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DOI:

[10.1016/j.cpr.2016.05.007](https://doi.org/10.1016/j.cpr.2016.05.007)

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Citation for published version (APA):

Harrison, A., de la Cruz, L. F., Enander, J., Radua, J., & Mataix-Cols, D. (2016). Cognitive-behavioral therapy for body dysmorphic disorder: A systematic review and meta-analysis of randomized controlled trials. *Clinical Psychology Review*. Advance online publication. <https://doi.org/10.1016/j.cpr.2016.05.007>

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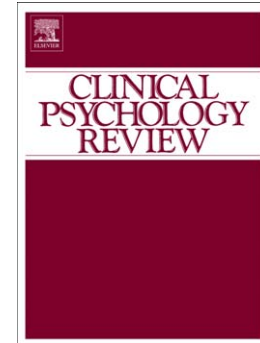
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PII: S0272-7358(15)30197-5
DOI: doi: [10.1016/j.cpr.2016.05.007](https://doi.org/10.1016/j.cpr.2016.05.007)
Reference: CPR 1529

To appear in: *Clinical Psychology Review*

Received date: 18 December 2015
Revised date: 15 April 2016
Accepted date: 28 May 2016



Please cite this article as: Harrison, A., de la Cruz, L.F., Enander, J., Radua, J. & Mataix-Cols, D., Cognitive-behavioral therapy for body dysmorphic disorder: A systematic review and meta-analysis of randomized controlled trials, *Clinical Psychology Review* (2016), doi: [10.1016/j.cpr.2016.05.007](https://doi.org/10.1016/j.cpr.2016.05.007)

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Cognitive-Behavioral Therapy for Body Dysmorphic Disorder:

A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Body dysmorphic disorder (BDD) is a chronic and disabling psychiatric disorder unlikely to remit without treatment. A systematic review and meta-analysis of randomized controlled trials (RCTs) of cognitive-behavioral therapy (CBT) for BDD was conducted, including published and unpublished trials to 26th November 2015. Primary outcomes were validated BDD measures; secondary outcomes included depression and insight. Meta-regressions were conducted to examine potential effects of variables on the primary outcome, including socio-demographic variables, comorbidity, symptom severity/duration, concomitant medication, treatment duration, and methodological quality of the RCTs. Seven RCTs (N = 299) met inclusion criteria. CBT was superior to waitlist or credible psychological placebo in reducing BDD (7 studies; delta = -1.22, 95% CI = -1.66 to -0.79) and depression symptoms (5 studies; delta = -0.49, 95% CI = -0.76 to -0.22). CBT was associated with improvements in insight/delusionality (4 studies; delta=-0.56, 95% CI=-0.93 to -0.19). Improvement in BDD was maintained after 2-4 months follow-up (3 studies; delta=-0.89, 95% CI = -1.24 to -0.54). Meta-regression analyses did not reveal any significant predictors of outcome. CBT is an efficacious treatment for BDD but there is substantial room for improvement. The specificity and long-term effects of CBT for BDD require further evaluation using credible control conditions. Additional trials comparing CBT with pharmacological therapies, as well as their combination, are warranted. Tele-care options, such as Internet-based CBT, hold great promise to increase access to evidence-based treatment for a majority of patients who need it, and should be evaluated further.

Keywords: Body Dysmorphic Disorder; Cognitive-Behavioral Therapy; Treatment; Meta-analysis; Systematic Review; Randomized Controlled Trial.

Introduction

Body dysmorphic disorder (BDD) is characterized by a persistent preoccupation with perceived defects or flaws in one's appearance, which are unnoticeable to others (American Psychiatric Association, 2013). This preoccupation leads to time-consuming rituals (e.g., mirror checking) and marked avoidance, which cause significant distress and impairment (Didie, Menard, Stern, & Phillips, 2008), and results in poor quality of life (Phillips, 2000). BDD is also linked with strikingly high suicidal behavior (Phillips, Menard, Pagano, Fay, & Stout, 2006a; Phillips, 2005; Phillips et al., 2005). Approximately one third of patients lack insight into their difficulties, which they attribute to objective physical flaws rather than being emotional in origin (Phillips et al., 2006b). BDD is relatively common, with prevalence estimates ranging from 1.7% to 2.4% (Buhlmann et al., 2010; Koran, Abujaoude, Large, & Serpe, 2008; Rief, Buhlmann, Wilhelm, Borkenhagen, & Brähler, 2006). The onset typically occurs during adolescence, with earlier onsets associated with a more insidious form of illness, a higher frequency of suicide attempts, and greater comorbidity (Bjornsson et al., 2013). High comorbidity with major depressive disorder, social anxiety disorder, and obsessive-compulsive disorder (OCD), amongst others, is frequently reported (Gunstad & Phillips, 2003).

BDD is unlikely to resolve without an evidence-based intervention (Phillips, Menard, Quinn, Didie, & Stout, 2013). Two principal forms of treatment are thought to be efficacious for BDD, namely serotonin reuptake inhibitors (SRIs) and cognitive-behavior therapy (CBT) adapted for BDD and including exposure with response prevention (ERP) techniques. Regarding pharmacotherapy, a limited number of double blind placebo-controlled trials have shown that clomipramine (relative to desimipramine; Hollander et al., 1999) and fluoxetine (relative to placebo; Phillips, Albertini, & Rasmussen, 2002) are efficacious in BDD, while SRI non-responders do not seem to benefit from augmentation with low doses of

antipsychotics (Phillips, 2005). A further relapse prevention trial has recently shown that, amongst responders to escitalopram, continuation of escitalopram was associated with lower relapse rates and longer time to relapse, compared to patients who were switched to placebo (Phillips et al., 2016).

Regarding CBT, a previous meta-analysis (Ipser, Sander, & Stein, 2009) identified three randomized controlled trials (RCT) – with available data for analyses from two studies (combined $n = 36$) – and concluded that CBT significantly reduced BDD symptoms, relative to waitlist/no treatment conditions (Weighted Mean Difference = -44.96 , 95% CI $-54.43 - -35.49$). Thus, the evidence base for CBT, upon which international guidelines like the National Institute for Health and Clinical Excellence (NICE) (National Institute for Health and Clinical Excellence, 2006) rely, was relatively weak. Since the publication of that meta-analysis, several additional RCTs of CBT for BDD have been conducted, motivating the current study.

The primary aim was to investigate the efficacy of CBT for BDD through a systematic review and meta-analysis of all published and unpublished RCTs for individuals with BDD of all ages, with primary outcomes of treatment response determined using validated measures of BDD. As a secondary aim, the effect of CBT on depressive symptoms and insight in patients with BDD was investigated. The planned analyses also included meta-regression to examine the potential effect of symptom severity, number of CBT sessions and therapy hours, comorbidities, insight, use of medication, previous cosmetic procedures, gender, age, and duration of the disorder on the outcomes studied.

Methods

The review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist and protocol outlined by the PRISMA Group (Moher, Liberati, Tetzlaff, & Altman, 2009).

Protocol and Registration

The protocol of this review was registered with the International Prospective Register for Systematic Reviews (PROSPERO), number CRD42015025513, available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015025513.

Eligibility Criteria

Studies were eligible for inclusion if they: A) Included patients with a diagnosis of BDD established using the Diagnostic and Statistical Manual of Mental Disorders (DSM) in any of its editions (DSM-III-R; (American Psychiatric Association, 1987); DSM-IV; (American Psychaitric Association, 1994); DSM-IV-TR; (American Psychiatric Association, 2000); DSM-5; (American Psychiatric Association, 2013), or the International Classification of Diseases (ICD) in its 9th or 10th editions (World Health Organisation, 1975, 1999); B) reported results of an RCT evaluating the efficacy of CBT (in all its varieties and formats) against a waitlist/no treatment, treatment as usual, other psychotherapies, or a credible psychological placebo; and C) contained sufficient data for analyses. No language or age restrictions were set.

Information Sources

Two of the authors (AH and LFC) conducted an independent systematic two-step literature search to identify relevant articles. First, EMBASE, MEDLINE®, and PsycInfo were searched to detect published and unpublished studies on CBT for individuals with BDD.

Databases were searched up to November 26th 2015. Second, manual searches of the reference lists of previous reviews and the retrieved articles were performed. Additionally, research teams in the field were contacted for unpublished RCTs, as were the contacts for the registered incomplete trials reported in the previous review (Ipser et al., 2009).

Search

The search was performed in the above-mentioned databases using the Ovid® search engine. No limits were set. The search algorithm included the terms BDD and related variants (*body dysmorphic disorder OR dysmorphophobia OR dysmorphia*), CBT and related variants (*cognitive behavio* therapy OR behavio* therapy OR cognitive therapy OR therapy OR treatment*), and RCT and related variants (*randomi* controlled trial OR controlled clinical trial OR random allocation OR double-blind method OR single-blind method OR clinical trial OR comparative study*). Results from the three blocks were combined and duplicates removed subsequently.

Study Selection

Abstracts were initially screened to ascertain whether the reported study met the eligibility criteria described above. If eligibility criteria were met, the full text article was retrieved and screened for the presence of sufficient data for analysis. Where this was not the case, the corresponding author of the article was contacted and data were requested.

The data extracted for the meta-analysis were taken from the controlled phase of the RCTs, comparing CBT with a waitlist or other control condition both during the active phase of the treatment and any follow-up points when available. Thus, if additional CBT sessions

were offered after the primary endpoints, or patients in the waitlist/control groups were offered to crossover to CBT after the primary endpoint, these were not analyzed.

Data Collection Process

Data extraction and quality assessment were independently performed by two of the authors (AH and LFC). Disagreement between the two authors concerning the extracted data was resolved via discussion until a consensus was reached. Any uncertainty regarding the extraction of data from a particular study was resolved via contact with the study authors.

Data Items

For each article, pre-treatment, post-treatment, and follow-up (when available) means, standard deviations, effect sizes of the difference in severity decrease between CBT and the waitlist/control group were recorded for both primary and secondary outcomes. The primary outcome measure was improvement in BDD symptoms, measured by either the Yale-Brown Obsessive Compulsive Scale for Body Dysmorphic Disorder (BDD-YBOCS; Phillips, Hollander, Rasmussen, & Aronowitz, 1997), or the Body Dysmorphic Disorder Examination (BDDE; Rosen & Reiter, 1996). The secondary outcomes were the improvement in depressive symptoms, measured by either the Montgomery-Åsberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979), the Beck Depression Inventory (BDI; Beck, Ward, & Mendelson, 1961), or the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983), and the improvement in insight, measured by the Brown Assessment of Beliefs Scale (BABS; Eisen et al., 1998), or the insight item of the BDD-YBOCS; Phillips et al., 1997).

Additionally, the following variables were recorded: year of publication, sample size, participant's gender, age, illness duration, use of psychoactive medication, comorbid diagnoses (confirmed by clinical interview/clinician assessment), content of the active treatment and control conditions, treatment dose (operationalized as the number of therapy sessions and therapy hours provided), percentage of responders, number of patients who dropped out of treatment during the treatment phase, and other clinical and methodological items objectively used to calculate the quality score of each study (see below).

Risk of bias in individual studies

The Cochrane Collaboration's Tool for Assessing Risk of Bias (Higgins et al., 2011) was used to explore possible bias in the individual studies. Studies were assessed across five domains: adequate sequence generation, allocation concealment, outcome assessment blinding, management of incomplete outcome data and selective reporting. Each study was scored using a three-item scale (low, high, or uncertain risk of bias).

Summary Measures

Effect size of the difference in severity decrease between groups (Cohen's delta, i.e. the standardized difference in mean decrease) was directly retrieved from the papers (Enander et al., In press; Mataix-Cols., 2015; Veale et al., 2014; Wilhelm et al., 2014) or derived from the reported statistics (Rabiei, Mulkens, Kalantari, Molavi, & Bahrani, 2012). Two other papers (Rosen, Reiter, & Orosan, 1995; Veale et al., 1996) reported the pre- and post-treatment means and variances but not the pre-post correlation, which is needed to calculate Cohen's delta. Rather than estimating a single constant correlation coefficient, the pre-post correlation coefficients were meta-analyzed using the MetaNSUE approach (Radua

et al., 2015), which yields multiple imputations of the (Fisher-transformed) unknown correlation coefficients according to the distribution parameters estimated from all other studies. Each set of imputed correlation coefficients was then used to create a set of imputed effect sizes. One study (Rosen et al., 1995) reported both the BDD-YBOCS and the BDDE; before the final analysis, the separate effect-sizes resulting from both measurements were combined into a single one (Rubia et al., 2014).

Synthesis of results

All effect sizes were corrected for small sample size (Hedges & Olkin, 1985) and separately meta-analyzed in each set of imputations using random-effects (in case of main analyses) or mixed-effects (in case of meta-regressions) models, which take both intra-study and between-study variability into account. The latter, also called “heterogeneity,” was estimated with the optimal restricted maximum likelihood (REML) technique (Viechtbauer, 2005).

Consistency of these differences was assessed: a) estimating the percentage of variability due to between-study heterogeneity (I^2) and the probability that this is statistically significantly different from 0% (so-called “Q test”, but using an F statistic due to the multiple imputations); and b) conducting leave-one-out jack-knife analyses (i.e. iteratively repeating the meta-analysis with all studies but one).

The multiple results originated from the different imputation sets were pooled taking imputation variability into account (Radua et al., In press). To allow other researchers easily follow our approach, we modified MetaNSUE software to automatically conduct meta-analysis of effect size based on imputation of correlations coefficients (software available at

<http://www.metansue.com/>; please use “referee” as username and “84bnf023” as password to access this website).

Separate meta-analyses were also conducted for depressive symptoms and for insight scores, as well as for follow-up severity, although due to the lower number of studies (five, four, and three, respectively), complementary analyses other than the jack-knife iterations were not conducted.

Drop-out analysis

Possible differences in the number of patients who dropped out prematurely from treatment were investigated between the two arms. Analyses were then repeated considering drop-out patients as non-responders, as follows. First, a meta-analysis of the (logarithm-transformed) relative risk that a patient dropped out from the CBT group (as compared to the control group) was conducted. Second, post-treatment means and variances including drop-out patients were estimated assuming post-treatment mean and variance in drop-out patients to be the same as pre-treatment mean and variance.

Risk of bias across studies

Funnel plots were used to explore the risk of publication or selective reporting bias and the possibility of missing studies. Potential bias was further assessed by meta-regressing the effect sizes by their standard errors in order to detect whether studies with larger standard errors (due to e.g. small sample sizes) report larger effect sizes.

Additional studies (meta-regression)

Meta-regressions by year of publication, number of sessions, hours of treatment, percentage of females, age, duration of illness, percentage of patients with depressive comorbidity, percentage of patients with any comorbidity, percentage of patients with delusional symptoms, percentage of patients on SSRI medication, percentage of patients who had received a previous cosmetic intervention, and quality/bias score were also conducted, correcting for multiple comparisons.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. Both first authors had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

Study selection and study characteristics

The PRISMA flowchart is shown in Figure 1. Seventeen studies out of a total 211 that were initially screened were analyzed for eligibility, leading to a total of seven studies finally included in the review, comprising 299 participants with BDD. All studies included adults with BDD except for Mataix-Cols et al., (2015) which included an adolescent sample. The majority of studies involved individually delivered face-to-face CBT sessions including ERP and differing amounts of additional cognitive techniques, compared to no treatment/waitlist (Rabiei et al., 2012; Rosen et al., 1995; Veale et al., 1996; Wilhelm et al., 2014), an enhanced waitlist (Mataix-Cols et al., 2015), or a credible psychological placebo (Enander et al., 2016; Veale et al., 2014). One study compared meta-cognitive therapy based on Wells (2000) with a waitlist control and was the only RCT that did not explicitly mention ERP (Rabiei et al.,

2012), although it included behavioural experiments. One study used a group format (Rosen et al., 1995). Another study compared Internet-delivered CBT (including ERP) with Internet-delivered supportive therapy (Enander et al., 2016) (see Table 1).

Risk of bias within studies

Table 2 provides data on the risk of bias measured using the Cochrane Collaboration's Tool for Assessing Risk of Bias.²⁹ Of the analyzed studies, four had unclear risk (Rabiei et al., 2012; Rosen et al., 1995; Veale et al., 1996; Wilhelm et al., 2014) and three were considered to have low risk of bias (Enander et al., 2016; Mataix-Cols et al., 2015; Veale et al., 2014).

Results of individual studies and synthesis of results

The final sample of the meta-analysis consisted of seven RCTs, totaling 299 individuals. At post-treatment, improvement on the primary outcome measure was significantly higher in patients receiving CBT than in patients on a waitlist or control treatment (delta = -1.22, 95% CI = -1.66 to -0.79; $p < 0.001$; Figure 2). There was moderate heterogeneity ($I^2 = 54\%$), but this did not reach statistical significance ($F = 1.3$; $p = 0.277$). Jack-knife sensitivity analyses showed that the exclusion of any single study from the analysis did not result in any meaningful differences in the overall effect size (Table 3). Controlled follow-up data was only available for three studies (Enander et al., 2016; Mataix-Cols et al., 2015; Rabiei et al., 2012). CBT remained superior to waitlist/control treatment 2 to 4 months after treatment (delta = -0.89, 95% CI = -1.24 to -0.54; $p < 0.001$).

CBT was also associated with significant improvements in comorbid depression scores and insight/delusionality, compared to waitlist/control treatments (depression delta [5

studies] = -0.49, 95% CI = -0.76 to -0.22; $p < 0.001$, Figure 3; insight delta [4 studies] = -0.56, 95% CI = -0.93 to -0.19; $p = 0.003$, Figure 4). Jack-knife analysis showed that these results were robust, that is, not driven by the effects of any single study (Table 3). Depression and insight/delusionality symptoms were not assessed at follow-up given that only two studies^{30,31} reported follow-up data.

Drop-out analysis

No differences in the number of drop-out patients were detected between the CBT and waitlist/control groups (relative risk = 1.01, 95% CI = 0.97 – 1.05; $p = 0.772$), and the results of the meta-analyses were similar when considering drop-out patients as non-responders (BDD severity: delta = -1.25, 95% CI = -1.84 to -0.65; $p < 0.001$; depression: delta = -0.37, 95% CI = -0.70 to -0.02; $p = 0.036$; insight: delta = -0.53, 95% CI = -0.85 to -0.21; $p = 0.001$).

Risk of bias across studies

Inspection of the funnel plot (Figure 5) showed potential reporting bias, though regression by standard error was not significant ($p = 0.238$).

Additional analyses (meta-regression)

None of the regressors investigated were predictive of changes in BDD severity across studies. Too few studies were available for analysis of the secondary outcome variables.

Discussion

The main finding of this meta-analysis was that CBT is an efficacious intervention for treating the main symptoms of BDD and some of its accompanying features (depressive symptoms and insight/delusionality). The meta-analysis also showed that gains are likely to be maintained at least in the short term (2-4 months after treatment). Effect sizes were large for BDD symptoms and medium for depressive symptoms and insight/delusionality, as would be expected from interventions primarily targeting BDD symptoms. The effect sizes were comparable to those reported in previous meta-analyses of CBT for OCD, a closely related disorder to BDD (Olatunji, Davis, Powers, & Smits, 2013; Öst, Havnen, Hansen, & Kvale, 2015; Ponniah, Magiati, & Hollon, 2013). Therefore, despite being perceived as difficult to treat, BDD patients can achieve meaningful symptom relief when a specialist team delivers CBT, at least under the highly controlled conditions of a clinical trial. These findings broadly support the recommendations currently included in the NICE guidelines for BDD (National Institute for Health and Clinical Excellence, 2006).

Sensitivity analyses revealed that, despite the substantial methodological heterogeneity of the trials conducted to date, which included various types of control groups (no treatment/waitlist, active controls), predominant CBT techniques (mainly ERP, cognitive therapy-based ERP, meta-cognitive therapy with no explicit ERP), methods of treatment delivery (individual, group, Internet-based), and age groups (adults, adolescents), the results were remarkably robust; exclusion of any given study at a time did not substantially modify the overall effect sizes. This suggests that CBT is probably suitable across a range of individuals and robust to the method of delivery, though the evidence for adolescents, group CBT, and Internet-based CBT is limited to single trials.

Employing the widely-used criteria suggested by (Chambless & Hollon, 1998), CBT for BDD can be said to be efficacious and possibly specific. Under this framework,

efficacious means that two or more independent research groups have found that the treatment is superior to no treatment or waitlist, and *possibly specific* means that CBT is probably superior to generic psychological treatment. We conservatively considered that only one study to date (Veale et al., 2014) employed a truly credible control treatment. Therefore, additional trials are required to test the specificity of CBT for BDD.

These generally optimistic results need to be tempered by having a closer look at the percentage of patients who achieved responder status in these trials. Four of the seven studies reported a percentage of responders using an empirically derived cut-off of at least 30% change on the BDD-YBOCS (Phillips, Hart, & Menard, 2014); 40% to 54% of patients were classified as responders, which is a substantially lower response rate than that typically obtained in CBT trials for OCD, where response rates range between 60% and 80%, depending on how response is defined (Mataix-Cols et al., 2016; Öst et al., 2015). Many participants had post-treatment severity scores in the mild/moderate range, which means that they would normally qualify for entry into a BDD clinical trial. It is also our clinical impression that many patients with BDD would drop out from treatment in naturalistic settings, compared to the ‘hot pursuit’ strategies employed in clinical trials of either CBT or pharmacotherapy. In a naturalistic 4-year prospective follow-up study of 166 patients with BDD, the cumulative probability of being in full remission was 0.20 (Phillips et al., 2013). This, coupled with the fact that many BDD patients may refuse or are unable to engage in CBT due to low insight, low mood, imminent suicide risk, or other reasons, suggests that there is significant room for improvement and that CBT may not be the best or single treatment option for *all* patients with BDD.

Clearly, there is further room to improve on the existing CBT protocols. For example, some patients may require a higher number of sessions. There is some uncontrolled trial data to suggest that adding additional sessions (beyond the standard 8-14 sessions employed in

previous trials) may lead to further improvement in BDD symptoms (Veale et al., 2014; Wilhelm et al., 2014). At present, there is insufficient data to suggest that any particular modality of CBT is superior to another. Like in OCD (Öst et al., 2015; Ponniah et al., 2013), both exposure-based and cognitive interventions may be comparably efficacious for BDD, arguably because these interventions may address the same maintaining factors (e.g., avoidance). Dismantling studies may be helpful to determine, for example, if adding cognitive techniques (such as metacognitive tools; Rabiei et al., 2012) enhances the efficacy of more purely behavioral interventions. As mentioned earlier, further studies comparing CBT with credible control treatments are needed to establish the specificity of this treatment.

Long-term follow-ups of CBT-treated BDD patients are rare (McKay, 1999; Veale, Miles, & Anson, 2015). These follow-up studies suggest that many patients maintain their gains but longer follow-up studies are needed to confirm this. The optimal strategies, pharmacological or psychological, for patients who require additional treatment after a course of CBT are unclear. Similarly, sequential trials of SSRI-resistant patients are needed to evaluate whether CBT offers additional clinical benefit, as it has been demonstrated in OCD (Franklin et al., 2011; Simpson et al., 2008). Unfortunately, no reliable predictors of outcome have been identified in BDD to guide clinical decision-making.

While the results broadly support the NICE guidelines, they do not inform clinicians as to which patients should be offered CBT and which should be offered a combination of CBT and SRI. Severity alone does not seem a reasonable criterion, since many patients included in the CBT trials were in the severe range, and severity did not reliably predict outcome. Trials comparing the efficacy and safety of CBT, SSRIs, and their combination are needed.

CBT for adolescents with BDD has only been tested in one small RCT, which compared developmentally tailored CBT with an enhanced waitlist control consisting of

written psychoeducation materials and weekly phone calls to monitor risk (Mataix-Cols et al., 2015). Since approximately 70% of patients report symptom onset during adolescence (Bjornsson et al., 2013), further trials are warranted in this age group, preferably in the incipient phases of the disorder, with the aim of preventing school failure, suicide risk, and chronicity. Unfortunately, the disorder often goes undetected in young people, as the symptoms of BDD may be mistakenly interpreted as normal developmental concerns (i.e., most teenagers worry about their appearance to some extent). More must be done to improve early detection and diagnosis of BDD in young people, particularly boys (Mataix-Cols et al., 2015).

The development and evaluation of Internet-based interventions for BDD is an emerging area that should be explored further. Data from a relatively large RCT (Enander et al., 2016) suggest that this can be a highly acceptable, safe, and efficacious way to reach a large majority of patients previously unable to access CBT. However, this may only be an option for less severe patients who have reasonably intact insight and are therefore motivated for treatment. Internet-based CBT may particularly useful in a stepped-care model, where mild to moderate cases could be offered the treatment by general practitioners, thus freeing resources for more severe and complex cases to be treated in specialized settings. Future stepped-care trials of Internet-based CBT in non-specialist settings are warranted. There is also preliminary evidence to support the efficacy of group-based CBT for BDD (Linde et al., 2015; Rosen et al., 1995), which has the potential to be cost-effective in specialist settings and should be evaluated further.

This study has several limitations. First, the studies included in the meta-analysis used a range of manualized CBT-based treatments with a degree of heterogeneity in the content and format of the CBT offered to patients. Similarly, control conditions were also heterogeneous, with most studies using a waitlist as a control, but others using a more active

control like anxiety management (Veale et al., 2014) or supportive therapy (Enander et al., 2016). However, despite this heterogeneity, jack-knife analyses indicated no significant differences in overall impact relative to the studies included in the meta-analysis, and a key common treatment component was ERP in all studies, with one exception (Rabiei et al., 2012) in which CBT was focused on developing metacognitive skills. Second, the current evidence is based on seven RCTs worldwide, including fewer than 300 patients, and conducted primarily in specialist clinics. This may potentially limit the generalizability of the results to other settings and to other populations systematically excluded from clinical trials, such as those with certain comorbidities (e.g., substance use disorders) or acute suicidal behavior. Results on secondary outcomes, namely depressive symptoms and insight/delusionality, should especially be interpreted with caution as they were based on reports in five and four studies, respectively. Given the relatively small sample, future meta-analyses of individual participant data may be helpful to further increase power and better control for potential confounds (Stewart et al., 2015). Finally, several studies failed to report on the ethnic background of their participants; over 80% of patients included in the trials that reported this information were from White backgrounds and, thus, it is unclear whether CBT is equally acceptable and efficacious in patients from ethnic minorities.

Conclusions

CBT is an efficacious treatment for BDD symptoms and associated features, but there is substantial room for improvement. The specificity and long-term effects of CBT in both adults and children/adolescents with BDD require further evaluation using credible control conditions. Additional trials comparing CBT with pharmacological therapies, as well as their combination, are warranted. Tele-care options, such as Internet-based CBT, hold great

promise to increase access to evidence-based treatment for a majority of patients who need it, and should be evaluated further.

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Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flowchart

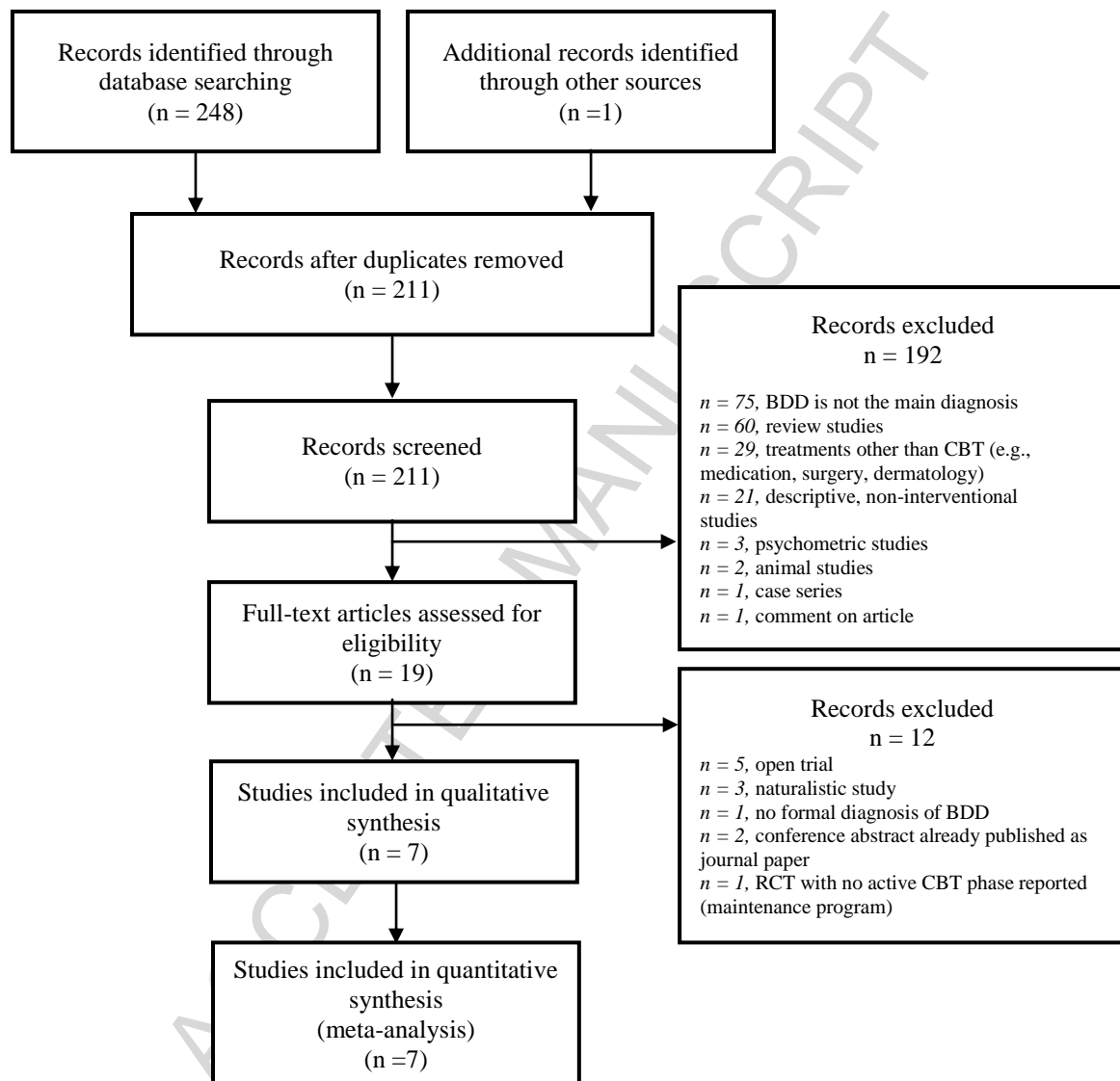
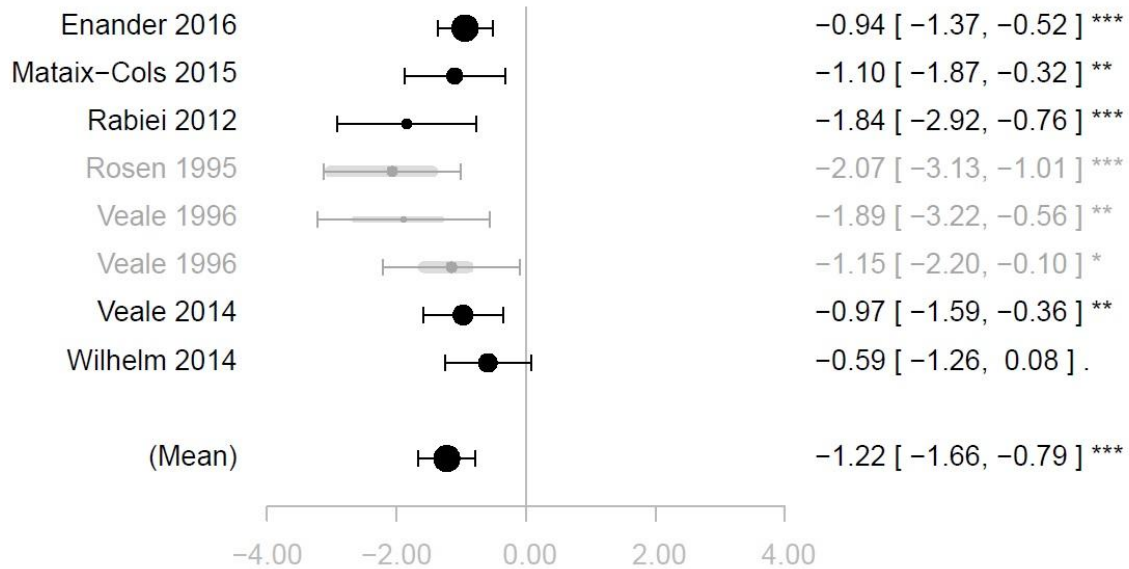


Figure 2: Forest Plot of Primary Outcome Variable: Effect of Cognitive-Behavior Therapy on Symptoms of Body Dysmorphic Disorder.



Footnote: Studies providing sufficient data to derive the exact effect size of the changes in the Body Dysmorphic Disorder Examination (BDDE) and the Yale-Brown Obsessive Compulsive Scale for Body Dysmorphic Disorder (BDD-YBOCS) are colored black, whereas studies with missing data, in which the effect size had to be imputed, are colored gray (see MetaNSUE approach in the text). Note that Veale 1996 appears twice: the upper row refers to the BDD-YBOCS score whereas the lower row refers to the BDDE score.

Figure 3: Forest Plot of Secondary Outcome Variable: Effect of Cognitive-Behavior Therapy on Symptoms of Depression.

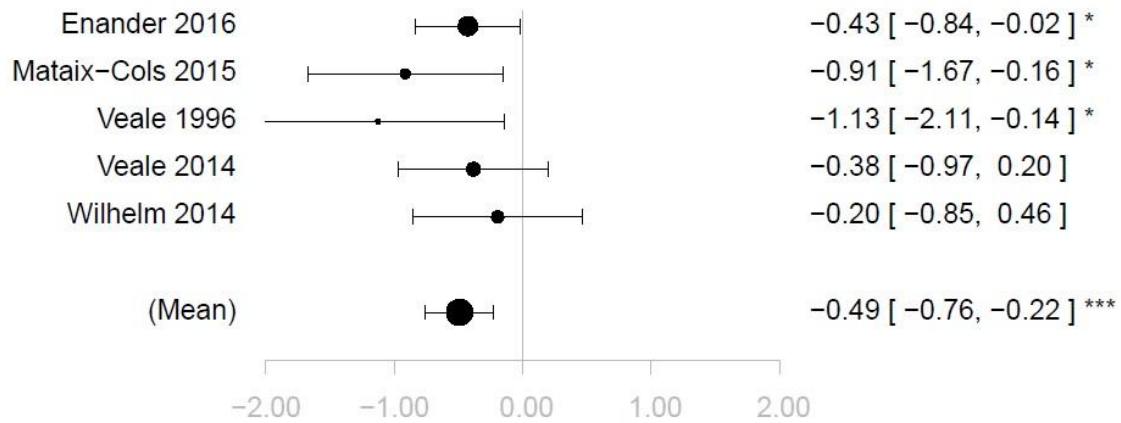


Figure 4: Forest Plot of Secondary Outcome Variable: Effect of Cognitive-Behavior Therapy on Insight/Delusionality.

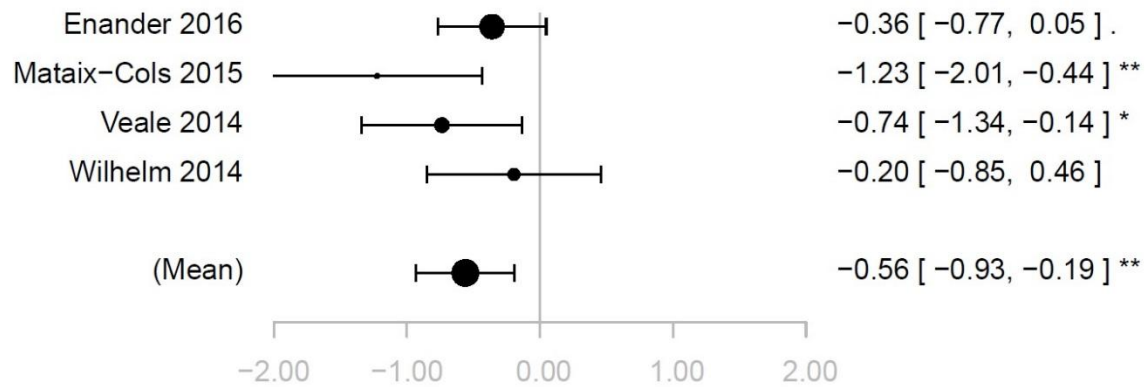
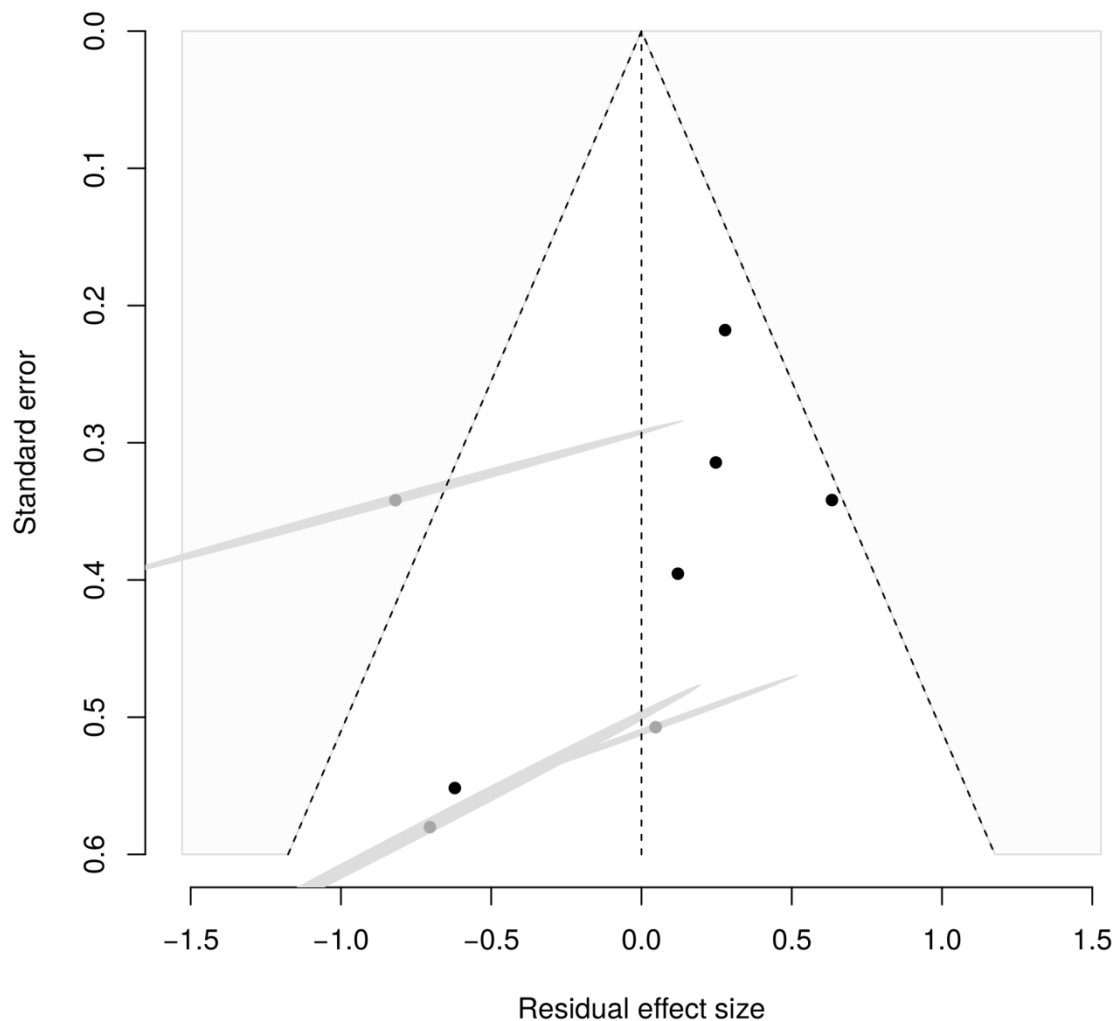


Figure 5: Funnel Plot for Primary Outcome Variable: Body Dysmorphic Disorder Severity.



Footnote: Studies providing enough data to derive the exact effect size of the changes in the Body Dysmorphic Disorder Examination (BDDE) and the Yale-Brown Obsessive Compulsive Scale for Body Dysmorphic Disorder (BDD-YBOCS) are colored black, whereas studies with missing data, in which the effect size had to be imputed, are colored gray (see MetaNSUE approach in the text). For each of the latter studies, the light gray shadow area shows the interval containing 95% of the imputed effect sizes, whereas the dark gray central point shows the mean.

Table 1: Characteristics of Studies Included in the Systematic Review.

Study	n	Setting	Active Condition	Control Condition	Primary outcome	Secondary outcome (Depressive Symptoms)	Secondary outcome (Insight)	Length of intervention	Dro p-outs	Females (%)	Mean age (years)	Length of illness (years)	Delusional (%)	Previous cosmetic procedure (%)	Presence of any comorbidities (%)	Use of SSRI (%)
Rosen et al., 1995	54	Group Face-to-face	CBT, including ERP	No treatment	BD DE	–	–	8 sessions (16 hours)	0	100	36.5	NR	NR	11	NR	NR
Veale et al., 1996	19	Individual Face-to-face	CBT, including ERP	Waitlist	BD DE BD D-YB OCS	HADS	–	12 sessions (Unknown number of hours)	NR	90	35.4	14.8	NR	NR	NR	NR
Rabiei et al., 2012	20	Individual Face-to-face	MCT	Waitlist	BD D-YB OCS	–	–	8 sessions (8 hours)	0	90	25.1	11.2	NR	NR	45	0
Wilhelm et al., 2014	36	Individual Face-to-face	CBT, including ERP	Waitlist	BD D-YB OCS	BDI	BABS	12 sessions (Unknown number of hours)	3 (CBT) 4 (Control)	61	34.8	NR	NR	NR	NR	NR
Veale et al., 2014	46	Individual Face-to-face	CBT, including ERP	Anxiety management	BD D-YB OCS	MA DRS	BABS	12 sessions (12 hours)	2 (CBT) 5 (Control)	58.7	30.0	NR	54.3	33.3	60.9	45.7
Matix-Cols et al., 2015	30	Individual Face-to-face	CBT, including ERP	Psychoeducation + weekly phone calls	BD D-YB OCS	BDI-Y	BABS	14 sessions (15 hours)	0	86.7	16.0	3.5	51.7	3.3	66.7	16.6
Enander et al., 2016	94	Individual Internet-delivered	CBT (BD D-NET), including ERP	Supportive therapy	BD D-YB OCS	MA DRS	DSM-5 insight specifier	12 weeks (Unknown number of hours)	1 (CBT)	85.1	32.6	19.0	14.9	22.3	73.4	13.8

Table 2: Indicators of Study Quality based on the Cochrane Collaboration's Tool for Assessing Risk of Bias (Higgins & Green, 2011).

Study (chronological order)	Adequate sequence generation	Allocation concealment	Blinding (outcome assessment)	Incomplete outcome data addressed	Free of selective reporting	Overall risk of bias
Rosen et al., 1995	Uncertain	Uncertain	Uncertain	Low	Low	Unclear
Veale et al., 1996	Uncertain	Uncertain	Uncertain	Uncertain	Low	Unclear
Rabiei et al., 2012	Uncertain	Uncertain	Uncertain	Low	Low	Unclear
Veale et al., 2014	Low	Low	Low	Low	Low	Low
Wilhelm et al., 2014	Low	Uncertain	Low	Low	Low	Unclear
Mataix-Cols et al., 2015	Low	Low	Low	Low	Low	Low
Enander et al., 2016	Low	Low	Low	Low	Low	Low

Table 3: Results of the leave-one-out jack-knife analysis for the primary and secondary outcomes.

Discarded study	Delta	95% Confidence Interval	p value
BDD severity			
Rosen 1995	-1.01	-1.28 to -0.75	<0.001
Veale 1996 (BDD-YBOCS)	-1.19	-1.63 to -0.76	<0.001
Veale 1996 (BDDE)	-1.24	-1.68 to -0.80	<0.001
Rabiei 2012	-1.14	-1.56 to -0.73	<0.001
Wilhelm 2014	-1.35	-1.85 to -0.84	<0.001
Veale 2014	-1.25	-1.73 to -0.77	<0.001
Mataix-Cols 2015	-1.27	-1.80 to -0.75	<0.001
Enander, in press	-1.32	-1.87 to -0.77	<0.001
BDD severity after follow-up			
Rabiei 2012	-0.88	-1.25 to -0.51	<0.001
Mataix-Cols 2015	-0.90	-1.32 to -0.49	<0.001
Enander, in press	-0.91	-1.51 to -0.32	0.003
Depressive symptoms			
Veale 1996	-0.44	-0.72 to -0.16	0.002
Wilhelm 2014	-0.55	-0.84 to -0.26	<0.001
Veale 2014	-0.52	-0.82 to -0.22	<0.001
Mataix-Cols 2015	-0.43	-0.72 to -0.15	0.003
Enander, in press	-0.55	-0.93 to -0.17	0.004
Insight/delusionality			
Wilhelm 2014	-0.68	-1.15 to -0.21	0.004
Veale 2014	-0.53	-1.06 to -0.00	0.050
Mataix-Cols 2015	-0.42	-0.72 to -0.12	0.006
Enander, in press	-0.69	-1.24 to -0.14	0.014

Highlights

- CBT for BDD is efficacious and associated with large sized symptom improvement
- Treatment gains are maintained 2-4 months after treatment
- CBT for BDD improves accompanying features (depression and insight/delusionality)
- Internet-based CBT may help improve access to evidence-based treatments for BDD
- Additional trials are required to test the specificity of CBT for BDD