contact other parties is not protected or confidential according to HIPAA standards.

The Swedish Personal Data Act (PUL)
Study information will be housed at Stockholm County Hospital (Healthcare Provision) in ongoing computer research databases. The responsible party for this information is the registry's Data Protection Officer, who can be contacted regarding data concerns: PO Box 179 14, 118 95 STOCKHOLM; phone: +46 8-123400 00. No one except the researchers involved in this project will be able to see your personal information. If you want find out what information is held about you, you can request this in writing directly to Stockholm County Council (contact details above). You are entitled to receive this information once per year at no cost. If you identify incorrect information about you, it can be corrected. After 15 years the data Passkey will be destroyed. Then it will no longer be possible to disclose any records.

Contact for further information:

- Christopher La Lima, co-investigator and project manager, XXXX (long distance charges may apply), Email: christopher.la.lima@ki.se
- Christian Rück, principal investigator, assistant professor, Email: christian.ruck@ki.se

Consent participation

I do not wish to participate in the BDD-NET treatment study
I do wish to participate in the BDD-NET treatment study

I ..... have taken note of the above written information on the implementation of the study and what participation means. I consent to the processing of personal data as described above. I am aware that my participation is voluntary and that I, at any time, and without explanation, have the right to cancel my participation without penalty.

Location .....

Date .....

Name (Printed) .....

Signed .....

Figure 4. BDD-NET Safety Plan

BDD-NET Safety Plan

Information for 24-hour psychiatric emergency center: (look up suggested centers based on location ahead of time and call to confirm they provide such services)

Phone number:

_____

(Fill out prior to interview)

Address/Location:

_____

(Fill out prior to interview)

Information for Alternative Emergency Center if Requested:

Phone number:

_____

Address/Location:

_____

Name of Emergency Contact Person/Next of Kin who can be contacted in the event of emergency:

_____

Emergency Contact Person's phone number:

_____

Figure 5. BDD-NET Accessibility and Confidentiality Interview

BDD-NET Accessibility and Confidentiality Interview

- Do you have access to computer with internet access at least once per day for 1 hour or more?

_____

- Where is this computer located?

_____

- Do you have a private email account where you can be notified of updates in the ICBT platform? (Please write below:)

_____

- Please choose a personalized password for access to your ICBT account:

_____

Figure 6. Screen Shot of an ICBT Treatment Platform

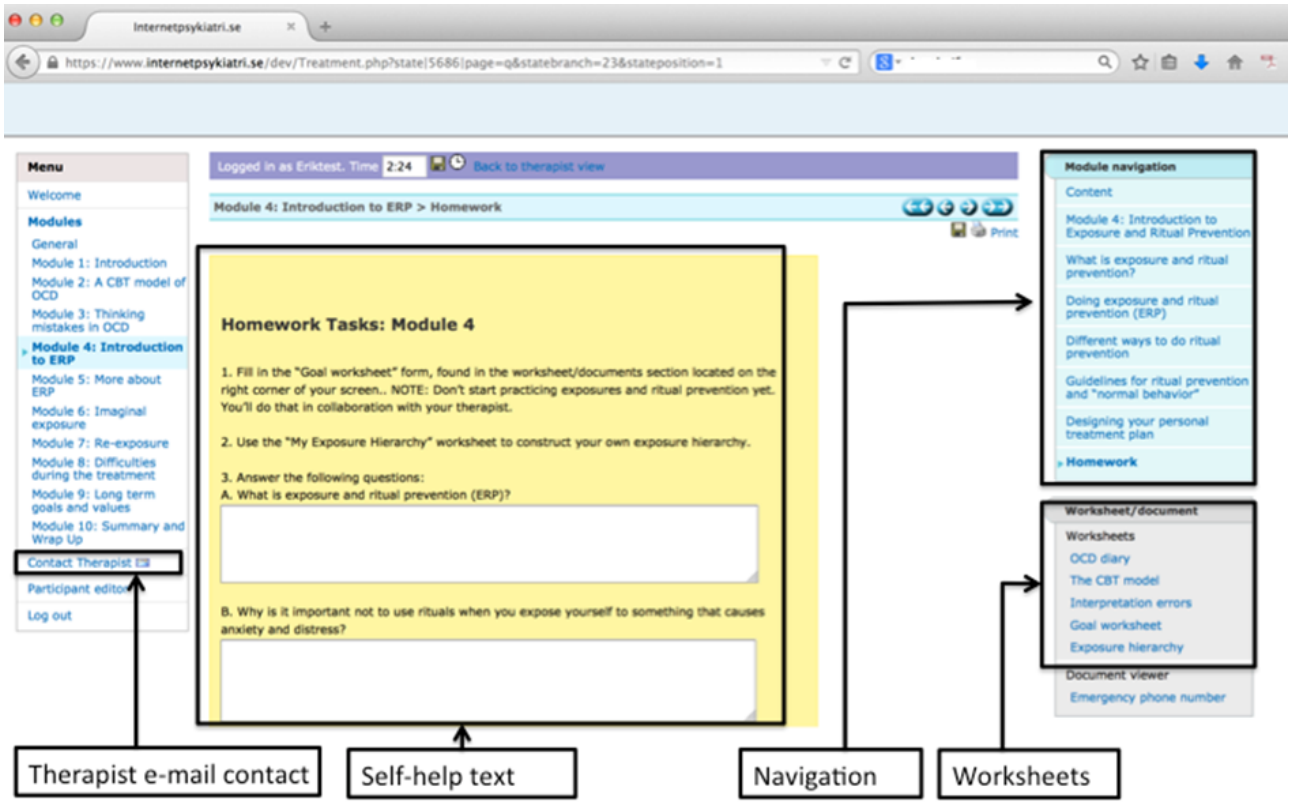
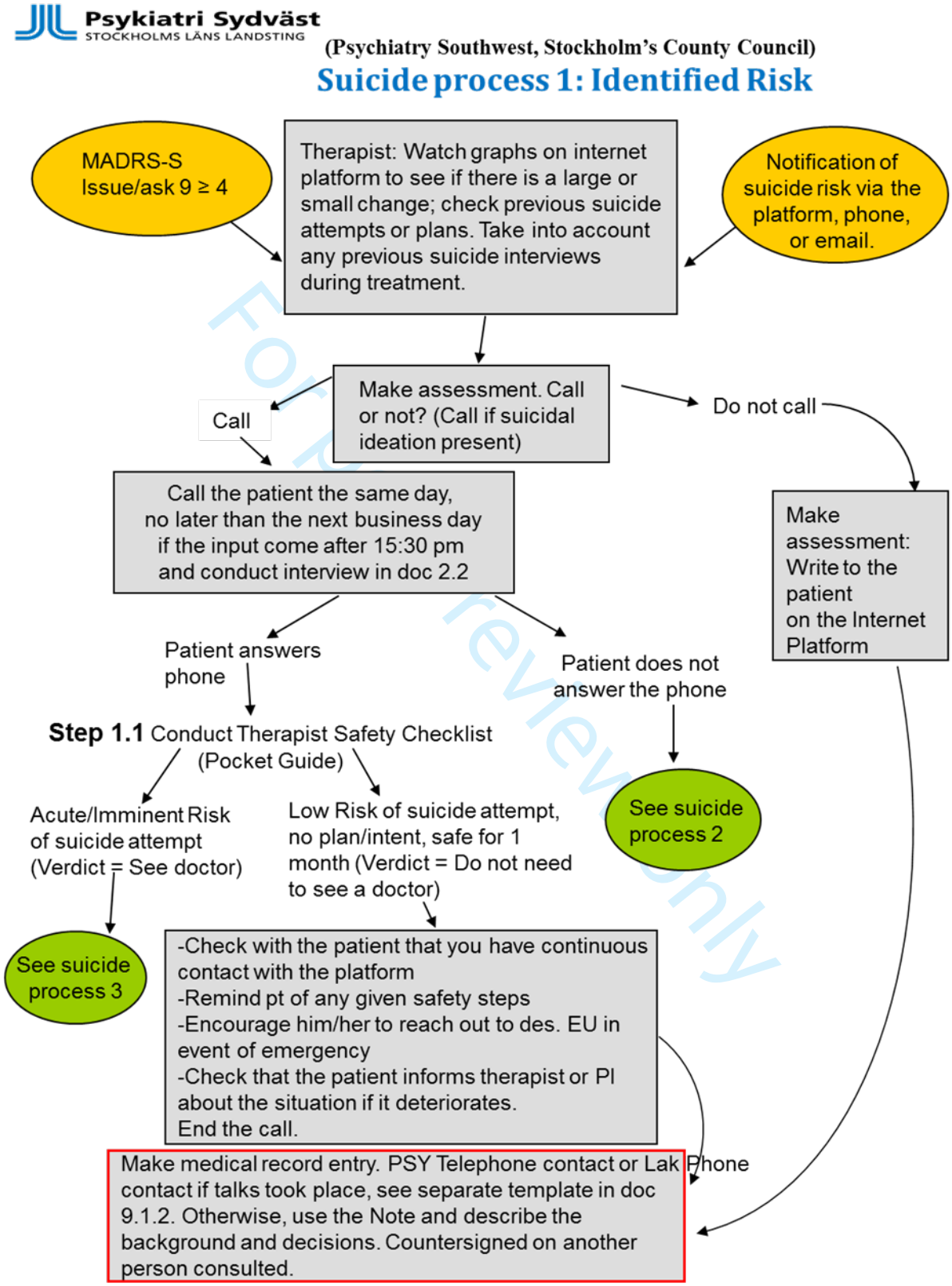
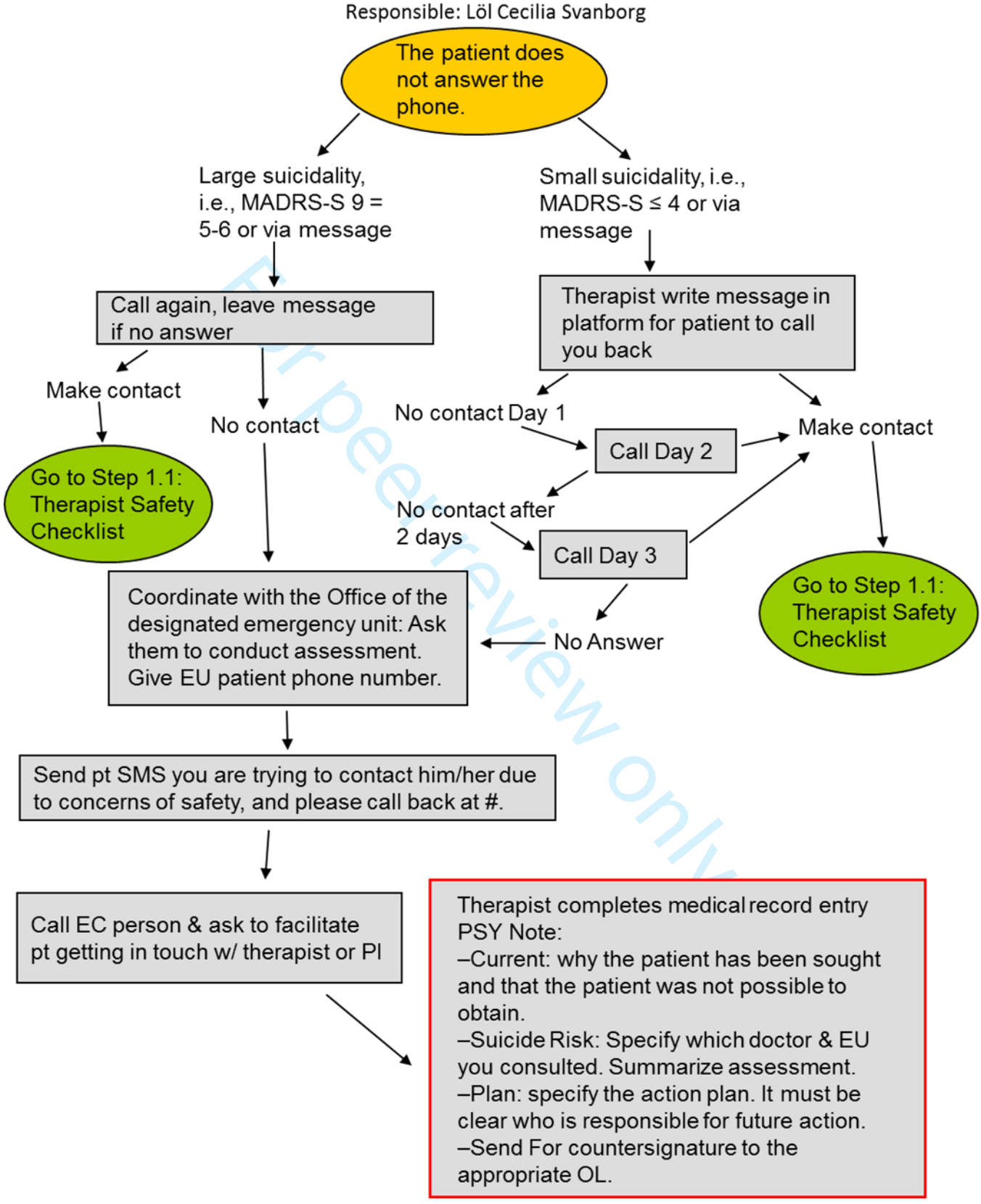

Internetpsykiatri.se
https://www.internetpsykiatri.se/dev/Treatment.php?state|5686|page=q&statebranch=23&stateposition=1
Menu
Welcome
Modules
General
Module 1: Introduction
Module 2: A CBT model of OCD
Module 3: Thinking mistakes in OCD
Module 4: Introduction to ERP
Module 5: More about ERP
Module 6: Imaginal exposure
Module 7: Re-exposure
Module 8: Difficulties during the treatment
Module 9: Long term goals and values
Module 10: Summary and Wrap Up
Contact Therapist
Participant editor
Log out
Logged in as Eriktest. Time 2:24
Back to therapist view
Module 4: Introduction to ERP > Homework
Print
Homework Tasks: Module 4
1. Fill in the "Goal worksheet" form, found in the worksheet/documents section located on the right corner of your screen.. NOTE: Don't start practicing exposures and ritual prevention yet. You'll do that in collaboration with your therapist.
2. Use the "My Exposure Hierarchy" worksheet to construct your own exposure hierarchy.
3. Answer the following questions:
A. What is exposure and ritual prevention (ERP)?
B. Why is it important not to use rituals when you expose yourself to something that causes anxiety and distress?
Module navigation
Content
Module 4: Introduction to Exposure and Ritual Prevention
What is exposure and ritual prevention?
Doing exposure and ritual prevention (ERP)
Different ways to do ritual prevention
Guidelines for ritual prevention and "normal behavior"
Designing your personal treatment plan
Homework
Worksheet/document
Worksheets
OCD diary
The CBT model
Interpretation errors
Goal worksheet
Exposure hierarchy
Document viewer
Emergency phone number
Therapist e-mail contact
Self-help text
Navigation
Worksheets

Figure 7. Suicide Process



Psykiatri Sydväst
STOCKHOLMS LÄNS LANDSTING

Suicide Process 2: Patient Doesn't Answer Phone



Psykiatri Sydväst
STOCKHOLMS LÄNS LANDSTING

Suicide Process 3: Phone Contact Made, Acute Risk

Responsible: Löl Cecilia Svanborg

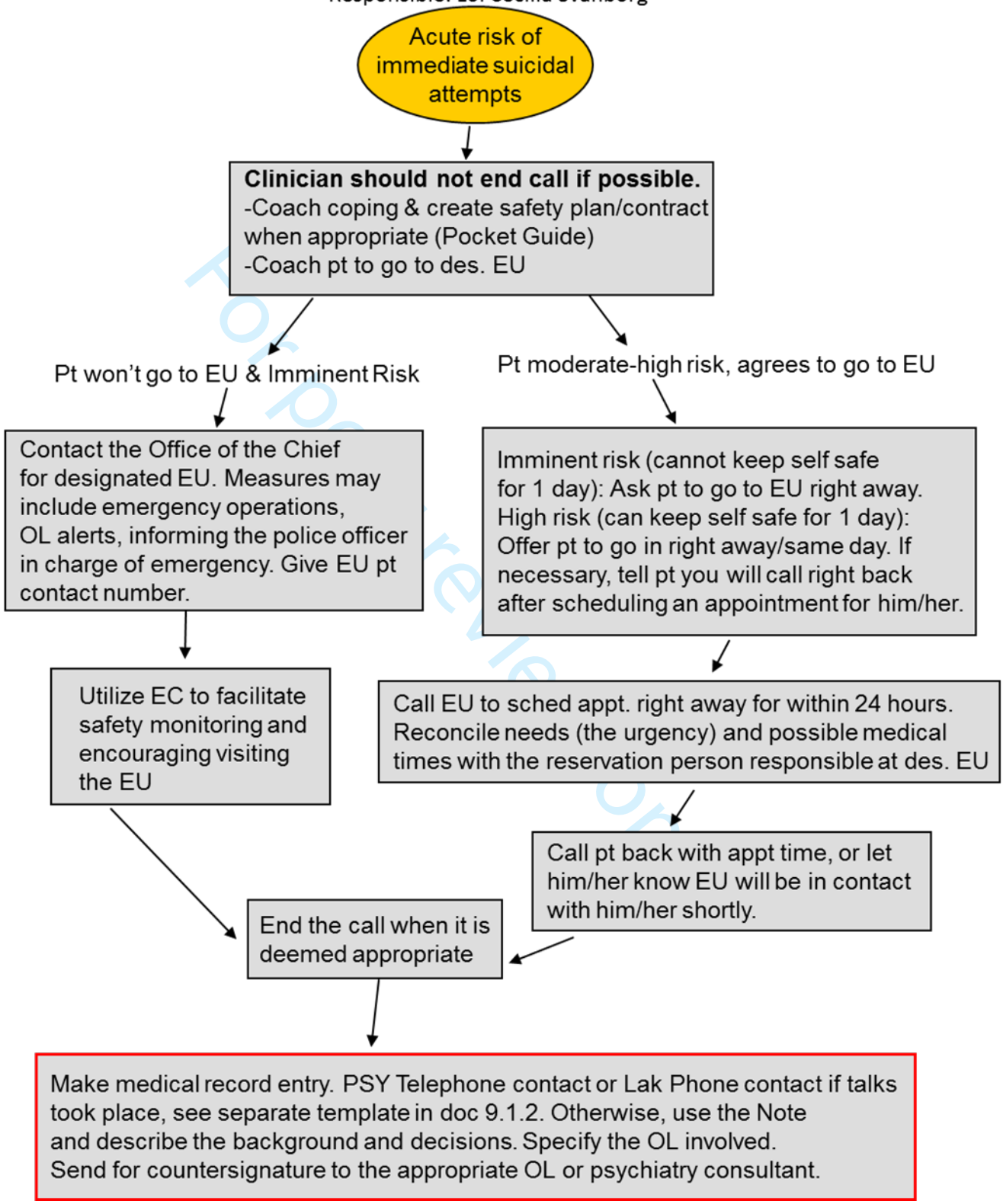


Figure 8. Therapist Safety Checklist and Tools for Crisis Coaching

STEPS

Example of suggested transition to risk conversation:

- I appreciate how difficult this problem must be for you at this time. Some of my patients with similar problems/symptoms have told me that they have thought about ending their life. I wonder if you have had similar thoughts?

When risk is indicated, follow…

SUICIDAL RISK ASSESSMENT CHECKLIST:

- Are you feeling hopeless about the present or future? _____

  If yes ask…
- Have you had thoughts about taking your life? _____

  If yes ask…
- When did you have these thoughts and do you have a plan to take your life? _____

_____

  If yes, inquire about plan: _____

_____

- Have you begun to carry out your plan? _____
- Are there any reasons you would not make a suicide attempt (pt may say not fair to family, religious values, etc.)? Look for protective factors here: _____

_____

- Have you ever had a suicide attempt? _____

  Before getting off phone, ask…
- Are you in any physical harm? _____
- Can you keep yourself safe for the next hour? _____
- " for the next day? _____
- " for the next week? _____
- " for the next month? _____

RESPONDING

If pt is **escalated and/or demonstrates imminent risk** of self-harm (SI or suicide) in same day, de-escalate and create a safer environment with the following steps:

- **Remove or secure any lethal means of self-harm** (e.g. weapons, pills)
- **Decrease isolation** (can be designated emergency contact)
- **Decrease anxiety and agitation**
    - E.g. paced breathing (5 seconds in, hold 1, 5 seconds out, or longer/shorter as pt is comfortable).
    - Progressive Muscle Relaxation (PMR)
    - Listen, allow expression of feelings
    - Being accepting and non-judgmental
    - Speak directly, openly, and matter-of-factly about suicide and your current concerns
    - Offer hope that there are alternatives available, but don't reassure that any 1 strategy will turn things around right away
- **Engage patient in a safety plan** (crisis management or contingency planning), with steps for follow-through. Can involve family members and others.
    - If pt feels the need to self-harm, what are his/her go-to coping strategies, distress tolerance skills, and replacement behaviors?
        - E.g. Paced breathing, diaphragmatic breathing, music, sensory behaviors for 5 senses (scented lotions/soaps, bubble bath, touching something textured), PMR, splash face w/ very cold water (drops heart rate to resting pace), 10 minutes of intense exercise, opposite emotion activity: e.g. watching a TV or YouTube video that is incompatible with current emotion (e.g. if sad, watch comedy), reach out to a friend or family member
    - In the future, should feelings of hopelessness or urges to self-harm or engage in suicidal behaviors occur, how will the pt keep him/herself safe?
        - Knowing who to reach out to and when: EU when formal assessment indicated or in risk of harm (*preferred bc they can work w/ pt in person), BDD-NET therapist or PI if in risk of harm, family and friends for social support.
        - When in risk of harm, keep reaching out until EU, therapist, or PI is reached, and notify therapist or PI when you can. If these parties cannot be reached right away, seek social support from emergency contact person or in appropriate ways until designated parties are reached.
    - Obtain agreement on this Safety Contract for designated amount of time depending on risk. E.g. can you agree to follow these steps for the next week?
    - You can recap the decided on contract in the platform.
    - Once safety plan and skills are agreed upon by the patient and therapist, remind patient to use the skills.
- **Reinforce all safe and healthy behaviors** of the patient along the way. E.g. you're doing a great job sticking with paced breathing and leading it on your own.

FOLLOWING CRISIS COUNSELING

- If sufficient patient risk is indicated, prompt him/her to receive a formal assessment at the designated EU. Follow procedures on Suicide Process 3.
- If patient is at low risk and not in need of EU, follow procedures on Suicide Process 1.

THERAPIST SELF-CARE

- Seek support for yourself when you feel you've been emotionally affected.

http://www.mentalhealth.va.gov/docs/suicide_risk_assessment_guide.doc
http://www.vbh-pa.com/provider/info/qual_mgt/Summary_and_Review_APA_Suicide_Guidelines_Review.pdf
http://www.apa.org/ethics/code/

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BMJ Open

Internet-based, therapist guided, cognitive behavioral therapy for body dysmorphic disorder with global eligibility for inclusion: An uncontrolled pilot study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024693.R1
Article Type:	Research
Date Submitted by the Author:	18-Oct-2018
Complete List of Authors:	Gentile, Andrew; Karolinska Institutet, Centre for Psychiatry Research, Department of Clinical Neuroscience La Lima, Christopher ; Karolinska Institutet, Centre for Psychiatry Research, Department of Clinical Neuroscience Flygare, Oskar; Karolinska Institutet Department of Clinical Neuroscience, Enander, Jesper; Karolinska Institutet Department of Clinical Neuroscience, Wilhelm, Sabine; Harvard Medical School, Department of Psychiatry Mataix-Cols, David; Karolinska Institutet, Department of Clinical Neuroscience Rück, Christian; Karolinska Institutet, Department of Clinical Neuroscience
Primary Subject Heading:	Mental health
Secondary Subject Heading:	Evidence based practice, Global health
Keywords:	Adult psychiatry < PSYCHIATRY, Anxiety disorders < PSYCHIATRY, Clinical trials < THERAPEUTICS, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, World Wide Web technology < BIOTECHNOLOGY & BIOINFORMATICS

Text word count: 3618
Abstract: 370
Tables: 2
Figures: 3

Internet-based, therapist guided, cognitive behavioral therapy for body dysmorphic disorder with global eligibility for inclusion: An uncontrolled pilot study

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ABSTRACT

Objectives: Cognitive–behavioural therapy (CBT) has been shown to be an effective treatment for body dysmorphic disorder (BDD) but access to treatment around the world is limited. One way to increase access is to administer CBT remotely via the internet. This study represents the first effort to remotely deliver a therapist-supported, internet-based CBT treatment with no restrictions on enrollment based on geographic location, and it aims to assess whether this treatment can be delivered safely across international borders, with outcomes comparable to previous BDD-NET trials.

Design: Uncontrolled clinical trial.

Participants: Patients (N=32) in 9 different countries were recruited primarily through internet advertisements.

Intervention: BDD-NET is a 12-week treatment, consisting of 8 treatment modules previously shown to be effective in a Swedish version.

Setting: Therapists based at a single, secondary care centre in Sweden provided active guidance and feedback throughout the treatment via asynchronous electronic messages.

Main outcome measure: The clinician-administered Yale-Brown Obsessive Compulsive Scale for BDD (BDD-YBOCS). Symptom severity was assessed pretreatment, mid-treatment (6 week), post-treatment, and at the 3-month follow-up.

Results: There were significant improvements on BDD-YBOCS scores (F[3, 71.63] = 31.79, p < .001), that were maintained at 3-month follow-up. Mean differences from baseline in BDD-YBOCS scores were -8.12 (week 6), -12.63 (post-treatment), and -11.71 (3-month follow-up). Forty-seven percent and 50% of participants were considered treatment responders at post and 3-month follow-up, respectively. Additionally, remission rates were 28% at post-treatment and 44% at 3-month follow-up. The treatment was also deemed acceptable by patients.

Conclusions: The results suggest that BDD-NET can be safely and effectively delivered across international borders to a culturally diverse sample. Larger scale randomized controlled trials with more participants from non-western cultures are warranted to further validate the cross-cultural generalizability of this treatment.

Trial registration number: Clinicaltrials.gov registration ID: NCT03517384

Article Summary:

Strengths and limitations of this study

- This is the first study to investigate the feasibility and acceptability of a therapist-guided, internet-based CBT intervention, delivered from a single centre, to an international sample with global eligibility for inclusion

- The absence of a control condition limits the ability to make inferences about what caused the changes observed
- Since most participants resided in western countries, it is unclear to what extent BDD-NET is generalizable to patients from non-western cultures

INTRODUCTION

Despite the enormous socio-economic costs and individual suffering caused by mental illness, there are far too few clinicians to meet the global need for mental health services [1,2]. Moreover, outpatient health services are usually open during normal working hours, and this current service model disenfranchises individuals who may have difficulties taking time off work or accessing care if living in remote and underserved areas. Furthermore, issues like stigma, lack of awareness, cost of treatment, and the symptoms of psychiatric disorders themselves can also be barriers to accessing care [3]. As a result, most individuals with a mental disorder do not receive treatment [4].

This treatment gap is particularly wide for under-recognized disorders such as body dysmorphic disorder (BDD), where the affected individual is preoccupied with perceived flaws or defects in one's appearance that are not noticeable to others [5]. In fact, only 10-17% of those with the disorder report receiving an evidence-based psychotherapy like cognitive behavioral therapy (CBT), despite its common prevalence and significant functional impairment for sufferers [3,6–10].

Internet-based CBT (ICBT) aims to increase accessibility and availability to specialised treatment and has been shown to be efficacious and cost effective for a range of disorders [11]. While ICBT has been studied for nearly 20 years [12], there has been a upsurge of promising research on technology-based mental-health interventions during the past several years [13,14]. Recently, BDD-NET, a therapist-guided, internet-based CBT program for BDD, was developed to improve access to evidence-based care, and the treatment has

been shown to be safe, efficacious, and highly acceptable by patients [15,16]. The treatment is delivered through a secure tailored online platform that contains the treatment content. Communication between therapist and patient is done through asynchronous messaging, requiring only a fraction of therapist time compared to conventional CBT. Crucially, BDD-NET removes key barriers to treatment, while yielding outcomes equivalent to traditional face-to-face CBT [17].

ICBT represents a promising solution for economically and efficiently targeting mental health disparities around the world. However, this integration of CBT with information technology has yet to realize its true potential to reach underserved populations. Therefore, our aim was to conduct the first investigation evaluating whether a therapist-guided, internet-based CBT intervention could be delivered safely and effectively across international borders, with no geographic restrictions for recruitment. In doing so, the current researchers hope to shed light on aspects of feasibility and ethical considerations that arise in this novel treatment context.

METHODS

Trial design

The aim of this investigation was to evaluate the feasibility and safety of a global treatment initiative using an English-language version of BDD-NET [15,16]. This uncontrolled pilot study was intended to assess different aspects of conducting the study remotely and across international borders; including recruitment, assessment, and treatment delivery. The central ethical review board in Sweden approved the protocol (CEPN Ö 7-2016), as well as institutional review boards (IRB) at Massachusetts General Hospital (approved

11/23/2015), and Hofstra University (1/14/2016). The study was registered at Clinicaltrials.gov (NCT03517384).

Procedure

Participants were recruited by clinician referral as well as using internet advertisements through Google AdWords, bddfoundation.org, and on internet forums. Individuals interested in participating in the study were directed to the study's website where they provided initial informed consent, and completed an online screening consisting of the Montgomery–Åsberg Depression Rating Scale (MADRS-S) [18,19], the Body Dysmorphic Disorder Questionnaire (BDDQ) [20], the Dysmporhic Concerns Questionnaire (DCQ) [21], the Alcohol Use Disorders Identification Test (AUDIT) [22] and the Drug User Disorders Identification Test (DUDIT) [23]. Following this initial screening, eligible individuals were invited for an assessment over VSee, a Health Insurance Portability and Accountability Act (HIPAA) compliant video-conferencing software. During the video-conference assessment, final screening and baseline measures were obtained, as well as verbal informed consent, identification documents, and emergency information. Measures administered at this time were the Body Dysmorphic Disorder modification of the Yale-Brown obsessive compulsive scale (BDD-YBOCS) [24], Columbia Suicide Severity Rating Scale (CSSR-S) [25], Brown Assessment of Beliefs Scale (BABS) [26], Clinical Global Impressions Scale of Severity (CGI-S) [27], and Global Adaptive Functioning (GAF) [5]. Additionally, the obsessive-compulsive and related disorders module of the Structured Clinical Interview for DSM 5 [28] and the Mini International Neuropsychiatric Interview (M.I.N.I. 7) [29] were also administered at this time as a means to establish a primary diagnosis of BDD. For full eligibility criteria and

details on recruitment and patient flow, see appendix A. Eligible participants were then granted access to treatment via the online platform. In order to guarantee participant confidentiality, we used a dedicated server with encrypted traffic and a strong authentication login function.

Participants

Thirty-two participants were included in the study. These individuals resided in 9 different countries and represented 12 different nationalities (Socio-demographic and clinical characteristics of participants are presented in Table 1). Inclusion criteria were that participants needed to be aged 18 years or older, meet DSM-5 criteria for a diagnosis of BDD with symptom severity measuring ≥ 20 on the BDD-YBOCS [24], be outpatient, be fluent in English, and have regular access to a computer with an internet connection. Patients who were able to navigate the online registration and screening process were considered to have sufficient computer skills to participate in the study.

Exclusion criteria were concurrent psychological treatment, having received CBT for BDD within 12 months preceding treatment, changes in psychotropic medications within 12 weeks before inclusion, not having access to a 24 hour psychiatric emergency center in their proximity, or if they could not provide an emergency contact person. Additional grounds for exclusion were current substance dependence, lifetime bipolar disorder or psychosis, MADRS-S score ≥ 35, personality disorder diagnosis, lifetime history of suicide attempts, or clinically significant current suicidal ideation (≥ 5 on item 9 of MADRS-S; C-SSRS (past month) - Most Severe Ideation score ≥ 4). Patients excluded from the study prior to enrollment due to excessive depression or suicidality were subjected to the same

safety procedures as patients who were included. They agreed to go to an identified, local 24 hour psychiatric emergency center in the event that they were at imminent risk, and were referred to mental health services in their area for ongoing care.

Patient and Public Involvement

Patients and the general public did not have direct involvement in the design of this study, recruitment, or the development of research questions or measures. Upon publication, patients will be sent a copy of the article which would not have been possible without their participation.

Primary Outcome

The primary outcome was the BDD-YBOCS, administered at baseline, mid-treatment (week 6), post-treatment (week 12), and 3 months after treatment completion. BDD-YBOCS is a semi-structured clinician-administered scale, considered to be the gold standard for measuring BDD symptom severity and has demonstrated good psychometric properties [30]. Scores range from 0-48 with higher scores indicating greater severity. Prior to subject enrollment, all evaluators were trained to a reliability criterion (intra-class correlation coefficient (ICC) of at least .85) with a gold standard rater on the BDD-YBOCS.

Secondary Outcomes

Participants with ≥ 30% reduction on the BDD-YBOCS were considered responders [30]. Participants no longer meeting full criteria for DSM-5 diagnostic criteria for body dysmorphic disorder were considered to be in remission.

Clinicians rated patient overall severity and symptom change on the clinical global impressions scale (CGI). The CGI-S ranges from 1 (normal, not ill at all) to 7 (among the most extremely ill of subjects). Similarly, the CGI-I ranges from 1 (very much improved) to 7 (very much worse) [27]. Secondary measures of symptoms included the Montgomery - Åsberg Depression Rating Scale – self-report (MADRS-S) [18,19], Global Assessment of Functioning (GAF) [5] and Brown Assessment of Beliefs Scale (BABS) [26]. See appendix A for a complete list of secondary outcome measures.

Treatment activity, completion, and acceptability

Therapist time spent on the platform reviewing patient progress and responding to messages, number of messages sent and received, and number of completed modules were automatically recorded for each patient. Patients rated working alliance every two weeks throughout treatment using the WAI-SR [31]. At post-treatment, patients rated treatment satisfaction on the client satisfaction inventory (CSI) [32]. Patient credibility and expectancy was also recorded every two weeks throughout treatment using the Credibility/Expectancy Questionnaire [33,34].

Adverse events monitoring

Each week patients were asked if they experienced any adverse events or side effects that could be attributed to treatment (e.g., sleep disturbances, increased anxiety, or depression symptoms). If so, they were asked to describe them in the form of free text [35].

For a full list of outcome measures used, as well as a detailed timetable for their administration, see protocol in appendix A.

Intervention

BDD-NET, a 12 week internet-delivered cognitive behavioral therapy intervention for BDD, was evaluated in Sweden in a pilot study (n=23) and then in a randomized controlled trial (n=94), and showed sustained effects at 2-year follow-up [15,16] (2-year follow-up under review). It was translated to English for the current study in order to reach an international sample (For a full description of the treatment content, see [15,16]. Throughout treatment, patients had unlimited access to their therapist from Monday through Friday via asynchronous electronic text messages. The therapist's primary role was to offer clarification and emotional support, and to help participants design and practice EX/RP exercises that targeted their treatment goals. They also reminded participants to complete treatment content in time via text message reminders. Therapists were doctoral level psychology students with no previous experience treating BDD, and were supervised by licensed psychologists and psychiatrists based at Karolinska Institutet. Similar to the delivery of the treatment itself, supervision was primarily delivered at least once per week, on a continuous basis, any time that decisions were made related to patient inclusion/exclusion or withdrawal from treatment, any time a patient reported elevated risk, and as needed to address other questions related to the delivery of the treatment itself.

Safety Procedures

Before the start of treatment, researchers verified the 24 hour emergency psychiatric centers in each participant's local area. Symptom levels and adverse events were evaluated weekly via the platform and considered along with patients' message content in order to

continuously assess risk. Any increase in suicidal ideation (e.g. MADRS-S item 9 ≥ 4) was automatically flagged by the system and prompted the therapist for further assessment (see appendix A for details on this procedure).

Statistical Analyses

All statistical analyses are reported according to "intention to treat" principles unless otherwise stated. Linear mixed models were used to assess continuous outcomes, with time as a fixed effect and random intercepts for each participant [36], and reported using maximum likelihood estimation with 95% confidence intervals around estimated means. We calculated Cohen's *d* by dividing the estimated change by the standard deviation of that measure at pre-treatment. For non-continuous outcomes, ordinal logistic regression was used with a fixed effect of time, reported as proportional odds ratios with 95% confidence intervals. To examine whether data could be deemed to be missing at random, we compared completers (i.e., those with BDD-YBOCS data at follow-up) with non-completers on baseline measurements from Table 1, using t-tests or chi-square tests where appropriate. Analyses were performed in R (version 3.4.4) and in SPSS version 25.

RESULTS

In total, 32 participants initiated treatment, 25 participants (78%) completed mid-treatment assessments, 21 (66%) post-treatment, and 25 participants (78%) follow-up assessments, respectively (see Figure 1 for patient flow throughout the study). There were no statistically significant differences between completers and non-completers on baseline demographic and clinical variables (*p*'s 0.29 - 0.91), except that non-completers, on average, had undergone more previous plastic surgeries ($p = 0.03$).

Primary Outcome

From baseline to week 6, participants made significant improvements on the BDD-YBOCS (Estimate = -8.12, 95% CI = -10.93 to -5.32, d = 1.66, p < .001). Further improvements were seen at post-treatment (Estimate = -12.63, 95% CI = -15.61 to -9.65, d = 2.57, p < .001) and were maintained at the 3-month follow-up (Estimate = -11.71, 95% CI = -14.52 to -8.91, d = 2.39, p < .001). The effect of time in a linear mixed effects model was significant (F[3, 71.63] = 31.79, p < .001). These outcomes were similar to those of the previous BDD-NET trials (see figure 2).

Secondary Outcomes

At post treatment, 15 participants (47%, 95% CI = 24% - 70%) were considered treatment responders, with 16 (50%, 95% CI = 29% - 71%) participants considered responders at 3-month follow-up. At post treatment, 9 participants (28%, 95% CI = 7% - 49%) no longer met criteria for BDD, which increased to 14 (44%, 95% CI = 23% - 65%) at the 3-month follow-up.

Participants showed statistically significant improvements on the CGI-S at post- (pOR = 0.17, 95% CI = .06 - .47, p < .001) and at 3-month follow-up (pOR = 0.22, 95% CI = .07 - .60, p = .004). The majority of participants who participated in post- and follow-up assessments were much improved or very much improved on the CGI-I after treatment (see figure 3).

Additionally, participants showed significant improvement in depressive symptoms measured using the MADRS-S (F[13, 243.83] = 5.85, p <.001), global functioning using the GAF (F[2, 46.89) = 10.46, p < .001), and insight using the BABS (F[2, 47.36] = 10.11, p <

0.001). See table 2 for estimated means and change on primary and secondary outcome measures.

Treatment activity, completion and acceptability

Therapists spent an average of 15.2 minutes supporting patients (SD = 12.1 minutes) per participant per week, and sent or received an average of 3.7 (SD = 2.7) messages per week. For each additional message sent, participants had on average a reduction of BDD-YBOCS score of 0.11 points (95% CI = -0.23 to 0.01), but the number of messages sent were not a statistically significant predictor of BDD-YBOCS score when controlling for time (F[1, 28.80] = 3.01, p = .09). In total, 18 (56%) participants completed the core treatment content (modules 1-5). Eight participants (25%) completed all 8 modules. The mean number of modules completed was 5.1 (SD = 2.47). Individuals who completed at least 5 modules had, on average, a lower score on the BDD-YBOCS over time (Estimate = -6.35, 95% CI = -11.72 to -0.99). The effect of number of modules completed was statistically significant when including time as a co-variate (F[1, 37.62] = 5.39, p = .03). The following results on acceptability measures reflect patient responses at post-treatment which could not be acquired from the entire sample, and therefore, are not intention to treat analyses. The mean WAI-SR score after treatment was 49.7 (SD = 10.7) out of a possible 60, indicating a strong therapeutic bond. Additionally, 95% of participants who gave feedback at post-treatment (20/21) reported that they felt well supported or very well supported by their therapist. Furthermore, despite the fact that some participants were not native English speakers, 95% of participants found the language used in treatment to be easy or very easy to understand. On average, participants were satisfied with the treatment and

found it to be credible. Treatment satisfaction on the CSI was moderate to high at post-treatment, with a mean score of 129.4 (SD = 32.6) out of a possible 175. Participants rated treatment credibility as moderate on the CEQ at post-treatment (mean = 33.1, SD = 9.8).

Adverse Events

During the course of treatment, (8/32) 25% of participants reported at least one mild adverse event, which did not pose any acute health risk. This included increased depressive symptoms (21.9%), a temporary increase in anxiety (15.6%), sleep disturbance or nightmares (9.4%), and feelings of shame (6.3%). Two adverse events needed further action due to increased suicidal ideation. One participant was admitted to high-intensive psychiatric care and ended participation in the study. In this case, researchers facilitated the connection to services in the participant's local area. Another participant who reported a high frequency of suicidal ideation remained in the study and was monitored by a local psychiatrist who had previously treated the patient.

DISCUSSION

Here we report the results of the first fully remote, psychological treatment, of BDD or any other disorder, without any geographic restrictions for enrollment. We found that BDD-NET was associated with a large reduction of BDD symptoms at post-treatment and follow-up. Participant-rated reductions in body dysmorphic symptoms and depressive symptoms were 46% and 34%, respectively. Remission rates were 28% at post-treatment and 44% at follow-up. Additionally, patients at post-treatment (n= 21) reported a strong therapeutic bond with mean Working Alliance Inventory scores at 49.8 (sd = 10.4) out of a possible 60.

The safety procedures tested in this study worked well. These results indicate that delivering BDD-NET across international borders is feasible, safe, and acceptable to clients. Furthermore, as required therapist time was minimal as compared to face-to-face CBT, our findings highlight international ICBT treatment as a promising solution to the global mental health epidemic in general.

Comparison to previous results

Current results are in line with previous evaluations of BDD-NET as well as face-to-face CBT for BDD [15–17]. These findings suggest that delivering BDD-NET across borders in a new language, to a more culturally diverse patient population, had little to no impact on treatment effects. That said, these data are not sufficient to conclude that the treatment effects are universally generalizable. While our sample comprises 12 different nationalities, only 25% came from non-western cultures. Post-hoc analyses did not identify nationality as a statistically significant predictor of BDD-YBOCS score, but larger samples recruiting more heavily from non-western countries are needed to detect differences between nationalities and to determine if adaptations should be made to the core treatment content.

Limitations

While the amount of missing data (35% at post-treatment and 21% at follow-up) is higher than previous investigations of BDD-NET (4% at post-treatment and 9% at follow-up in BDD-NET pilot), it is similar to estimates from recent meta-analyses of both face-to-face and Internet CBT [37,38]. Furthermore, our sensitivity analysis showed that participants with incomplete data at post-treatment did not differ from participants with complete

post-treatment data on most baseline measures. However, participants with missing data did report more cosmetic surgeries. This could potentially be related to poorer insight or higher overall severity, which in turn could have impacted their commitment to treatment. Also, since there was no active comparison group, one cannot conclusively say that treatment caused the improvements that were observed. However, this was not the primary aim of the current study since the specific treatment effects of BDD-NET have already been established in comparison with online supportive therapy [16].

Challenges for clinical trials with global inclusion

Legal considerations

Trials are currently regulated by ethical review boards at universities and health care providers. These typically oversee research at their specific site. While multi-center trials may be international, this is to our knowledge the first one-site therapist-guided ICBT treatment study with global eligibility for inclusion. Legislation on ethical vetting is by default national and there are presently no clear guidelines on how trials with international participation of study subjects should be regulated. Internet treatment may also be subject to regulations that govern communications as well as clinical practice. Any legal ambiguity could potentially put some patients at risk when receiving treatment. Therefore, it is essential that international treatment programs protect patients' privacy and safety in this new context.

Risk management

Another challenge for studies with global eligibility for inclusion is to ensure adequate care for at-risk patients while also reaching those in need of treatment. While high-risk patients may make clinicians uncomfortable due to liability concerns, many patients seek out ICBT because it is their only viable treatment option. Our procedure for monitoring and responding to suicidality was effective in ensuring patient safety despite the distance between patients and clinicians. One strategy used in this study to manage higher risk patients was to partner with local mental health practitioners who could facilitate risk assessment and expedite a safety plan in their local area if necessary. Psychiatrists can function particularly well in this role, as pharmacological treatment (when indicated) could complement ICBT treatment with minimal redundancy or interference. It is our view that offering remotely delivered evidence-based treatment will always be safer for patients than not having access to treatment at all.

Cultural differences

International ICBT treatment also poses some novel challenges to cultural competence. Patients not only have different cultural backgrounds, but are currently residing in a different cultural context. Therefore cultural considerations in treatment may be magnified. Special care should be taken when establishing treatment goals and designing exposure exercises that are culturally appropriate. While our results suggest that a competent therapist can adapt the treatment to the needs of patients from different cultural backgrounds, it should be noted that the participants in this trial were relatively homogeneous (mainly from industrialised nations, highly educated, good command of

English language, availability of local psychiatric services). Therefore, it is not yet clear to what extent ICBT can be made available in other settings. Furthermore, while the assessment instruments used in the current study are the most widely used and accepted among BDD researchers, they were developed and validated within western cultures, with primarily native English speakers. Therefore, it is not yet clear to what extent these instruments assess the same psychological constructs for participants from non-western backgrounds.

Conclusion

This is, to our knowledge, the first investigation of a fully remote, therapist-guided psychological treatment with recruitment efforts deployed on a global scale. We found large reductions in core BDD symptomatology, with 44% of patients in remission at follow-up. Participants accepted the treatment and rated their therapist as supportive in the majority of cases. Future trials should evaluate the specific effects of BDD-NET compared to a credible control condition and strive to include more participants from non-western cultures. In summary, we found that an internet-delivered treatment for BDD can be delivered fully remotely with intact treatment effects, and in a safe way, across countries.

Author Contributions: CR was he primary investigator for the study and drafted the design of the study with CL, JE and D-MC. AG and CL both independently served as project manager during different periods of time. The treatment manual was written by JE with notable influence from work by SW, and was translated to English by CL. CL also developed the study website, protocol, drafted the ethics submissions, and international regulations pertaining to treatment. AG was in charge of the recruitment, assessment, and treatment of participants, with significant contributions by CL and additional work by OF. Data analysis was primarily conducted by OF and AG. CR, AG, CL, and OF had full access to data and are guarantors for the accuracy of raw data and statistical analyses.The manuscript was primarily written by AG, with significant contributions by OF, CR, JE, SW, D-MC, and CL.

Funding: This study was funded through the regional agreement on medical training and clinical research (ALF) between the Stockholm County Council and Karolinska Institutet. CR was supported by the Swedish Research Council (grant No: K2013-61X-22168-01-3). The funders had no role in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication.

Competing interests: All authors declare: No support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Data sharing statement: No additional data are available.

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Table 1

Socio-demographic and Clinical Characteristics of the Sample (N = 32)

Variable	
Gender, n (%)	
Men	8 (25)
Women	24 (75)
Age, mean (SD)	31.91 (7.44)
Highest education, n (%)	
Primary school	1 (3.1)
High school	6 (18.8)
Bachelor's degree	14 (43.8)
Master's degree	10 (31.2)
Doctorate degree	1 (3.1)
Occupational status, n (%)	
Working, full time	9 (28.1)
Working, part time	10 (31.2)
Student	7 (21.9)
Unemployed	5 (15.6)
Disability pension	1 (3.1)
Years with BDD, mean (SD)	16.22 (9.10)
Number of areas of concern, mean (SD)	12.16 (5.84)
Comorbid conditions, n (%)	
Major depressive disorder	10 (31.2)
Panic disorder	2 (6.2)
Social anxiety disorder	5 (15.6)
Generalized anxiety disorder	5 (15.6)
Current medication, n (%)	
SSRI	2 (6.2)
SNRI	3 (9.4)
Benzodiazepines	1 (3.1)
Stimulants	1 (3.1)
Previous psychological treatment, n (%)	25 (78.1)

CBT	8 (32.0)
PDT	2 (8.0)
Non-specific counseling	12 (48.0)
Religious counseling	1 (4.0)
Unknown	2 (8.0)
Plastic surgery	
Previous plastic surgery, n (%)	13 (40.6)
Number of surgeries, mean (SD)	1.38 (2.46)
Nationality, n (%)	
American	12 (37.5)
Swedish	7 (21.9)
Indian	1 (3.1)
Bulgarian	1 (3.1)
Finnish	1 (3.1)
English	4 (12.5)
Serbian	1 (3.1)
South Korean	1 (3.1)
Irish	1 (3.1)
Norwegian	1 (3.1)
Sri Lankan	1 (3.1)
Lithuanian	1 (3.1)
Dysmorphic concerns questionnaire, mean (SD)	15.63 (2.50)

Abbreviations: BDD, Body dysmorphic disorder; SSRI, Selective serotonin reuptake inhibitor; SNRI, Serotonin and norepinephrine reuptake inhibitor; CBT, Cognitive behavior therapy; PDT, Psychodynamic therapy

Table 2. Estimated means and change on primary and secondary outcomes

Outcome	Time	Estimated mean (SE)	Estimated change [95% CI]	d	p
BDD-YBOCS	Pre	28.72 (1.35)			
	Mid	20.6 (1.43)	-8.12 [-10.93 to -5.32]	-1.66	0.001
	Post	16.09 (1.52)	-12.63 [-15.61 to -9.65]	-2.57	0.001
	Follow-up	17.01 (1.43)	-11.71 [-14.52 to -8.91]	-2.39	0.001
MADRS-S	Pre	20.16 (1.59)			
	Week 1	19.54 (1.08)	-0.62 [-2.74 to 1.51]	-0.07	0.57
	Week 2	17.02 (1.09)	-3.14 [-5.28 to -1]	-0.38	0.004
	Week 3	17.24 (1.11)	-2.91 [-5.1 to -0.73]	-0.35	0.01
	Week 4	16.15 (1.16)	-4.01 [-6.29 to -1.72]	-0.48	0.001
	Week 5	16.8 (1.13)	-3.35 [-5.57 to -1.14]	-0.4	0.003
	Week 6	16.7 (1.23)	-3.46 [-5.86 to -1.06]	-0.42	0.005
	Week 7	14.76 (1.25)	-5.4 [-7.84 to -2.95]	-0.65	0.001
	Week 8	15.37 (1.28)	-4.78 [-7.29 to -2.28]	-0.58	0.001
	Week 9	14.88 (1.25)	-5.27 [-7.72 to -2.82]	-0.63	0.001
	Week 10	16.37 (1.21)	-3.78 [-6.14 to -1.42]	-0.46	0.002
	Week 11	13.5 (1.34)	-6.66 [-9.28 to -4.03]	-0.8	0.001
	Post	13.36 (1.17)	-6.8 [-9.08 to -4.51]	-0.82	0.001
	Follow-up	12.37 (1.3)	-7.78 [-10.34 to -5.23]	-0.94	0.001
BABS	Pre	14.75 (1.06)			
	Post	10.1 (1.18)	-4.65 [-6.96 to -2.34]	-0.98	0.001
	Follow-up	10.72 (1.1)	-4.03 [-6.19 to -1.87]	-0.85	0.001
GAF	Pre	57.34 (1.73)			
	Post	67.43 (2.2)	10.08 [5.76 to 14.4]	0.94	0.001
	Follow-up	61.55 (2.07)	4.21 [0.15 to 8.27]	0.39	0.048

Abbreviations: SE, standard error; CI, confidence interval; d, Cohen's d; p, p-value (estimated change); BDD-YBOCS, Body dysmorphic disorder modification of the Yale-Brown obsessive compulsive scale; MADRS-S, Montgomery-Åsberg depression rating scale – self-rated; BABS, Brown assessment of beliefs scale; GAF, Global adaptive functioning.

Figure legends

Figure 1. Participant flow through the study

Figure 2. Clinician-rated BDD-YBOCS, Comparison with previous BDD-NET trials

Figure 3. CGI improvement

Figure 1. Participant flow through the study

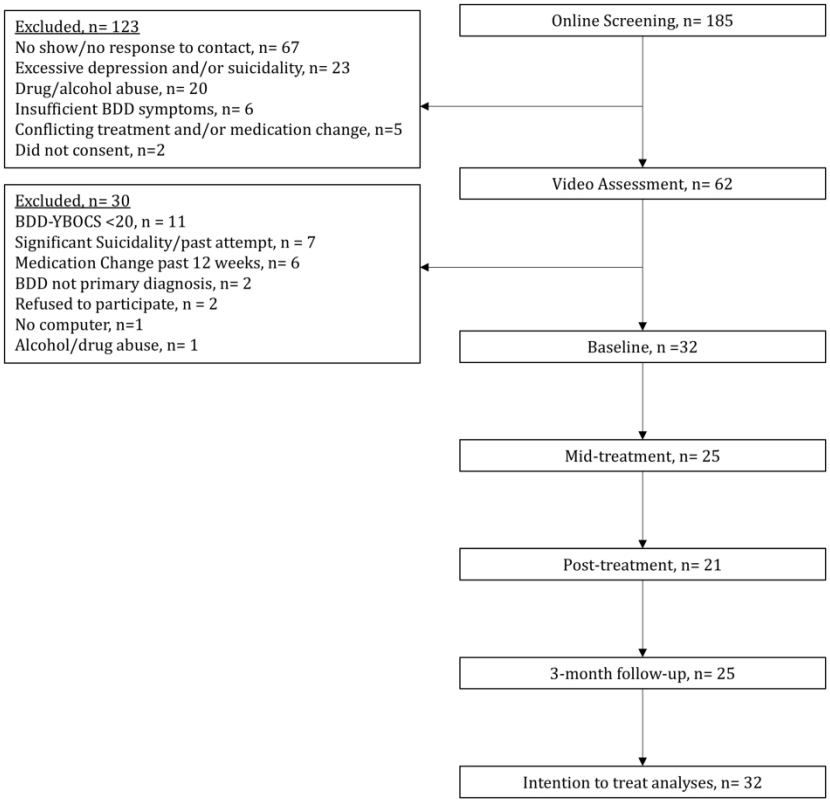

Figure 1

297x420mm (300 x 300 DPI)

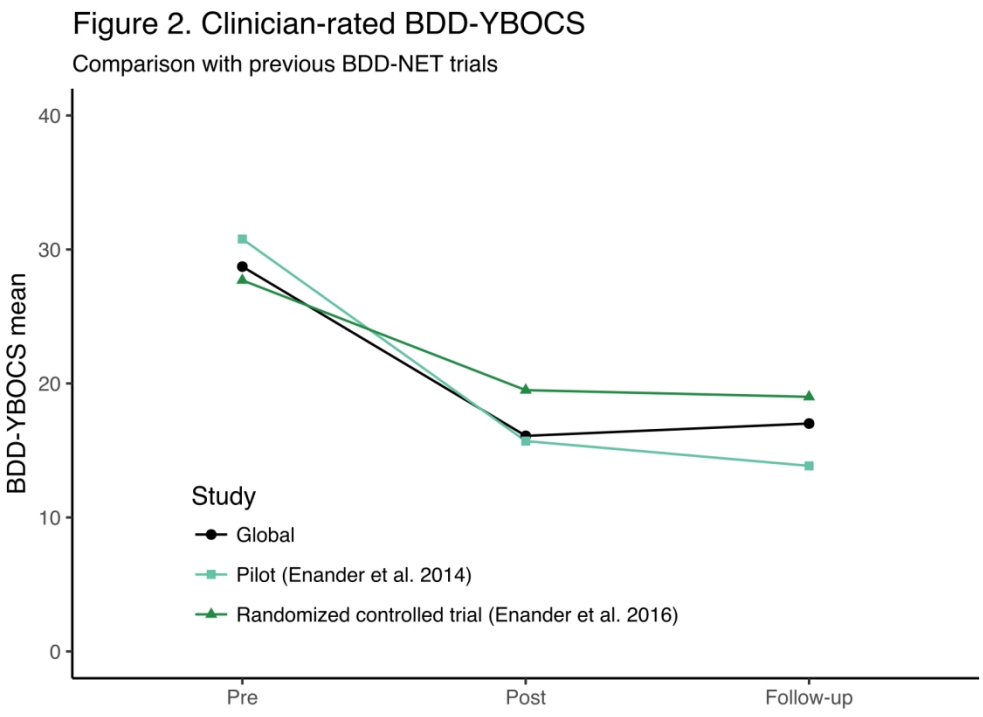

Figure 2. Clinician-rated BDD-YBOCS: Comparison with previous BDD-NET trials

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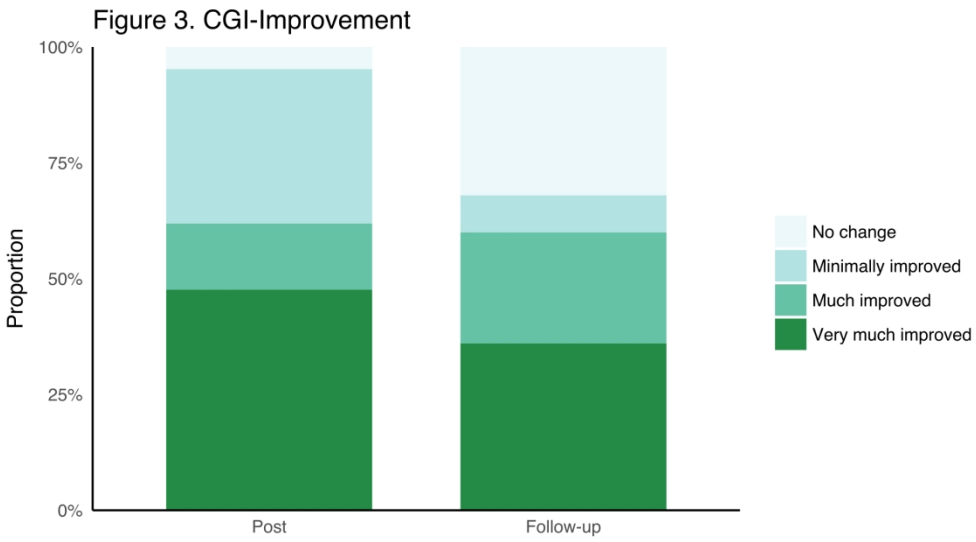


Figure 3. CGI Improvement

178x101mm (300 x 300 DPI)

Appendix A

Methods

Supplementary table 1. Overview of inclusion and exclusion criteria
Inclusion criteria
Fluent in English
Outpatient
≥ 18 years of age
BDDQ ≥ 4 at internet screening
DCQ ≥ 9 at internet screening
Primary diagnosis of BDD according to DSM-5
BDD-YBOCS ≥ 20
Verbal consent via video-conference and check yes to consent via treatment platform
Regular access to a computer with internet connection
Adequate skills to use the internet
Photo ID with name and age
Exclusion criteria
Psychotropic medication changes within 12 weeks prior to treatment
Completed CBT for BDD within 12 months prior to treatment
AUDIT ≥ 8 or DUDIT ≥ 8
Lifetime bipolar disorder or psychosis
MADRS-S ≥ 35
Clinically significant suicidal ideation or lifetime history or suicide attempts
Personality disorder that could jeopardize treatment participation (e.g. borderline personality disorder with self-harm)
Other current psychological treatment

No access to a 24 hour psychiatric emergency care center
No specific emergency contact person or emergency contact person phone number

Measures

Appearance Anxiety Inventory (AAI)

The AAI is a self-report, process measure that identifies cognitive processes and behaviors in the treatment of BDD. The maximum total score is 40, with higher scores indicating greater frequency of a process [1].

Brown Assessment of Beliefs Scale (BABS)

The BABS is a 7 item, clinician administered measure with excellent psychometric properties [2]. Scores can range from 0 to 24 with higher scores indicating poorer insight.

EuroQol – 5 Dimension Questionnaire (EQ-5D)

The EQ-5D is used as a non-disease specific assessment of quality of life and global functioning. It measures these constructs along 5 dimensions: Mobility, self-care, main activity, pain, and mood [3,4]. EQ-5D scores range between 0 (dead) and 1 (perfect health).

Sheehan Disability Scale (SDS)

The SDS has 3 items measuring functional impairment and disability regarding work/school, social life/leisure, and family life/home responsibilities on a likert scale between 0 (no interference) to 10 (extreme impairment). Two items measure days lost at work/school and days being underproductive at work/school. Items are on a likert scale of 0 (not at all) to 10 (very severe) [5,6].

Skin-Picking Scale – Revised (SPS-R)

The SPS-R is a self-report measure containing 8 items evaluating skin-picking severity. Scores range from 0 to 32 with higher scores indicating higher severity [7].

ICBT – EX/RP Adherence Scale

The ICBT – EX/RP Adherence Scale is modified from the Patient EX/RP Adherence Scale (PEAS) [8]. This measure assesses a patient's overall level of engagement in treatment with particular emphasis on quality and quantity of exposure and response prevention exercises. It looks at number of days, total hours, and quality of approach behaviors in EX/RP practice. In addition, it also looks other aspects of internet treatment adherence such as reading psychoeducational content and communicating with their therapist.

Results

Self-reported symptoms of BDD were significantly reduced over the course of treatment (F[13, 244.7] = 16.93, p <.001).

There were statistically significant reductions in delusionality on the BABS (F[2, 47.36] = 10.11, p < 0.001), as well as skin-picking using the SPS-R (F[2, 34.64] = 6.41, p = .004).

Changes in overall quality of life using the EQ-5D were not statistically significant (F[2, 36.28] = 1.35, p = .273). There were statistically significant improvements in functioning on the SDS (F[2, 35.07] = 12.78, p < .001).

Self-reported adherence to treatment (PEAS) increased over the course of treatment, from 16.83 (se = 1.88) at week 1, to 29.09 (se = 2.33) at post-treatmen

Supplementary table 2. Estimated means and change on secondary outcome measures

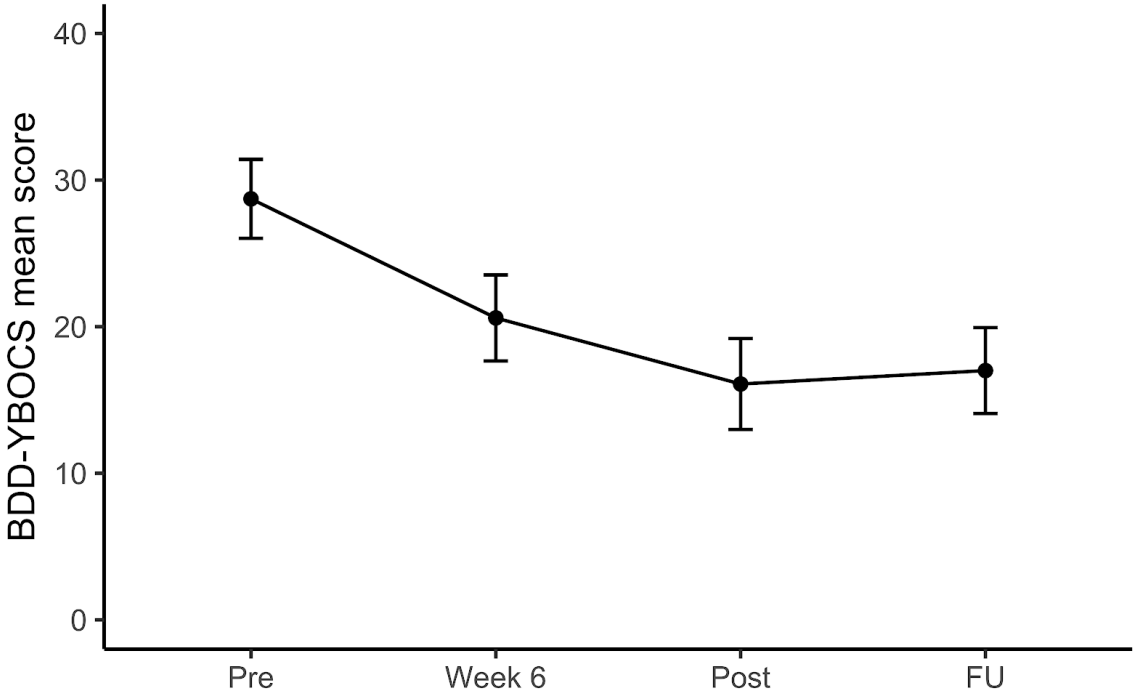
Outcome	Time	Estimated mean (SE)	Estimated change [95% CI]	d	p
AAI	Pre	26.66 (1.36)			
	Week 1	24.88 (1.11)	-1.78 [-3.95 to 0.39]	-0.26	0.109
	Week 2	22.25 (1.12)	-4.41 [-6.6 to -2.22]	-0.66	0.001
	Week 3	20.73 (1.14)	-5.93 [-8.16 to -3.69]	-0.88	0.001
	Week 4	19.09 (1.19)	-7.56 [-9.89 to -5.23]	-1.13	0.001
	Week 5	18.96 (1.15)	-7.69 [-9.95 to -5.43]	-1.14	0.001
	Week 6	18.52 (1.25)	-8.13 [-10.59 to -5.68]	-1.21	0.001
	Week 7	17.18 (1.28)	-9.48 [-11.98 to -6.97]	-1.41	0.001
	Week 8	17.47 (1.3)	-9.18 [-11.74 to -6.63]	-1.37	0.001
	Week 9	16.63 (1.28)	-10.03 [-12.53 to -7.53]	-1.49	0.001
	Week 10	16.86 (1.23)	-9.8 [-12.21 to -7.39]	-1.46	0.001
	Week 11	16.42 (1.37)	-10.23 [-12.91 to -7.56]	-1.52	0.001
	Post	14.38 (1.19)	-12.28 [-14.61 to -9.94]	-1.83	0.001
	Follow-up	13.45 (1.33)	-13.21 [-15.82 to -10.6]	-1.97	0.001
EQ-5D	Pre	0.75 (0.03)			
	Post	0.82 (0.04)	0.07 [-0.02 to 0.15]	0.33	0.126
	Follow-up	0.8 (0.05)	0.05 [-0.04 to 0.15]	0.25	0.302
SDS	Pre	14.56 (1.35)			
	Post	9.33 (1.43)	-5.17 [-7.93 to -2.41]	-0.6	0.001
	Follow-up	7.13 (1.6)	-7.43 [-10.57 to -4.29]	-0.86	0.001
SPS-R	Pre	6.38 (1)			
	Post	4.34 (0.74)	-2.03 [-3.49 to -0.58]	-0.33	0.01

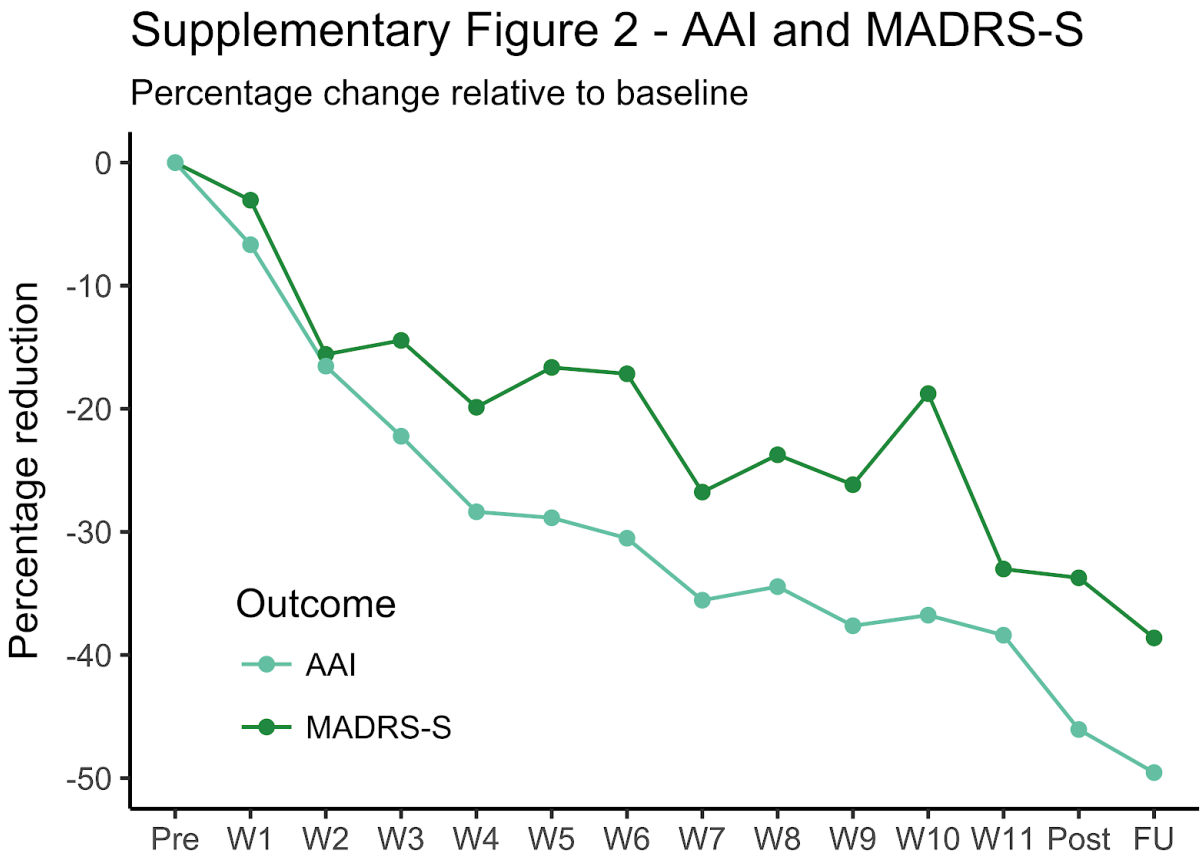
	Follow-up	3.66 (0.85)	-2.72 [-4.38 to -1.06]	-0.44	0.003
PEAS	Week 1	16.83 (1.88)	-12.26 [-15.95 to -8.57]	-1.22	0.001
	Week 2	18.49 (1.91)	-10.6 [-14.33 to -6.86]	-1.05	0.001
	Week 3	24.83 (1.96)	-4.26 [-8.1 to -0.41]	-0.42	0.031
	Week 4	23.82 (1.98)	-5.27 [-9.15 to -1.39]	-0.52	0.008
	Week 5	26.62 (2.08)	-2.47 [-6.54 to 1.59]	-0.25	0.235
	Week 6	28.54 (2.1)	-0.55 [-4.68 to 3.57]	-0.06	0.793
	Week 7	29.22 (2.05)	0.13 [-3.9 to 4.16]	0.01	0.949
	Week 8	28.47 (2.07)	-0.63 [-4.68 to 3.43]	-0.06	0.763
	Week 9	28.19 (2.06)	-0.9 [-4.94 to 3.14]	-0.09	0.664
	Week 10	32.18 (2.18)	3.09 [-1.18 to 7.36]	0.31	0.157
	Week 11	36.1 (4.04)	7 [-0.91 to 14.92]	0.7	0.084
	Post	29.09 (2.33)			
WAI-SR	Week 2	43 (1.33)	-4.64 [-7.25 to -2.04]	-0.48	0.001
	Week 4	45.28 (1.34)	-2.37 [-4.99 to 0.25]	-0.25	0.08
	Week 6	46.02 (1.37)	-1.62 [-4.31 to 1.07]	-0.17	0.24
	Week 8	46.19 (1.38)	-1.45 [-4.16 to 1.26]	-0.15	0.296
	Week 10	46.75 (1.4)	-0.9 [-3.65 to 1.85]	-0.09	0.524
	Week 12	46.88 (2.53)	-0.77 [-5.73 to 4.2]	-0.08	0.763
	Post	47.65 (2.05)			
CSI	Pre	110.77 (5.72)			
	Post	124.27 (4.85)	13.49 [3.99 to 23]	0.43	0.011

Abbreviations: SE, standard error; CI, confidence interval; d, Cohen's d; p, p-value (estimated change); AAI, Appearance anxiety inventory; EQ-5D, EuroQol – 5 dimension questionnaire; SDS, Sheehan disability scale; SPS-R, Skin-picking scale – revised; PEAS, ICBT – exposure and response prevention adherence scale; WAI-SR, Working alliance inventory – short revised; CSI, Client satisfaction inventory.

Supplementary Figure 1. BDD-YBOCS

Estimated means with 95% confidence intervals





Protocol

Therapist-Guided, Internet-Based Cognitive Behavioral Therapy for Body Dysmorphic Disorder – English Version (BDD-NET): A Feasibility Study

Principal Investigator: Christian Rück, MD, PhD, Department of Clinical Neuroscience

Version: XXXX

Date: XXXX

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1. Protocol Summary

PROTOCOL IDENTITY AND OBJECTIVES	
Protocol Title:	Therapist-Guided, Internet-Based Cognitive Behavioral Therapy for Body Dysmorphic Disorder – English Version (BDD-NET): A Feasibility Study
Trial Objectives:	Primary: Establish ICBT for BDD, English version (BDD-NET), as an acceptable, feasible, and potentially efficacious treatment.

METHODOLOGY	
Trial Design:	Uncontrolled clinical trial with within-subjects repeated measures design.
Treatment/Duration:	Internet-based cognitive behavioral therapy for 12 weeks.
Primary Endpoints:	Change from W0 to W12, 3 and 12-month follow-ups.
Efficacy Parameters:	Clinician-administered BDD-YBOCS[41]
Safety Parameters:	Designated emergency care centers, adverse events assessed weekly via the internet and also at post-treatment and 3-month follow-up using clinician assessments via video-conference or telephone.

POPULATION OF TRIAL SUBJECTS	
Description of Trial Subjects:	Adults, fulfill DSM-5 diagnostic criteria for BDD.
Number of Subjects:	30

TRIAL TIMETABLE	
First Subject In:	December 2015
Last Subject In:	January 2016
Last Subject Out:	April 2016

2. Administration Information

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PERSONNEL INFORMATION

Personnel	Background	Role	Affiliation
Christopher La Lima, MA	Clinical Psychology PhD student at Hofstra University	Co-Investigator, Project Manager	Karolinska Institutet (KI) and Hofstra University
Christian Rück, MD, PhD	Psychiatrist, associate professor, senior lecturer. Co-founder of Internetpsykiatrienheten, the world's largest implementation of ICBT in mental health. Research group leader in a group specializing in ICBT for OCD, BDD, and related disorders (www.rucklab.com)	Principal Investigator	KI
Jesper Enander, MSc	Doctoral candidate, psychologist, KI. Has written the ICBT program for BDD (BDD-NET).	Development and monitoring psychological treatment, IT platform	KI
Sabine Wilhelm, PhD	Chief of Psychology, Massachusetts General Hospital (MGH) Director, OCD and Related Disorders Program, MGH Professor, Harvard Medical School	Treatment development, recruitment, design	Harvard, MGH
David Mataix-Cols, PhD	Professor at KI. The most cited European researcher in OCD and related disorders (ISI Web of Science).	Supervising, study design	KI

3. Research field overview

WHAT IS BDD?

Body Dysmorphic Disorder (BDD) is a disabling illness characterized by excessive preoccupation with minor or imagined defect(s) in one's physical appearance, followed by

repetitive behaviors (e.g. mirror checking, camouflaging, mentally comparing one's appearance to another) and avoidance. This preoccupation leads to clinically significant distress and/or impairment[1]. BDD is associated with decreased social, emotional, and occupational functioning, as well as reduced quality of life[2, 3]. It is a chronic disorder linked to high rates of hospitalization[3, 4]. Individuals with BDD tend to have elevated rates of suicidal ideation and suicide attempts[5-7]. Furthermore, preliminary results suggest that they have a higher rate of completed suicide[6].

BDD is a prevalent disorder, affecting 0.7 % to 2.4 % of the general population across a variety of nationalities and geographic locations[7-12]. Specifically, it has a point prevalence of 2.4 % in the United States, exceeding schizophrenia and bipolar I disorder, and 2.1% among Swedish women[8, 9]. Additionally, BDD is a heritable disorder, with genetic factors accounting for approximately 44% of the variance in dysmorphic concerns[13].

While relatively common, many individuals with BDD are not receiving proper treatment. BDD is underdiagnosed in mental health care settings, and patients often do not express body image concerns to physicians due to feelings of shame[5, 14, 15]. Furthermore, individuals with BDD often have poor insight and seek non-psychiatric care, such as dermatological treatments and cosmetic surgery. Such treatments are rarely effective and can lead to a worsening of symptoms[16-18].

CBT FOR BDD

Evidence based treatments for BDD include cognitive behavioural therapy (CBT) and pharmacotherapy with serotonin reuptake inhibitors (SRIs)[19-22]. Veale et al. (2014) conducted the only RCT comparing CBT with an active comparison group to date. They reported superiority of CBT over anxiety management, including progressive muscle relaxation and breathing techniques. Wilhelm et al. (2013) developed a multimodal treatment manual for BDD that was tested in one open trial and one wait-list controlled trial. Both studies resulted in improved BDD symptoms at post-treatment and maintained gains at a 6-month follow-up[21, 23]. Wilhelm et al. (2014) additionally found that depression, insight, and disability significantly improved with this treatment. These studies show promising results that CBT is effective and can have a lasting effect on symptom reduction in the months following treatment. However, to date there are relatively few studies of CBT treatment for BDD, and they include relatively small samples, so larger studies are needed to better understand this area.

While studies of CBT for BDD suggest that this treatment is efficacious, few patients are in fact receiving it[24]. In an online survey, 17.4% of participants diagnosed or self-diagnosed with BDD had received empirically supported psychotherapy (i.e. CBT) for body dysmorphic concerns, and 34.4% had been treated with SSRIs[25]. In another internet survey, 19.8% of people with body dysmorphic concerns were participating in psychosocial treatment, and 18.6% were receiving psychotropic medications[24]. Participants in both studies reported that shame associated with talking openly about one's appearance concerns was a major factor in not seeking help. In addition to underreporting symptoms associated with shame, underdiagnosis of BDD in mental health settings, and patients seeking non-psychiatric treatments that are ineffective or potentially worsen symptoms, individuals face restricted access to CBT[5, 14, 15, 16-18, 25-27]. This includes cost of services, a lack of trained therapists, and not having a specialized healthcare provider

nearby[25-27]. Furthermore, scheduling difficulties and transportation to healthcare providers hinder help-seeking efforts[25]. Therefore, it is clear that improved access to CBT treatments is needed.

ICBT FOR BDD

In response to limited CBT availability and accessibility, internet-based CBT (ICBT) with therapist support has been developed. In ICBT, the patient, instead of going to a clinic, logs onto a secure website and works with written self-help materials and homework assignments, supported online by a clinician. It has the advantage of being more accessible and requiring less therapist time than face-to-face[28]. ICBT has been shown to be effective in treating a variety of psychiatric disorders, such as obsessive-compulsive disorder, social anxiety disorder, depression, and panic disorder[29-31]. When compared to face-to-face CBT, a recent meta-analysis suggests no difference in treatment outcomes between the two, although there might be disorder-specific differences[32]. Additionally, ICBT is cost-effective and has been employed as a part of healthcare systems in Sweden, Australia, and the Netherlands[30, 32-36].

Recently, members of our research group (Enander et al. 2014)[37] developed ICBT for BDD (BDD-NET), based on existing BDD CBT manuals[38, 39], and tested it with a Swedish-speaking sample in an uncontrolled clinical trial. Results indicated BDD-NET was effective, with 82% of participants responding to treatment and large effect sizes. Participants also showed improvement in the areas of depression, skin picking, global functioning, and body image-related quality of life. Treatment gains in this study were maintained at a 3-month follow-up, and ICBT for BDD was highly accepted by participants[37]. Additionally, therapist interaction time was lower than that of typical CBT. Enander et al. (2015)[40] then conducted an RCT comparing BDD-NET with an active control (supportive therapy). In this trial, BDD-NET was superior to supportive therapy and associated with significant improvements in symptom severity, depression, and quality of life (submitted manuscript). Furthermore, self-reported satisfaction with BDD-NET was high.

ICBT for BDD may be especially important to address restricted access to treatment, including therapist availability, costs of services, and proximity to a clinician with specialized training. In addition, patients with BDD who have difficulties seeking face-to-face care may be easier reached via the internet. To test the BDD ICBT protocol (BDD-NET) in an English-language adaptation may be a first step to greatly increasing the availability of evidence-based treatment in the United States, Great Britain, India, and other areas with English-speaking populations. The current study aims to do just that in a pilot trial.

4. Purpose and Objectives

GENERAL PURPOSE

We plan to establish ICBT for BDD, English version (BDD-NET), as an acceptable, feasible, and potentially efficacious treatment for English-speakers across national borders. To achieve these goals, we need to:

PRIMARY OBJECTIVES

O1: Gain evidence that BDD-NET with therapist support leads to decreased symptoms of BDD.
O2: Assess patient satisfaction with the BDD-NET treatment platform and online therapist guidance.

O3: Evaluate patient engagement and ability to utilize tools and services offered in BDD-NET.

RESEARCH QUESTIONS

Q1: Does BDD-NET lead to a decrease in BDD symptom severity, dysmorphic concerns, and appearance concerns in English-speaking patients diagnosed with BDD?
Q2: Does BDD-NET improve insight/delusionality in these patients?
Q3: Does BDD-NET reduce symptoms of depression in these patients?
Q4: Does BDD-NET improve global functioning, quality of life, and disability in these patients?
Q5: Are these patients satisfied with BDD-NET and do they report a good working alliance with BDD-NET therapists?
Q6: Do these patients see BDD-NET as a credible intervention?
Q7: Are these patients compliant with the BDD-NET treatment protocol and able to complete treatment behaviors with its given resources?
Q8: Does the completion of EX/RP exercises and/or other treatment behaviors in BDD-NET predict outcome?

5. Hypotheses

H1. English-speakers diagnosed with BDD will decrease their BDD symptom severity, dysmorphic concerns, and appearance concerns at the end of the BDD-NET program (week 12), and at 3 and 12 month follow-ups, as compared to pretreatment.
H2. These patients will improve in insight/delusionality at week 12, and 3 and 12 month follow-ups, as compared to pretreatment.
H3. These patients will reduce in depression symptoms at week 12, and 3 and 12 month follow-ups, as compared to pretreatment.
H4: These patients will improve in global functioning, quality of life, and disability at week 12, and 3 and 12 month follow-ups, as compared to pretreatment.
H5: These patients will report satisfaction with treatment at W2, W7, and W12, and good working alliance with therapists.
H6: These patients will report treatment credibility for BDD-NET throughout treatment.
H7: These patients will complete BDD-NET core treatment modules (1-5) within 12 weeks of treatment, including module homework questions, written worksheets, and monitoring completed EX/RP exercises, provided BDD-NET resources and online therapist guidance.
H8: Reported EX/RP behaviors throughout treatment will predict outcome, with more EX/RP practice leading to greater improvement.

6. Endpoints

PRIMARY ENDPOINT

H	Measure	Utility	Time Points by Week															
			S	0	1	2	3	4	5	6	7	8	9	10	11	12	Post (12)	3m	12m
H1	Clinician-rated Body Dysmorphic Disorder	BDD symptom severity		x						x							x	x	x

	Modification of Y-BOCS; BDD-YBOCS[41]																	

SECONDARY ENDPOINTS

H	Measure	Utility	Time Points by Week															
			S	0	1	2	3	4	5	6	7	8	9	10	11	12	Post (12)	3m	12m
	Structured Clinical Interview for DSM 5 – Research Version (SCID-5-RV) module G[42]	BDD Remission status, comorbid anxiety diagnoses (e.g. social phobia)		x													x	x	x
	Mini-International Neuropsychiatric Interview – version 7.0 (M.I.N.I. 7.0)[43]	Current major depressive episode, comorbid diagnoses		x													x	x	x
H1	Dysmorphic Concerns Questionnaire (DCQ)[44]	BDD screening/ dysmorphic concerns	x	x													x	x	x
H1	Appearance Anxiety Inventory (AAI)[45]	BDD symptoms	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
H2	Brown Assessment of Beliefs Scale (BABS)[46]	Conviction and insight regarding beliefs/ obsessions		x													x	x	x
H3	Montgomery-Åsberg Depression Rating Scale, self-report (MADRS-S)[47]	Depressive symptoms	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Columbia-Suicide Severity Rating Scale (C-SSRS)	Suicide severity, suicidal		x													x	x	x

	Lifetime Recent – Clinical Version[48]	ideations and behaviors																	
	Skin-Picking Scale – Revised (SPS-R)[49]	Skin-picking severity		x												x	x	x	
H4	Global Assessment of Functioning (GAF)[50]	Global functioning		x												x	x	x	
H4	Clinical Global Impressions Scale – Severity (CGI-S)[51]	Global severity		x												x	x	x	
H4	Clinical Global Impressions Scale – Improvement (CGI-I)[51]	Global Improvement														x	x	x	
H4	EuroQol – 5 Dimension Questionnaire (EQ-5D)[52]	Quality of life		x												x	x	x	
H4	Sheehan Disability Scale (SDS)[53]	Functional Impairment		x												x	x	x	
H5	Client Satisfaction Inventory (CSI)[54]	Client satisfaction				x				x						x			
H5	Working Alliance Inventory – Short Revised (WAI-SR)[55]	Therapeutic alliance				x		x		x		x		x		x			
H6	Credibility Scale (Credibility/Expectancy Questionnaire)[56]	Treatment Credibility and expectancy		x		x		x		x		x		x		x			
H7	Completion of core treatment modules (1-5)	Treatment compliance	Continually monitored throughout treatment																
H7	Early Termination Checklist (Appendix Figure 1)	Reasons for early discontinuation or withdrawal	Continually monitored throughout treatment																

H8	ICBT – EX/RP Adherence Scale (modified from the Patient EX/RP Adherence Scale (PEAS)[57])	EX/RP adherence and practice; treatment adherence				x	x	x	x	x	x	x	x	x	x	x	x	

7. Efficacy of Data Collection

CLINICIAN-ADMINISTERED INTERVIEWS AND MEASURES

Clinician-Rated Body Dysmorphic Disorder Modification of Y-BOCS (BDD-YBOCS)[41]. The BDD-YBOCS is a modification of the Yale-Brown Obsessive Compulsive Scale designed to rate BDD symptom severity. It is a 12-item, semi-structured, clinician-administered interview with a total score of 0-48. Higher scores indicate more severe BDD symptoms[41]. In a recent study examining the psychometric properties of the BDD-YBOCS, it was found to have excellent interrater intra-class correlation coefficients (ICC), [.77 to 1.00 (p's < .001)] on all items, good test-retest ICCs for individual items [.73 to .93 (p's < .001)], and strong internal consistency [Cronbach's α = .92][41].

Structured Clinical Interview for DSM 5 – Research Version (SCID-5-RV), module G[42]. The SCID-5-RV is a semi-structured, clinician-administered interview designed to diagnose disorders according to the DSM-5[42]. For the purposes of the present study, only module G (obsessive-compulsive and related disorders) will be utilized.

Mini-International Neuropsychiatric Interview – Version 7.0 (M.I.N.I. 7.0)[43]. The M.I.N.I. 7.0 is a reliable and valid, brief, structured diagnostic assessment administered by a clinician[43]. It covers a range of disorders, including Agoraphobia, Alcohol Dependence/Abuse, Anorexia Nervosa, Antisocial Personality Disorder, Bulimia Nervosa, Generalized Anxiety Disorder, (Hypo) Manic Episode / Bi-Polar Disorder, Major Depressive Episode, Obsessive Compulsive Disorder, Panic Disorder, Posttraumatic Stress Disorder, Psychotic Disorders, Social Phobia (Social Anxiety Disorder), Substance Dependence/Abuse, and Suicidality[43]. This instrument will be used to screen and assess comorbid disorders and co-occurring pathology.

Columbia-Suicide Severity Rating Scale (C-SSRS) Lifetime Recent – Clinical Version[48]. The C-SSRS was designed to assess the severity of suicidal thoughts and behaviors. The C-SSRS has good convergent, divergent, and predictive validity, as well as sensitivity and specificity[48]. The ideation and behavior subscales show strong convergent validity with established suicidal ideation and behavior scales. In this study, exclusion during the W0 screen is based on a Most Severe Ideation score ≥ 4 (Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts) in the past month, or any reported lifetime actual attempt, interrupted attempt, aborted attempt, or preparatory behavior for suicide[48].

Global Assessment of Functioning (GAF)[50]. The GAF is a clinician rating of 1 to 100 indicating a patient's overall level of functioning. A higher score indicates greater functioning[50].

Clinical Global Impressions Scale - Severity (CGI-S)[51]. The CGI-S is a clinician global rating of a patient's overall severity. It ranges from 1 (normal, not ill at all) to 7 (among the most extremely ill of subjects)[51].

Clinical Global Impressions Scale – Improvement (CGI-I)[51]. The CGI-I is a clinician global rating of a patient's overall symptom change. It ranges from 1 (very much improved) to 7 (very much worse)[51].

SELF-REPORT MEASURES

Body Dysmorphic Disorder Questionnaire (BDDQ)[58]. The BDDQ is a BDD screening tool with good sensitivity and specificity[15]. A BDDQ cut-off score of at least 4 (positive BDD-screening) will be used to screen eligible participants for this study[59].

Dysmorphic Concerns Questionnaire (DCQ)[44]. The DCQ is a 7-item questionnaire assessing dysmorphic concerns in which patients compare their degree of concern with that of others for each item. It has good internal consistency (Cronbach's $\alpha = .88$), and strong correlations with other measures of distress and work and social impairment[44]. A DCQ cut-off score of 9 will be used to determine a positive BDD screen following the initial internet screening, as it has been shown to correctly identify 96.4% of BDD patients and 90.6% of undergraduates[60].

Brown Assessment of Beliefs Scale (BABS)[46]. The BABS is a clinician-administered, 7-item scale designed to assess delusional beliefs and insight in a range of psychiatric disorders. Total scores range from 0 to 24, with higher scores indicating greater delusionality or lack of insight. This instrument has good internal consistency (Cronbach's $\alpha = .87$), test-retest reliability (individual item test-retest ICCs = .79-.98, median = .95), interrater reliability (ICC = .96), and sensitivity to change, and very good convergent validity[46]. There is evidence to suggest that a score of 4 on the first item (conviction) in addition to a total score of at least 18 out of 24 is an empirically supported criteria for classifying a patient's beliefs as delusional[46].

Appearance Anxiety Inventory (AAI)[45]. The AAI was designed to be a process measure that identifies cognitive processes and behaviors possibly mediating outcome in the treatment of BDD[45]. It consists of 10 self-report items, each scored on a 5-point Likert scale ranging from 0 (not at all) to 4 (all the time). The maximum total score is 40, with higher scores indicating greater frequency of a process[45]. It has good internal consistency (Cronbach's $\alpha = .86$), test-retest reliability (ICC = .87, $p < .001$), convergent validity for the measurement of appearance anxiety, and sensitivity to change[45].

Skin-Picking Scale – Revised (SPS-R)[49]. The SPS-R is a self-report measure containing 8 items evaluating skin-picking disorder severity. It has acceptable internal consistency for the total score (Cronbach's $\alpha = .83$), as well as the symptom severity (Cronbach's $\alpha = .81$) and impairment (Cronbach's $\alpha = .79$) subscales[49]. Preliminary evidence supports convergent/concurrent and discriminant validity for the 2 subscales[49].

Montgomery - Åsberg Depression Rating Scale – self-report (MADRS-S)[47]. The MADRS-S contains 9 items evaluating depressive symptoms. It has satisfactory test-retest reliability and internal consistency (ICC = .78, Cronbach's alpha = .84), and good sensitivity to change[61]. It correlates well with the Beck Depression Inventory (BDI) [$r = .87$ ($p < .0001$)][62]. Holländare, Andersson, and Engström (2010) found a high correlation between total scores on the MADRS-S paper and internet versions [$r = .84$ ($p < .001$)][63]. Additionally, their results indicated no significant main effect for administration format between paper and internet versions. The MADRS-S was found to have good discriminative validity with the physician-rated Montgomery - Åsberg Depression Rating Scale (MADRS) in detecting a score of at least 35 (severe) during a current depressive episode[61].

Client Satisfaction Inventory (CSI)[54]. The CSI contains 25 items evaluating overall satisfaction with treatment. Total scores on this measure range from 0 % to 100 % satisfied. It is reliable, with very good internal consistency (Cronbach's $\alpha = .93$), and a standard error of measurement less than 5 % of the full range of scores[52]. Additionally, there is evidence to support good content and construct validity (μ item-total $r = .57$)[54].

Working Alliance Inventory – Short Revised (WAI-SR)[55]. The WAI-SR measures 3 aspects of therapeutic alliance: agreement on the tasks of therapy, agreement on the goals of therapy, and development of an affective bond. The WAI-SR correlates well with the original Working Alliance Inventory total score (r = .94-.95), as well as other alliance measures[55].

Credibility/Expectancy Questionnaire[56]. The Credibility/Expectancy Questionnaire is divided into 2 subscales that assess beliefs about the credibility of a treatment and thoughts/feelings of treatment expectancy. It was found to have a high internal consistency across 3 studies (expectancy factor standardized α = .79-.90; credibility factor Cronbach's α = .81-.86; whole scale standardized α = .84-.85). Additionally, it had good test-rest reliability over the course of 1 week (expectancy: .82, credibility: .75)[56].

EuroQol – 5 Dimension Questionnaire (EQ-5D)[52]. The EQ-5D is used as a non-disease specific assessment of quality of life and global functioning. It measures these constructs along 5 dimensions: Mobility, self-care, main activity, pain, and mood, and has shown some evidence for construct validity and good test-retest reliability[52, 64].

Sheehan Disability Scale (SDS)[53]. The SDS is a 4-item questionnaire measuring functional impairment and disability. Items 1-3 assess the domains of disability regarding work, social life and leisure, and family life and home responsibilities. They are on a likert scale of 0 (not at all) to 10 (very severe). Item 4 measures overall impairment and is on a likert scale of 1 (no symptoms) to 5 (symptoms radically change or prevent normal work or social life). In a study conducted by Leon, Olfson, Portera, Farber, and Sheehan (1997), this instrument was found to have high internal consistency (Cronbach's α = .89) and good construct validity, with over 80 % of patients with psychiatric disorders having an elevated SDS score[53].

ICBT – EX/RP Adherence Scale (modified from the Patient EX/RP Adherence Scale (PEAS)[57]). The ICBT EX/RP Adherence Scale is loosely based on the Patient EX/RP Adherence Scale (PEAS)[57]. It is a questionnaire designed for this study measuring number of days in which EX/RP was practiced, total hours EX/RP was conducted, quality of approach behaviors (1, (Didn't do exposure, 0% approach/100% avoidance) to 7 (Most, > 90%)) and ritual prevention (0, (0% response prevention) to 7 (Most > 90%)) during planned EX/RP practice, and quality of approach behaviors and ritual prevention outside of planned EX/RP practice in the past week. It also assesses number of days and total hours in which other ICBT treatment behaviors were completed in the past week (E.g. messaging therapist and reading psychoeducational materials).

BEHAVIORAL OUTCOME DATA

Completion of core treatment modules (1-5). Modules 1-5 contain the core components of treatment (psychoeducation, EX/RP hierarchy formation, cognitive restructuring, and EX/RP practice). Patients will be granted access to subsequent modules after completion of the previous one unless otherwise clinically indicated. In order to consider a module completed, subjects must provide written text relevant to symptoms, concerns, and treatment, according to module prompts, for all module homework assignments and written worksheets, as well as monitor their SUDS levels related to EX/RP practice.

Treatment termination (as measured by the Early Termination Checklist). The Early Termination Checklist is to be completed by the therapist of each subject immediately following early discontinuation for any reason. It provides the reason(s) for ending treatment prematurely, whether related to early termination or voluntary withdrawal.

8. Project description

DESIGN

A pilot study with within-subjects repeated measures design. Analysis of primary (BDD-YBOCS[41]) and secondary outcome measures between baseline and post treatment will be conducted to determine if the treatment significantly reduced symptoms associated with BDD. In a comparable study using a Swedish-language version of BDD-NET, Enander et al. (2014) [N = 23] found effect sizes of $d = 2.01$ ($p < .01$) at post-treatment and $d = 2.04$ ($p < .01$) at a 3-month follow-up, with 82% of completers being responders (≥ 30% decrease on the BDD-YBOCS)[37]. Furthermore, Enander et al. (2015) [N = 94] had effect sizes of .95 ($p < .001$) and .87 ($p < .001$) at post-treatment and 3-month follow-up, respectively, in an RCT comparing BDD-NET to supportive therapy[40]. Given 80% power, 30 participants are needed to be able to detect an effect size of $d = 0.66$. Clinical assessments of treatment effects and feedback from participants will be utilized to improve upon the BDD-NET treatment protocol.

SELECTION, WITHDRAWAL, AND DISCONTINUATION OF SUBJECTS

INCLUSION CRITERIA

Criteria	Method of Ascertainment
1. Fluent in English	Video-conference inclusion evaluation. If English is not subject's native language, he/she will be asked to read through 1 page of non-CBT treatment text and follow prompts; assessment based on the judgment of the evaluator
2. Outpatient	Self-report
3. At least 18 years of age	Self-report
4. Positive screening for BDD on BDDQ[58]	BDDQ score ≥ 4 at initial internet screening[59]
5. Positive screen for BDD on DCQ[44]	DCQ score ≥ 9 at initial internet screening[44]
6. Primary Diagnosis of BDD according to DSM-5[1]	SCID-5 module G[42]
7. A score of at least 20 on the BDD-YBOCS at baseline[41]	BDD-YBOCS[41]
8. Signed Informed Consent	Verbal consent via video-conference and check yes to consent on secure webpage
9. Regular access to a computer with internet capabilities	BDD-NET Accessibility and Confidentiality Interview
10. Adequate skills to use the internet	Self-report, completion of initial internet screening
11. Photo ID with name and age	Shown via video-conference at inclusion evaluation

EXCLUSION CRITERIA

Criteria	Method of Ascertainment
1. Psychotropic medication changes within 12 weeks prior to treatment	Self-report
2. Completed CBT for BDD within 12 months prior to treatment (defined as at least 12 sessions of EX/RP)	Self-report
3. Current substance dependence	Alcohol Use Disorders Identification Test (AUDIT) score ≥ 8[65], Drug User Disorders Identification Test (DUDIT) score ≥ 8[66], Mini-International Neuropsychiatric Interview – version 7.0 (M.I.N.I. 7.0)[43]
4. Lifetime bipolar disorder or psychosis	Self-report and M.I.N.I. 7.0[43]
5. Severe Depression	MADRS-S[47] score ≥ 35
6. Clinically significant suicidal ideation or lifetime history of suicide attempts	Video-conference inclusion evaluation; ≥ 5 on item 9 of MADRS-S[47]; C-SSRS Lifetime Recent – Clinical Version: Recent (past month) - Most Severe Ideation score ≥ 4, or any lifetime actual attempt, interrupted attempt, aborted attempt, or preparatory behavior for suicide[48].
7. Personality disorder that could jeopardize treatment participation (e.g. borderline personality disorder with self-harm)	PD diagnosis based on self-report and video-conference inclusion evaluation.
8. Other current psychological treatment	Self-report
9. No access to a 24 hour psychiatric emergency care center	Self-report; Co-investigator will confirm access based on subject's location and contact with emergency care center
10. No specified emergency contact person or emergency contact person phone number	BDD-NET Safety Interview

CRITERIA FOR WITHDRAWAL

1. Consent withdrawal by patient.
2. High suicide risk determined by the investigators.
3. Attempt at suicide during treatment.
4. Worsening of BDD symptoms better addressed by treatment incompatible with this protocol, as determined by the investigators' clinical judgment.
5. Psychiatric hospitalization during treatment.

OTHER REASONS FOR PREMATURE DISCONTINUATION OF TREATMENT

1. Adverse event or circumstances justifying the discontinuation of treatment as determined by the investigators.

2. Protocol deviation that jeopardizes the patient's safety.
3. Patient lost to follow-up: In the event that a patient is non-responsive following treatment, the investigators are to make efforts to contact him/her, establish a reason for discontinuation of treatment, and suggest the subject participate in an end-of-study video-conference interview. If these attempts to contact the participant fail, the investigators declare him/her "lost to post-treatment assessment." The previous contact attempts should be documented in the patient's medical file.

SUBJECT LOG

- The investigators must record the reason and date of premature discontinuation of treatment both in Take Care (electronic medical records system) and on the Early Termination Checklist (Appendix Figure 1). If the investigator gives more than one reason, he/she must indicate the main reason. Specifically if a subject withdraws, his/her therapist will ask him/her the reason for withdrawal.
- In the case of treatment discontinuation, participants will be asked to participate in all remaining scheduled assessments, including all measures for weekly internet self-reports and video-conference interviews at W12, 3 month follow-up, and 12 month follow-up. If subject is unable to complete the remaining video-conference assessments, he/she will be asked to complete the same assessment measures via phone.

PROCEDURES

A flow diagram of procedures can be found in Figure 2 of the appendix.

INITIAL INTERNET SCREENING

Participants can be referred by a clinician or self-referred. Participants interested in partaking in the study first do an Internet-administered screening on an encrypted webpage using the BDDQ[58], MADRS-S[47], Alcohol Use Disorders Identification Test (AUDIT)[65], Drug User Disorders Identification Test (DUDIT)[66], DCQ[44], and AAI[45], and filling out general demographic information. Before partaking in the screening, the participant is given written information about the study (objectives, requirements for participation, etc.). Participants will be excluded from the study at this point if they: *a)* score an 8 or higher on the AUDIT, which was found to have sensitivity of 92 % and specificity of 94 % for hazardous and harmful alcohol use[65], *b)* score an 8 or higher on the DUDIT[66], which was found to correspond to impairing drug issues with 90 % sensitivity and 85 % specificity[63], *c)* score at least 5 on item 9 of the MADRS-S[47], *d)* score less than 9 on the DCQ, as 9 was determined to be an optimal cut-off when screening for BDD[44], or *e)* score less than 4 on the BDDQ, as 4 was determined to be an appropriate cut-off for a positive screening of BDD[59].

VIDEO-CONFERENCE INCLUSION/BASELINE ASSESSMENT

If the participant fulfils selection criteria, he/she is interviewed by a psychiatrist/psychologist/supervised Masters level clinician at Karolinska Institutet via video-conference. The aims of this visit are to *a)* discuss informed consent and obtain verbal consent *b)* verify diagnosis of BDD, *c)* assess symptom severity and global functioning, *d)* confirm subject's identity, *e)* evaluate English language competency, *f)* establish a safety plan while in treatment, *g)* assess subject's access to a computer, *h)* obtain subject's treatment history, and *i)* inform patient of treatment protocol. This interview includes the Protocol # XXXX BDD-NET

Informed Consent form (Appendix Figure 3), BDD-YBOCS[41], SCID-5-RV module G[42], M.I.N.I. 7.0[43], BABS[46], C-SSRS Lifetime Recent-Clinical version[48], GAF[50], clinician-rated CGI-S[51], BDD-NET Safety Interview (Appendix Figure 4), and BDD-NET Accessibility and Confidentiality Interview (Appendix Figure 5). Subjects will be evaluated for English language competency via real time conversation during the inclusion evaluation. They will also be asked if English is their native language. If it is not, they will be prompted to read through 1 page of a non-CBT treatment text and to follow prompts to further assess English language proficiency. Additionally, subjects will be asked to hold up a government-issued form of photo identification to confirm name, age, gender, and country of citizenship or residency. During this interview, subjects will be asked about their treatment history related to BDD and mental health concerns.

VIDEO-CONFERENCE INCLUSION/BASELINE ASSESSMENT FOLLOW-UP

Following the video-conference inclusion/baseline assessment, the interviewer will complete an inclusion criteria checklist and review it with a consulting psychiatrist. If the participant meets all criteria for enrolment, he/she will have a follow-up video-conference with a psychiatrist/psychologist/supervised Masters level clinician at Karolinska Institutet in order to *a)* review informed consent and *b)* orient patient to the platform. Participants entered into the study are presented with the informed consent via a secure webpage in order to check yes to consent. Through this webpage, they are then administered baseline assessment measures, including the MADRS-S[47], AAI[45], SPS-R[49], EQ-5D[52], SDS[53], and Credibility/Expectancy Questionnaire[56] prior to beginning treatment.

WEEKLY ASSESSMENTS

Weekly assessments (weeks 1-12) are done in the secure internet platform with the MADRS-S[47], AAI[45], and a form asking about involvement with concomitant medications and/or therapies. Additionally, subjects will be administered the WAI-SR[55] and the Credibility/Expectancy Questionnaire[56] during weeks 2, 4, 6, 8, 10, 12, and post-treatment; the CSI[54] at the beginning of W2 and W7 (mid-treatment), and post-treatment; and the ICBT – EX/RP Adherence Scale weeks 2-12 and post-treatment through the secure platform.

MID-TREATMENT ASSESSMENT

Subjects will be administered the BDD-YBOCS at W6 via video-conference by a psychiatrist/psychologist/Master's level clinician to assess BDD symptom severity.

POST-TREATMENT ASSESSMENT

At post-treatment, a psychiatrist/psychologist/Master's level clinician will administer the same instruments used at the video-conference screening, as well as the CGI-I[51]. Post treatment assessment will also be made via a secure webpage with the MADRS-S[47], DCQ[44], AAI[45], SPS-R[49], WAI-SR[55], ICBT – EX/RP Adherence Scale, and CSI[56]. Additionally, subjects will be asked to complete a treatment feedback form via the internet. If subjects are unable to follow-through with a video-conference evaluation (e.g. no computer access), they will be asked to complete a phone interview containing the same assessment measures.

3-MONTH FOLLOW-UP

A psychiatrist/psychologist/Master's level clinician will administer the BDD-YBOCS[41], SCID-5-RV module G[42], M.I.N.I. 7.0[43], BABS[46], C-SSRS Lifetime Recent-Clinical version[48], GAF[50],

clinician-rated CGI-S[51], and clinician-rated CGI-I[51]. Participants will complete self-ratings via the secure webpage, including the MADRS-S[47], DCQ[44], AAI[45], SPS-R[49], EQ-5D[52], and SDS[53]. If subjects are unable to follow-through with video-conference evaluation (e.g. no computer access), they will be asked to complete a phone interview containing the same assessment measures.

12-MONTH FOLLOW-UP

A psychiatrist/psychologist will administer the same instruments used at video-conference 3-month follow-up. Participants will also complete the same self-ratings as the in the 3-month follow-up via the secure webpage. If subjects are unable to follow-through with video-conference evaluation (e.g. no computer access), they will be asked to complete a phone interview containing the same assessment measures.

MEASURES TO MINIMIZE BIAS

- Prior to subject enrollment, all evaluators will be trained to a reliability criterion (intra-class correlation coefficient (ICC) of at least .85) with a gold-standard rater on the BDD-YBOCS. All video-conferencing inclusion evaluations and post-treatment and 3-month follow-up BDD-YBOCS assessments will be recorded. 10% of videos from each of these assessment points for enrolled subjects will be randomly selected using simple randomization through a true random number service (www.random.org) to be evaluated by a gold-standard rater. If at any point throughout the trial an evaluator's BDD-YBOCS ratings fall below an ICC of .85 with a gold-standard rater, he/she will be retrained to meet this criterion.
- Inclusion evaluators will complete an inclusion criteria checklist for each potential subject and review it with a consulting psychiatrist/psychologist to determine patient suitability for the study prior to enrollment.

TREATMENT

Treatment will utilize an English-language version of the BDD-NET platform employed by Enander, et al. (2015)[40], which uses a hospital server with encrypted traffic and an authentication login function to guarantee participant confidentiality. Treatment starts within seven days after inclusion and is 12 weeks long. BDD-NET incorporates the established CBT techniques of psychoeducation, self-monitoring, cognitive restructuring, exposure with response prevention (EX/RP), and a relapse prevention program. Information in the internet treatment platform is provided in text and divided into 8 modules, with the first 5 containing the core treatment components. Worksheets accompany modules to apply concepts, gather patient information related to symptoms, and monitor EX/RP exercises. Modules 1-4 focus on psychoeducation, functional behavior analyses, cognitive restructuring of meta-cognitions, and individual EX/RP hierarchy formation. Modules 5-8 focus on daily in-vivo EX/RP exercises, monitoring of subjective units of distress (SUDS) levels, and a relapse prevention program. Throughout treatment participants are assigned a psychologist with whom they can communicate through a secure online messaging system. The role of the psychologist is to support patient efforts, trouble-shoot skills applications, and give feedback on written material. Psychologists also use clinical judgement based on each patient's needs and homework completion of each module to grant participants access to subsequent modules[40]. A screen shot of an ICBT platform format can be found in Appendix Figure 6.

CONTINUATION OF TREATMENT

- Patients will not be receiving therapist support beyond W12, but are recommended to continue EX/RP in accordance with the CBT model for BDD.
- Patients will have unlimited access to the BDD-NET platform, including access to all 8 modules, written communications with therapist from W0-W12, and worksheets, but not including ongoing platform communication with a therapist, for 12 months following treatment.
- Referrals will be given to subjects who request them only if the BDD-NET research team is adequately able to provide such recommendations given the location and needs of the patient.

TRIAL TIMETABLE

Goal	Date
Ethical Approval	Jan 2016
Inclusion of First Subject	Feb 2016
Inclusion of Last Subject	Feb 2016
Treatment Completion of Last Subject, first manuscript	May 2016
Last 3-month Follow-up, second manuscript	September 2016
Last 12-month Follow-up, 1-year follow-up manuscript	June 2017

SAFETY

CLINICAL SAFETY ASSESSMENTS

- C-SSRS[48] administration via video-conference will be obtained prior to inclusion to ensure included subjects are at low risk for suicide. It will also be administered at post-treatment and 3 and 12-month follow-up assessments.
- The MADRS-S[47] will be administered via the internet weekly to monitor mood symptoms and suicidal ideations during treatment.
- All platform communications will be monitored by each subject's assigned therapist within 36 hours on weekdays and utilized in clinician risk assessment.
- The AAI[45] will be administered weekly via internet to monitor fluctuations in appearance anxiety.
- Suicidal ideation or risk, as indicated by clinician interview, internet self-report, or platform communication, will be quickly responded to according to a modified version of the Psychiatry Southwest, Stockholm's County Council suicide process (located in Figure 7 of Appendix). This protocol includes criteria for making decisions related to risk and action steps for responding to situations in which sufficient risk is indicated. The main forms of clinician response to further evaluate risk and intervene are reaching out to patients via the secure internet platform, calling, referring subjects to their designated emergency unit, coping skills coaching, developing safety plans, and coordinating services with designated emergency units. Therapists will utilize a safety checklist and structured steps for conducting and responding to risk assessments (Appendix Figure 8). Incidents of risk or suicidal behavior will be documented in patients' medical files, reviewed, and countersigned by a consulting psychiatrist.

PROCEDURES FOR MINIMIZING RISK

- *Informed Consent:* Prior to treatment, subjects will be fully informed of the study procedures, amount of time required of them, and possible benefits and risks of participating in this study. Additionally, they will be advised of the voluntary nature of their participation, their right to refuse participation, and their right to terminate participation at any time. Verbal informed consent will be obtained via video-conference, and subjects will check a box indicating consent in the secure online platform. At request, patients will be sent a paper copy of their informed consent to their mailing address. Subjects will be given the name and telephone number of the Co-Investigator.
- *Confidentiality:* Patients will be notified in the informed consent that all information they provide and all study findings will be kept confidential, with limited access to research staff. All staff involved will be informed of measures to protect patient confidentiality. All communications and handling of protected health information (PHI) will be compliant with standards set forth by the United States Federal Health Information Portability and Accountability Act (HIPAA). This act establishes a number of rules related to ethical healthcare practices and health insurance coverage, including steps for the handling of PHI. Subjects access the secure treatment platform through their internet browsers, and platform data is stored on a KI server running MySQL. This server is owned by Stockholm County Council, and protected by the Swedish data act and Swedish health care laws, as well as the Helsinki declaration. Methods of HIPAA compliance for 4 major areas of privacy are described below.
    1. *Treatment platform access:* Subjects will be given personalized usernames and passwords to access the secure treatment platform.
    2. *Transfer of data in the platform:* Internet communications between subject and therapist will be done via a secure messaging system on a confidential platform. Information entered into the platform through subjects' internet browsers will be sent to the MySQL database at the Stockholm County Council. Data will be transmitted using Secure Socket Layers (SSL) (128 bit encryption), in line with HIPAA security requirements.
    3. *Data storage:* Platform information will be stored behind a Stockholm County Council firewall. Medical records will be stored in the Stockholm County Council TakeCare electronic medical records system. Additionally, certain patient PHI will be kept in a research database on a secure KI server with password encryption.
    4. *Data auditing:* Time points in which data are accessed and parties accessing are tracked by the MySQL system. Only study personnel will have access to patient PHI.
- Video-conferences will be completed using software that is secure and compliant with standards set forth by HIPAA. Video-conference software will be provided by VSee. VSee agreed to sign a Business Associate Agreement stating that their members and employees will not have access to patient videos, will not save patient videos, can provide audit trails of parties viewing videos if asked, and will notify covered entities at KI in the event of a confidentiality breach. Videos between evaluator and patient will not operate through a VSee server, but will require a relay server, likely in patients' home countries, to connect with their computers. If relay servers were to be breached, videos would remain inaccessible, but usernames may not. Therefore, to fully protect PHI and pertinent information, subjects will be assigned a random username composed of digits

and letters that they can log into VSee with. Subjects can download a free version of VSee software and will be covered under KI's Business Associate Agreement with VSee for video-communication with designated parties at KI. Subjects will be advised that they are not covered for VSee communications with outside parties under the VSee-KI Business Associate Agreement. The VSee package used in this study is FIPS-140 level 2 compliant and utilizes 256-bit AES encryption. It also abides by the criteria established in the HIPAA Privacy and Security Rules, as well as the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009.

- Careful pre-treatment assessment to identify and exclude participants who are at high risk for suicide or adverse treatment effects.
    1. Steps for minimizing risk for participants excluded prior to enrollment:
        - Following completion of the initial internet screening, participants will be presented with a form that notifies them when and how they will be contacted by phone if they are eligible for inclusion at this point. This form also includes contact information for the research team and outlines steps for participants to take if they are experiencing acute mental health concerns or do not receive a call within 14 days indicating they are eligible at this point of the study (e.g. visiting an emergency care unit, consulting with mental health specialists). In order to proceed, participants will have to check a box stating that they understand the appropriate steps to take following the initial internet screening.
        - Participants excluded during or after the W0 evaluation or W0 follow-up video-conference will be offered mental health recommendations during these video-conferences as appropriate. Specific types of specialists will be suggested to fit mental health needs. E.g. CBT therapist, licensed psychologist, outpatient care provider with experience treating depression/alcohol abuse/substance abuse, psychiatric consultation, psychiatric evaluation at a local emergency care center. Consultation with emergency care centers and crisis counseling will be offered on the spot if the patient is in imminent risk during the W0 and W0 follow-up video-conferences.
- Monitoring any deterioration of symptoms, adverse treatment effects, and suicidal ideations, and terminating treatment when in the patient's best interest.
    1. Deterioration of anxiety and mood symptoms and suicidal ideations are measured weekly via internet self-report forms. Patients will be contacted via platform or phone call if their MADRS-S[47] item 9 score reaches 4 or higher, or if suicidal ideation or intent is otherwise indicated (e.g. via platform). Deterioration of symptoms will be monitored using the MADRS-S[47] total score and AAI[45] total score. Subjects will be contacted in the event that their MADRS-S[47] and AAI[45] scores increase by 20% of the respective total score ranges. For the MADRS-S[47], deterioration is measured by a 5-point increase, and for the AAI[45], an 8-point increase.
- Offering treatment recommendations and referrals following discontinuation of treatment or treatment withdrawal when a suitable mental health care provider can be located.

- When a subject is withdrawn for reasons related to self-injury or suicidal behaviors, the BDD-NET team will provide ongoing consultation with a designated emergency unit while he/she is stabilized. Additionally, referral options will be offered when feasible.
- Following up completion of the BDD-NET protocol with referrals when patients are interested and a suitable mental health care provider can be located.
- Staff being informed of the modified Psychiatry Southwest, Stockholm County Council's suicide process, and implementing it when suicidal ideation and/or elevated risk of suicide are present.

ADVERSE EVENTS

WHAT IS AN ADVERSE EVENT (AE)?

- Unwanted events caused by treatment (adverse treatment reactions), adverse reactions caused by the correct treatment (side effects), and adverse reactions caused by inappropriate treatment (malpractice effects), will all be considered in the assessment of adverse events.

SERIOUS ADVERSE EVENTS (SAEs)

AEs can be categorized by the investigators as either serious or non-serious. An AE is considered a SAE if it:

- Requires psychiatric hospitalization
- Results in attempt at suicide
- Results in significant deterioration of symptoms or large increase in impairment in daily routines or social or occupational functioning.

PROCEDURES FOR IDENTIFYING AND RESPONDING TO ADVERSE EVENTS

- *Assessment:* AEs will be clinician-evaluated at post-treatment and 3-month follow-up using a checklist by video-conference. AEs will also be assessed weekly using an online adverse events questionnaire. AEs will also be assessed at post-treatment and at 3-month follow-up via video-conference with a clinician.
- *Reporting:* All SAEs or situations in which sufficient risk of a SAE is indicated, as determined by the investigators, will be reported immediately to the Karolinksa Institutet IRB.
- *Responding:* AEs detected by an online weekly adverse events questionnaire will be followed up immediately with a call. In the event that treatment is likely leading to a significant deterioration of symptoms or increased risk of suicide, patients will be withdrawn from treatment. Investigators will offer mental health referrals to patients withdrawn from treatment due to AEs when suitable, appropriate, and feasible. When appropriate, investigators and clinicians will refer patients to emergency care centers and work with them to inform acute treatment.
- *Following up:* Follow-up information regarding the outcome of SAEs and actions taken will be reported to the KI IRB as soon as it's available. The investigators must ensure that actions taken in response to AEs are appropriate to the nature of the event, and that actions continue to be taken until resolution.
- *Documenting:* All AEs will be recorded in KIs TakeCare medical records system. Follow-up information describing the outcome of the SAEs and actions taken will also be recorded in patients' medical records.

QUALITY CONTROL & ETHICS

- The Karolinska Trial Alliance will monitor the study regularly.
- The study will follow Good Clinical Practice (GCP).
- It will be subject to approval of the Regional Ethics Board in Stockholm.
- It will be registered on the ClinicalTrials.gov trial registry.

9. Patient Benefit/Significance for the Health Service

Access to CBT therapists in the United States and elsewhere is limited, and individuals with BDD face substantial barriers to treatment. There is a lack of trained professionals available, face-to-face CBT comes with geographic, financial, and scheduling limitations, and people commonly have difficulty reporting BDD symptoms associated with shame. As a result, too few people with BDD symptoms are left receiving treatments that are not evidence-based, and too often ineffective or harmful. ICBT could start to address these issues, dramatically increasing patient access to evidence-based treatment for BDD. For the individual who cannot afford face to face CBT, does not have a specialized therapist close to home, or has long work hours, BDD-NET can provide a more time flexible option that can be utilized from home. For those who experience shame associated with their appearance and do not want to openly talk about their symptoms and concerns with a therapist face to face, BDD-NET provides another avenue for treatment.

Enander et al. (2014) has shown promising preliminary support for BDD-NET as an efficacious, acceptable, and feasible treatment in Sweden in an uncontrolled pilot study[37]. Enander et al. (2015) then showed BDD-NET to be superior to an active control group in an RCT[40]. If BDD-NET – English version proves to be effective, future directions for research include conducting a larger randomized controlled trial testing the efficacy of this intervention among English-speakers, globally or within certain English-speaking subpopulations and nationalities. Long term goals for this treatment are to either implement it as a part of healthcare systems and private clinics globally, or to continue to treat those with limited access to CBT through the Internet Psychiatry Unit (Internetpsykiatrienheten) at the Stockholm County Council.

10. References

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Appendix

Figure 1. Early Termination Checklist

Reason(s) for Early Treatment Termination (Check all that apply):

Specify details of early termination in comments below

Reason	Comments
Need for higher level of care (e.g. hospitalization)	
Current clinically significant suicidality and/or MADRS-S suicide item (Q9) score ≥ 5	
PI decision	
Lost to follow-up	
Experienced NSAE	
Experienced SAE	
Protocol Violation	
Life Circumstances	
Treatment No Longer Needed	
Patient Not Willing to Continue	
Time commitment too great	
Noncompliance with protocol	
Voluntary withdrawal due to not enough time/other priorities (subject report)	
Voluntary withdrawal due to treatment not right fit (subject report)	
Voluntary withdrawal due to problems with treatment itself (subject report)	Problems:
Voluntary withdrawal Other (subject report)	
Other	

Figure 2. Flow Diagram of Procedures

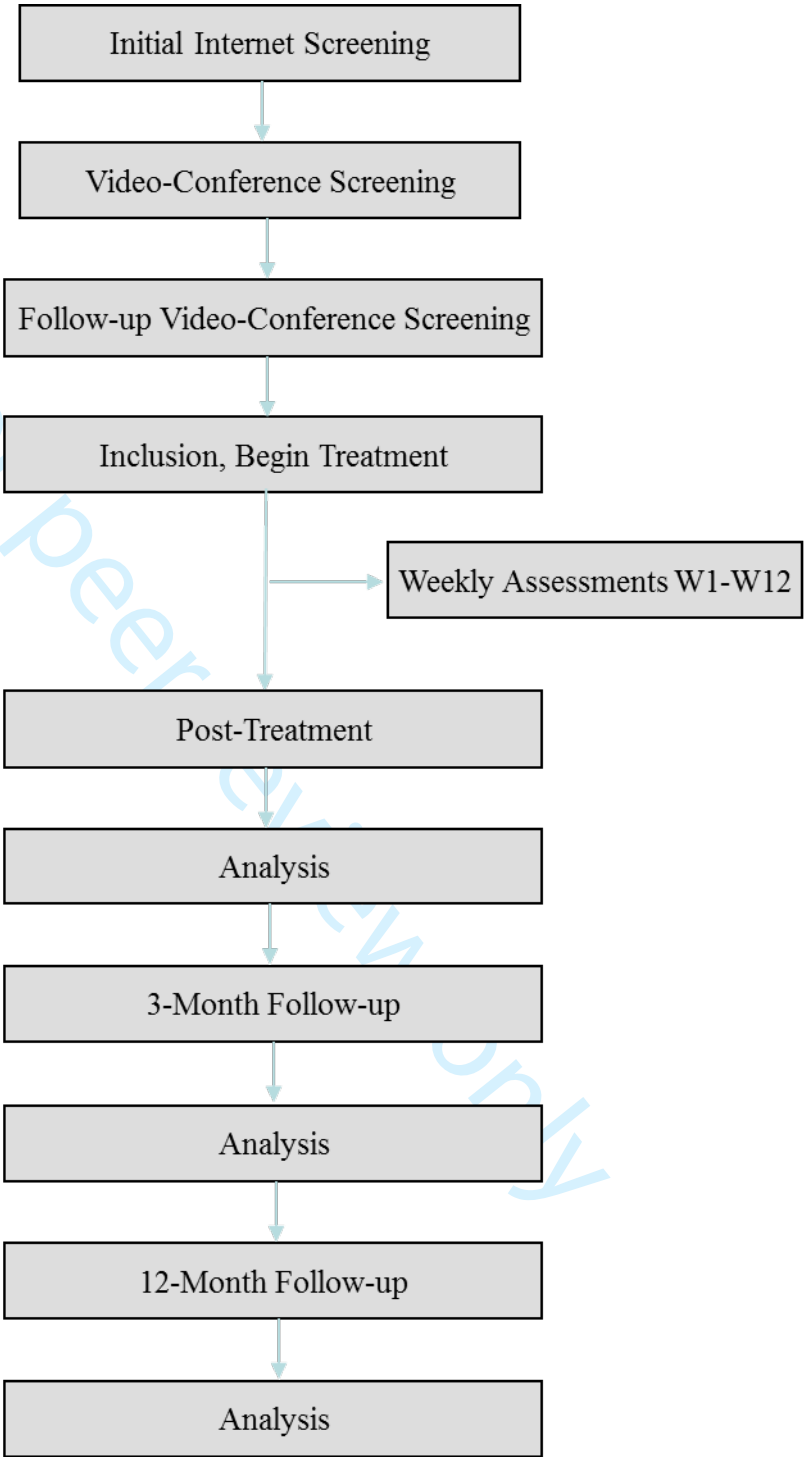


Figure 3. Informed Consent Form

Department of Clinical Neuroscience

Informed Consent Form

Therapist Guided, Internet-based Cognitive Behavioral Therapy for Body Dysmorphic Disorder – English Version (BDD-NET): A Feasibility Study

You have expressed interest in participating in this study at BDDstudy.com.

Objectives of this study
There is evidence to support that cognitive behavioral therapy (CBT) may be an effective treatment for people with body dysmorphic disorder (BDD). However, global access to specialized CBT therapists is very limited. Internet-based CBT (ICBT) has been developed, showing promising evidence as an effective treatment for BDD, but is currently only available in Sweden. Karolinska Institutet (Sweden) is conducting this study in order to investigate the efficacy and feasibility of CBT for BDD administered through a global internet platform.

Methods used and why they are used
In order to participate in the project, you must meet pre-determined criteria for body dysmorphic disorder and not suffer from other serious psychiatric problems, such as bipolar disorder. This is assessed by a diagnostic interview via video-conference where you will have to answer questions about body dysmorphic disorder and other psychiatric conditions. Video-conference assessments will generally take approximately 90 minutes. Minimum age for participation is 18 years. In order for us to be able to evaluate the results of treatment you will be given various questionnaires before, during, and after treatment. You will be contacted for video-conference evaluations once during treatment, immediately after completing treatment, and 3 and 12-months after completing treatment.

Internet treatment consists of a self-help program with therapist support via e-mail. ICBT has shown to be effective for treating a number of disorders, and the current treatment is based on proven CBT principles. The name of this treatment program is BDD-NET – English version. It is in English only and fully available through the internet.

Treatment is free of charge.

Participation
To be considered for this study, it is required that you have access to an internet connected computer, that you have the opportunity to work with the material for at least six hours per week, and that you are fully fluent in English, including reading, writing, and speaking. All participants will receive 12 weeks of treatment.

Participation is completely voluntary. You can choose not to participate and you can cancel participation at any time, for any reason, without having to disclose the reason, and without penalty. Your participation will not affect your ability to get other care. You will be able to take part in the results in the form of a scientific publication, but will not see your own results.

Duration of participation

Treatment lasts for twelve weeks. Video-conference interviews will be conducted before, during, and after the completion of treatment, as well as three and twelve months after treatment. The treatment will take about 6 hours per week.

Privacy and Confidentiality

All results of surveys, questionnaires, and interviews, as well as private or personal information provided to BDD-NET research personnel by participants in this study will be treated as confidential. The continued scientific processing of the information gathered from surveys, questionnaires, interviews, and communications with therapists will be done without identifying information of patients. The primary person held responsible for this is Associate Professor Christian Rück at Karolinska Institutet.

All information you provide is protected under Swedish secrecy and privacy regulations. Additionally, the current study has taken steps to by fully compliant with the United States federal Health Information Portability and Accountability Act (HIPAA) Privacy and Security Rules, as well as the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009. Protected Health Information (PHI) will be protected in accordance with these legislations for all forms of communication with study personnel, including all access, storage, transfer, and auditing of private and personal information.

HIPAA Privacy Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/index.html
HIPAA Security Rule: http://www.hhs.gov/ocr/privacy/hipaa/administrative/securityrule/index.html
HITECH Act of 2009:
http://www.hhs.gov/ocr/privacy/hipaa/administrative/enforcementrule/hitechenforcementifr.html

This study will utilize secure video-conference technology to conduct assessments. Please note that information transmitted with this technology is only secure for communications with designated research personnel at Karolinksa Institutet. The use of this technology to contact other parties is not protected or confidential according to HIPAA standards.

The Swedish Personal Data Act (PUL)

Study information will be housed at Stockholm County Hospital (Healthcare Provision) in ongoing computer research databases. The responsible party for this information is the registry's Data Protection Officer, who can be contacted regarding data concerns: PO Box 179 14, 118 95 STOCKHOLM; phone: +46 8-123400 00. No one except the researchers involved in this project will be able to see your personal information. If you want find out what information is held about you, you can request this in writing directly to Stockholm County Council (contact details above). You are entitled to receive this information once per year at no cost. If you identify incorrect information about you, it can be corrected. After 15 years the data Passkey will be destroyed. Then it will no longer be possible to disclose any records.

Contact for further information:

- Christopher La Lima, co-investigator and project manager, XXXX (long distance charges may apply), Email: christopher.la.lima@ki.se
- Christian Rück, principal investigator, assistant professor, Email: christian.ruck@ki.se

Consent participation

I do not wish to participate in the BDD-NET treatment study
I do wish to participate in the BDD-NET treatment study

I ..... have taken note of the above written information on the implementation of the study and what participation means. I consent to the processing of personal data as described above. I am aware that my participation is voluntary and that I, at any time, and without explanation, have the right to cancel my participation without penalty.

Location .....

Date .....

Name (Printed) .....

Signed .....

Figure 4. BDD-NET Safety Plan

BDD-NET Safety Plan

Information for 24-hour psychiatric emergency center: (look up suggested centers based on location ahead of time and call to confirm they provide such services)

Phone number:

_____

(Fill out prior to interview)

Address/Location:

_____

(Fill out prior to interview)

Information for Alternative Emergency Center if Requested:

Phone number:

_____

Address/Location:

_____

Name of Emergency Contact Person/Next of Kin who can be contacted in the event of emergency:

_____

Emergency Contact Person's phone number:

_____

Figure 5. BDD-NET Accessibility and Confidentiality Interview

BDD-NET Accessibility and Confidentiality Interview

- Do you have access to computer with internet access at least once per day for 1 hour or more?

_____

- Where is this computer located?

_____

- Do you have a private email account where you can be notified of updates in the ICBT platform? (Please write below:)

_____

- Please choose a personalized password for access to your ICBT account:

_____

Figure 6. Screen Shot of an ICBT Treatment Platform

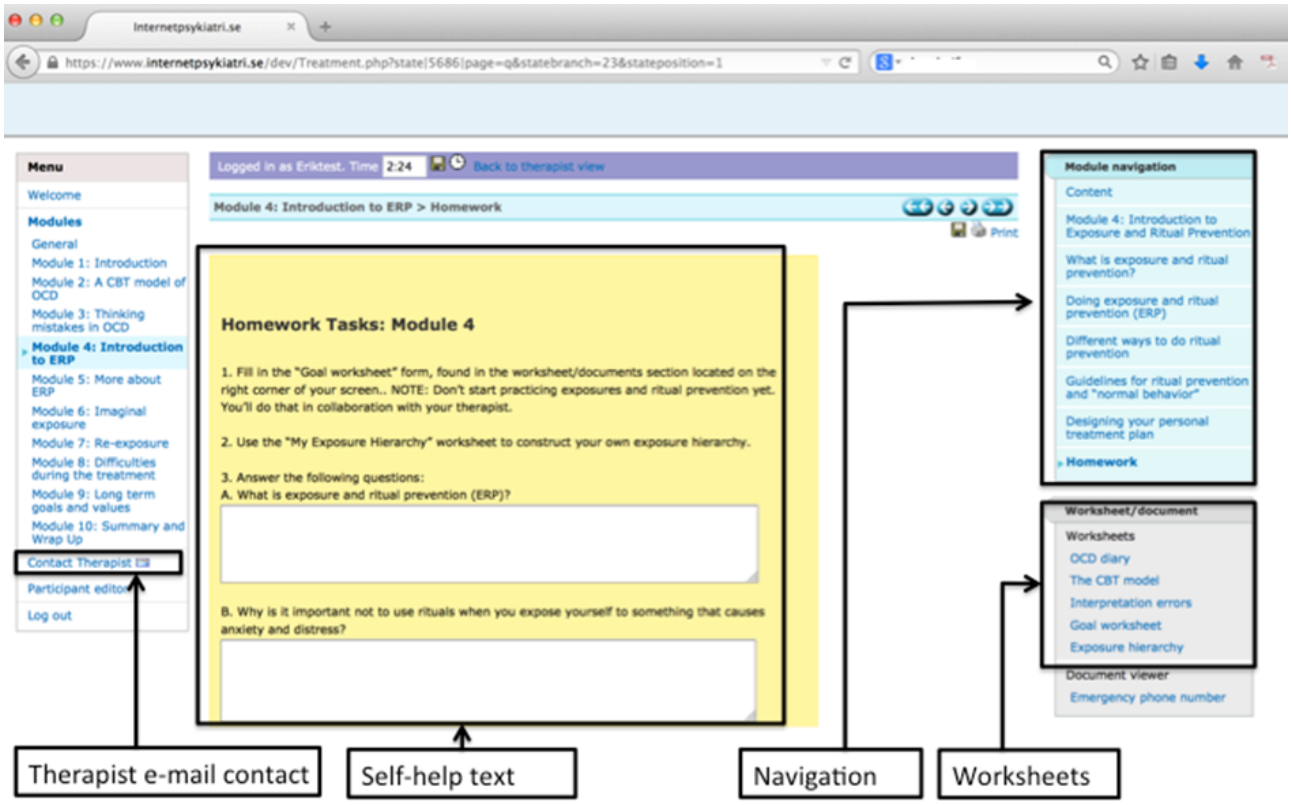
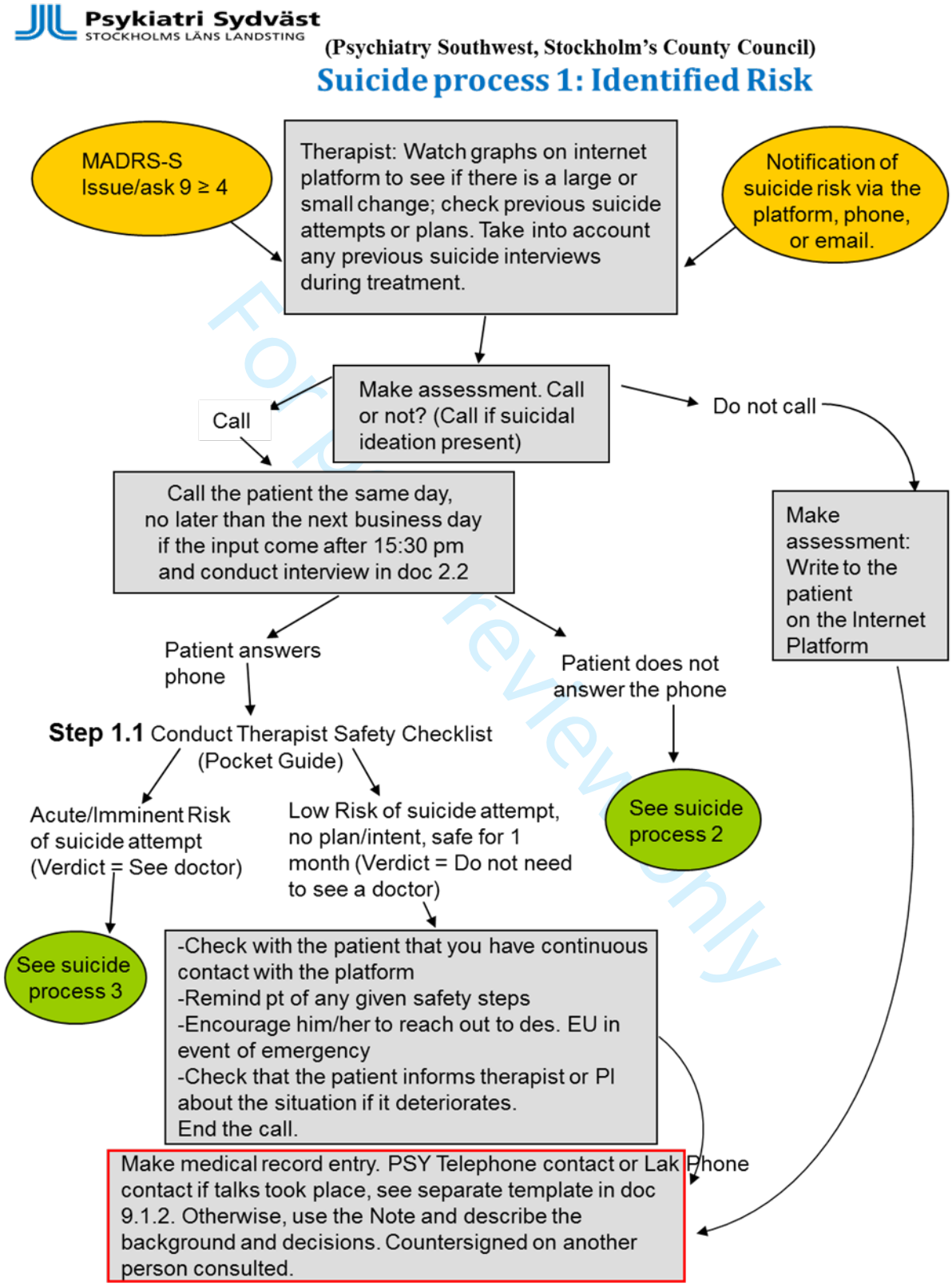


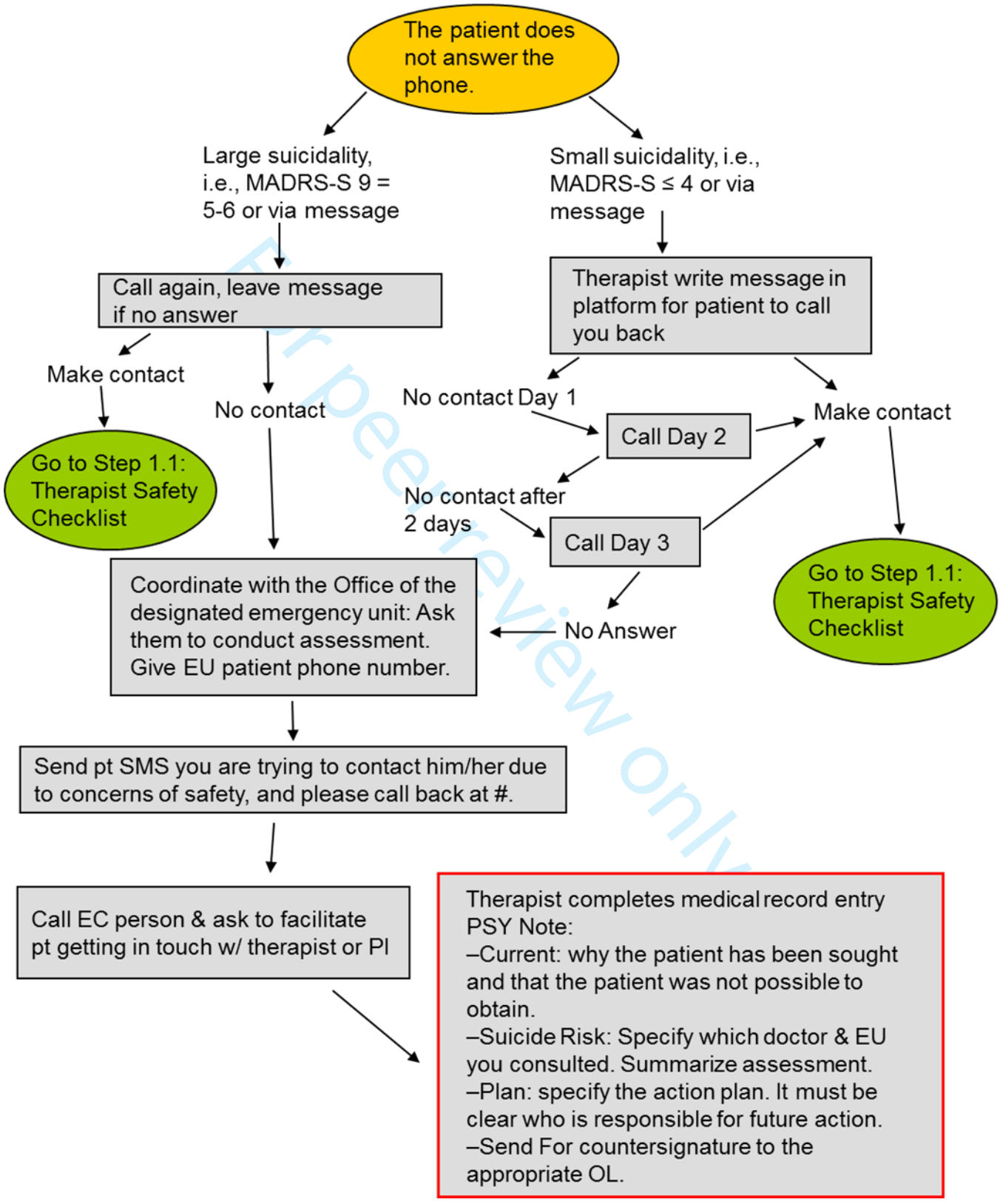
Figure 7. Suicide Process



Psykiatri Sydväst
STOCKHOLMS LÄNS LANDSTING

Suicide Process 2: Patient Doesn't Answer Phone

Responsible: Löl Cecilia Svanborg



Psykiatri Sydväst
STOCKHOLMS LÄNS LANDSTING

Suicide Process 3: Phone Contact Made, Acute Risk

Responsible: Löl Cecilia Svanborg

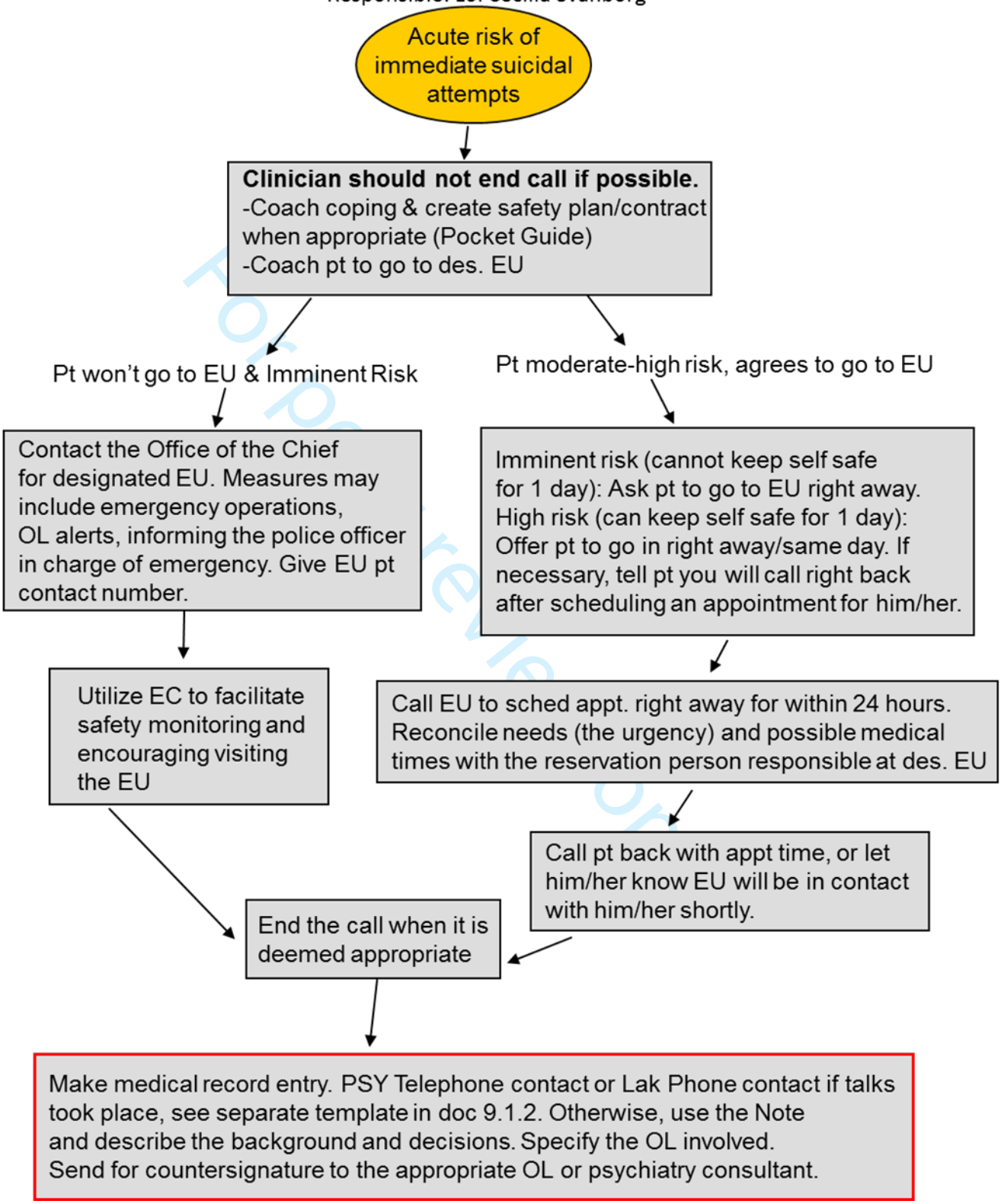


Figure 8. Therapist Safety Checklist and Tools for Crisis Coaching

STEPS

Example of suggested transition to risk conversation:

- I appreciate how difficult this problem must be for you at this time. Some of my patients with similar problems/symptoms have told me that they have thought about ending their life. I wonder if you have had similar thoughts?

When risk is indicated, follow…

SUICIDAL RISK ASSESSMENT CHECKLIST:

- Are you feeling hopeless about the present or future? _____

  If yes ask…
- Have you had thoughts about taking your life? _____

  If yes ask…
- When did you have these thoughts and do you have a plan to take your life? _____

_____

  If yes, inquire about plan: _____

_____

- Have you begun to carry out your plan? _____
- Are there any reasons you would not make a suicide attempt (pt may say not fair to family, religious values, etc.)? Look for protective factors here: _____

_____

- Have you ever had a suicide attempt? _____

  Before getting off phone, ask…
- Are you in any physical harm? _____
- Can you keep yourself safe for the next hour? _____
- " for the next day? _____
- " for the next week? _____
- " for the next month? _____

RESPONDING

If pt is **escalated and/or demonstrates imminent risk** of self-harm (SI or suicide) in same day, de-escalate and create a safer environment with the following steps:

- **Remove or secure any lethal means of self-harm** (e.g. weapons, pills)
- **Decrease isolation** (can be designated emergency contact)
- **Decrease anxiety and agitation**
    - E.g. paced breathing (5 seconds in, hold 1, 5 seconds out, or longer/shorter as pt is comfortable).
    - Progressive Muscle Relaxation (PMR)
    - Listen, allow expression of feelings
    - Being accepting and non-judgmental
    - Speak directly, openly, and matter-of-factly about suicide and your current concerns
    - Offer hope that there are alternatives available, but don't reassure that any 1 strategy will turn things around right away
- **Engage patient in a safety plan** (crisis management or contingency planning), with steps for follow-through. Can involve family members and others.
    - If pt feels the need to self-harm, what are his/her go-to coping strategies, distress tolerance skills, and replacement behaviors?
        - E.g. Paced breathing, diaphragmatic breathing, music, sensory behaviors for 5 senses (scented lotions/soaps, bubble bath, touching something textured), PMR, splash face w/ very cold water (drops heart rate to resting pace), 10 minutes of intense exercise, opposite emotion activity: e.g. watching a TV or YouTube video that is incompatible with current emotion (e.g. if sad, watch comedy), reach out to a friend or family member
    - In the future, should feelings of hopelessness or urges to self-harm or engage in suicidal behaviors occur, how will the pt keep him/herself safe?
        - Knowing who to reach out to and when: EU when formal assessment indicated or in risk of harm (*preferred bc they can work w/ pt in person), BDD-NET therapist or PI if in risk of harm, family and friends for social support.
        - When in risk of harm, keep reaching out until EU, therapist, or PI is reached, and notify therapist or PI when you can. If these parties cannot be reached right away, seek social support from emergency contact person or in appropriate ways until designated parties are reached.
    - Obtain agreement on this Safety Contract for designated amount of time depending on risk. E.g. can you agree to follow these steps for the next week?
    - You can recap the decided on contract in the platform.
    - Once safety plan and skills are agreed upon by the patient and therapist, remind patient to use the skills.
- **Reinforce all safe and healthy behaviors** of the patient along the way. E.g. you're doing a great job sticking with paced breathing and leading it on your own.

FOLLOWING CRISIS COUNSELING

- If sufficient patient risk is indicated, prompt him/her to receive a formal assessment at the designated EU. Follow procedures on Suicide Process 3.
- If patient is at low risk and not in need of EU, follow procedures on Suicide Process 1.

THERAPIST SELF-CARE

- Seek support for yourself when you feel you've been emotionally affected.

http://www.mentalhealth.va.gov/docs/suicide_risk_assessment_guide.doc
http://www.vbh-pa.com/provider/info/qual_mgt/Summary_and_Review_APA_Suicide_Guidelines_Review.pdf
http://www.apa.org/ethics/code/

Supplementary References

1 Veale D, Eshkevari E, Kanakam N, *et al.* The Appearance Anxiety Inventory: validation of a process measure in the treatment of body dysmorphic disorder. *Behav Cogn Psychother* 2014;**42**:605–16. doi:10.1017/S1352465813000556

2 Eisen JL, Phillips KA, Baer L, *et al.* The Brown Assessment of Beliefs Scale: reliability and validity. *Am J Psychiatry* 1998;**155**:102–8. doi:10.1176/ajp.155.1.102

3 Brooks R. EuroQol: the current state of play. *Health Policy* 1996;**37**:53–72.https://www.ncbi.nlm.nih.gov/pubmed/10158943

4 Rabin R, Charro F de. EQ-SD: a measure of health status from the EuroQol Group. *Ann Med* 2001;**33**:337–43. doi:10.3109/07853890109002087

5 Sheehan DV. Sheehan disability scale. In: Rush J, First MB, Blacker D, eds. *Handbook of psychiatric measures*. Washington DC: : American Psychiatric Association 2008. 100–2.

6 Sheehan DV, Harnett-Sheehan K, Raj BA. The measurement of disability. *Int Clin Psychopharmacol* 1996;**11 Suppl 3**:89–95.https://www.ncbi.nlm.nih.gov/pubmed/8923116

7 Snorrason I, Ólafsson RP, Flessner CA, *et al.* The Skin Picking Scale-Revised: Factor structure and psychometric properties. *J Obsessive Compuls Relat Disord* 2012;**1**:133–7. doi:10.1016/j.jocrd.2012.03.001

8 Simpson HB, Maher M, Page JR, *et al.* Development of a patient adherence scale for exposure and response prevention therapy. *Behav Ther* 2010;**41**:30–7. doi:10.1016/j.beth.2008.12.002

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Where to find
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 2
	2b	All items from the World Health Organization Trial Registration Data Set	See clinicaltrials.gov (NCT03517384)
Protocol version	3	Date and version identifier	See clinicaltrials.gov (NCT03517384) for version identifier
Funding	4	Sources and types of financial, material, and other support	Page 19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 19
	5b	Name and contact information for the trial sponsor	Christian Rück, MD, PhD (christian.ruck@ki.se). See clinicaltrials.gov (NCT03517384) for detailed contact information.
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Page 19

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Page 19
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Page 4
	6b	Explanation for choice of comparators	N/A
Objectives	7	Specific objectives or hypotheses	Page 6
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Page 6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	See clinicaltrials.gov (NCT03517384) for study site.
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 10

	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Pages 10-11
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Page 10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Page 7
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1 (flowchart)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Based on results from previous studies (Enander et al., 2014 & 2016). See clinicaltrials.gov (NCT03517384)
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 6
Methods: Assignment of interventions (for controlled trials)			

Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Page 6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Assessors were supervised by experienced clinicians, see Page 10. See Appendix A for detailed descriptions of study questionnaires. Data collection forms can either be found online or from the authors upon request.
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Data analyzed according to intention-to-treat principle, i.e. all available data used for individuals who discontinue treatment.
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Inspection of raw data to check that model assumptions are valid. Version control of statistical scripts to ensure reproducibility of analyses.
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Page 11
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Page 11
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Page 11
Methods: Monitoring			

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A, small scale pilot study.
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Pre-specified number of participants served as stopping point, no interim analyses.
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Page 9
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A, small scale pilot study.
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	IRB approval obtained prior to inclusion of first subject, pages 5-6
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Updates made to clinicaltrials.gov when necessary.
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 6

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Page 7
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Page 19
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Page 14
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Page 8
	31b	Authorship eligibility guidelines and any intended use of professional writers	Page 19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Page 19
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Page 6

Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.