Clinical Psychology Review 42 (2015) 72–82

Contents lists available at ScienceDirect

Clinical Psychology Review

Response rates for CBT for anxiety disorders: Need for standardized criteria

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HIGHLIGHTS

- Response across disorders averaged 49.5% at post-treatment and 53.6% at follow-up.
- Response rates varied as a function of the properties used to define them.
- We make recommendations for specific properties for operationalization of response.

ARTICLE INFO

Article history:
Received 16 February 2015
Received in revised form 17 July 2015
Accepted 12 August 2015
Available online 14 August 2015

Keywords:
CBT
Anxiety disorders
Response rates
Effectiveness

ABSTRACT

Full appreciation of the effectiveness of cognitive behavioral therapy (CBT) requires both effect size data and individual rates of positive response. Response rates are particularly helpful for clinicians when choosing among treatment options. However, systematic reviews on cross-study response rates have not been conducted, possibly due to the absence of a standardized metric for calculating response rates. We conducted a systematic review of the treatment outcome literature to determine overall response rates to CBT for anxiety disorders and whether current methods of defining treatment response influence overall response rates. Our database search (2000–2014) resulted in 87 studies that reported response rates and included at least one CBT condition. Results showed that overall treatment response rates across anxiety disorders averaged 49.5% at post-treatment and 53.6% at follow-up. Response rates varied significantly as a function of the properties used to define them. Measures that incorporated more than one criterion, the combination of a reliable change index with a clinical cutoff (a clinically significant change), and intent-to-treat samples yielded lower response rates at post-treatment. Blinded independent assessors yielded higher response rates than unblinded assessors. Based on previous empirical and theoretical work, we recommend that future studies use a clinically significant change index, in an intent-to-treat analysis (using a mixed-model approach), reflecting multiple modalities, and assessed by independent blinded assessors. Our results indicate that such measures are likely to reduce response rates, but may result in a less biased and more accurate representation of improvement and achievement of normative functioning.

Contents

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http://dx.doi.org/10.1016/j.cpr.2015.08.004
0272-7358/

1. Introduction

Anxiety disorders are among the most prevalent mental disorders, with close to one third of the population meeting diagnostic criteria at some point during their lifetimes (Kessler et al., 2005). Cognitive and behavioral therapies, herein referred to as CBT, are considered to be the most efficacious and empirically supported psychosocial interventions for anxiety disorders (Hofmann & Smits, 2008; Norton & Price, 2007; Tolin, 2010). Several meta-analyses show that CBT for anxiety disorders yields effects considerably higher than no-treatment, wait-list, or placebo controls (Hedges g = .73 to 1.53, depending on whether wait-list conditions are included or excluded; Butler, Chapman, Forman, & Beck, 2006; Hofmann & Smits, 2008; Norton & Price, 2007). These findings also extend to technology-supported CBT relative to waitlist conditions (Hedges g = 0.88; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010). Furthermore, CBT has been shown to be more effective than alternative psychosocial treatments, such as psychodynamic therapies (d = 0.22; Tolin, 2010).

Meta-analyses generate summary effect sizes based on group level data (treatment vs. control) and statistical tests that pool effect sizes across studies. Effect sizes are invaluable metrics for evaluating the relative size of treatment effects. However, an effect size does not indicate how many participants responded positively to treatment, nor does it indicate clinically meaningful response. Even though effect sizes can be substantial, as is the case for CBT for anxiety disorders, a significant number of individuals may remain symptomatic following CBT. Full appreciation of the effectiveness of CBT requires knowing both group level effect size data, to index statistical significance compared to control conditions, and individual rates of positive response.

By response rates, we refer to the percentage of the treatment group that was classified as "responders." Response rates are particularly helpful for clinicians when choosing among treatment options. Furthermore, response rates can inform clinical decision-making when evaluating moderators of different treatments (i.e., who responds best to one treatment versus another treatment; Meuret, Hofmann, & Rosenfield, 2010; Wolitzky-Taylor, Arch, Rosenfield, & Craske, 2012). Given the potential value of response rates, a commonly accepted metric for their operationalization is paramount. Yet, large variations exist in the way in which responder status is operationalized, including the number of dependent measures used to determine response, type of measures, and cut-offs used to dichotomize outcomes as "responder" versus "non-responder" (Kazdin, 2014). Using CBT for anxiety disorders, the goal of the current study was twofold: first, to examine the overall response rate of CBT for anxiety disorders (as well as the differential response rates for individuals with different anxiety disorders), and second, to describe and evaluate the current approaches used to determine response rates and their effects on overall outcome. By so doing, we aim to provide information that can be used for evaluating the effectiveness of a particular treatment, given the criteria used to define "response", and for formulating a standardized response rate measure which can be used to compare response rates across studies.

Eight issues regarding the measurement of response rates were investigated. First is the *number of measures* utilized, with some studies relying on a single measure and others relying on multiple measures to define responder status. Psychometrically, multiple measures (e.g., percent reduction on more than one scale) are preferred over a single measure (e.g., percent reduction on a single scale) for reasons of reliability and construct validity (Strauss & Smith, 2009). Observation of favorable treatment response rate based on only a single measure is vulnerable to inflated estimation of response rate compared to the same observation across multiple measures (Campbell & Fiske, 1959).

Second, and related to the first, is the *number of modalities* of response used to determine responder status, with some studies relying on a single modality and others relying on multiple modalities. Modalities include self-report, clinician-report, other-report, behavioral observation, and biological responses. Generally, more than one modality is preferred in order to improve measurement of a particular construct above and beyond the variance due to the particular method employed (Campbell & Fiske, 1959). Furthermore, multi-modal assessment has long been critical to the assessment of anxiety disorders, given their multifaceted nature that extends beyond subjective judgments to cognitive, behavioral and (neuro)physiological responding (e.g., Craske et al., 2009; Lang, 1971).

Third is assessment by an *independent assessor*, blinded to treatment condition. Blinding is an important safeguard against bias, especially with outcomes that are subjective (e.g., distress ratings) rather than objective (e.g., weight); effect estimates can be exaggerated when blinding is inadequate (Wood et al., 2008). Also, participants and assessors who are aware of treatment condition may overestimate response rate due to demand characteristics and desire to demonstrate improvement. For these reasons, blinding of assessors is recommended by CONSORT (2010).

Fourth is the *degree of change from baseline* that is considered sufficient to be classified as a responder. This sometimes involves a simple reduction from baseline, either as a percentage or a point reduction (e.g., 30% or 10-point reduction scores on a questionnaire). A more stringent and statistically reliable approach is the *reliable change index* (RCI; Jacobson & Truax, 1991; Maassen, 2004; our fifth measurement issue). The RCI provides an index of change in standardized units, and meeting criterion for RCI (1.96 or greater) indicates that the change is statistically significant (Jacobson & Truax, 1991). However, a limitation

of using only "degree of change from baseline" (irrespective of approach) is that some individuals, especially those more severe, may show a clinically meaningful amount of change from baseline (e.g., a drop of 50% in the amount of the day spent worrying or a RCI of 1.96 or greater), but remain symptomatic (e.g., continue to worry 40% of the day). Consequently, to the degree that response rate is used to judge how many individuals respond positively to treatment, sole reliance on change from baseline may present a somewhat inflated estimate for those individuals who remain significantly symptomatic.

Sixth is the use of a *clinical cut-off*. Such methods seek to identify whether a participant has achieved a nonclinical status (sometimes referred to as "high end state") and is based either on normative data (e.g., within one standard deviation of the mean of a healthy population; or more than two standard deviations from the mean of a clinical population) or by an absolute value on a clinical severity scale (e.g., total score of ≤3, with all individual items ≤1 on the Panic Disorder Severity Scale (Shear, Clark, & Feske, 1998) or 2 or less on a Clinical Global Improvement scale). A limitation of a clinical cut-off is that some individuals, especially those less severe, may change to a degree that is not clinically meaningful (e.g., a drop of 10% in scores on a questionnaire) and yet achieve a score below the clinical cut-off. This could lead to an inflation of response rates in those particular cases.

Hence, the most comprehensive method for determining outcome may be *clinically significant change* (Jacobson & Truax, 1991; our seventh property). This criterion combines the use of the RCI with a clinical cut-off: the magnitude of change has to be statistically reliable and end-of-treatment scores have to be in a range that renders them indistinguishable from well-functioning samples.

A final and eighth measurement issue pertains to the *selected sample* used to determine responder status: the completer sample or the intent-to-treat sample. Completer samples sometimes achieve higher effect sizes than intent-to-treat samples in meta-analyses (e.g., Hofmann & Smits, 2008), albeit not always (Mitte, 2005), possibly because some participants drop out due to an unfavorable response to treatment. The best determination of response is insured by analytic methods that account for all participants (e.g., multilevel modeling) which allow the inclusion of all patients, regardless of missing data or completer status (Hamer & Simpson, 2009).

We hypothesized that minimal or methodologically inferior methods for defining response rate (i.e., single measure, single modality of measurement, lack of independent assessors, change from baseline via either an RCI or a degree of change score alone, clinical cut-offs alone, or reliance on a completer sample) would be associated with higher response rates. By contrast, we hypothesized that clinically significant change (the interaction of RCI and clinical cut-offs) would be associated with lower response rates.

Because response rates in individual studies are likely to vary widely due to various study characteristics and type of CBT, we controlled for a number of variables whose effects otherwise might incorrectly be relegated to "error variance". These control variables were: principal anxiety disorder treated, the format in which CBT was delivered (e.g., individual or group CBT, in person or phone/teleconference/internet CBT), sample size, number of CBT sessions, attrition rate, age group studied, and whether the study was published or not. Failing to control for these differences between studies would result in inflated Type II error, and could bias results if these characteristics were correlated with any of the variables of interest.

2. Method

2.1. Data sources

Four approaches were used to identify studies. First, the first and fifth authors independently conducted extensive literature searches in PubMed, MEDLINE, and PsychInfo. They searched English-language publications on treatment outcome studies for anxiety disorders that used cognitive–behavioral therapy (CBT) from January 2000 to November 2014. The terms "random" and "open" were used to identify randomized controlled and open trials and the terms "CBT", "cognitive behavior therapy", and "cognitive behavioral therapy" were used to identify studies that used at least one form of CBT. To target specific anxiety disorders, the following terms were used: panic, panic disorder, agoraphobia, SAD, social anxiety disorder, social phobia, social anxiety, GAD, generalized anxiety disorder, generalized anxiety, PTSD, posttraumatic stress disorder, OCD, obsessive–compulsive disorder, specific phobia, and phobia. Additionally, the ProQuest Dissertation Abstracts International Database was searched for unpublished dissertations to account for publication bias that might occur from using published studies only (Ferguson & Brannick, 2012). Finally, the references of the originally identified articles, published meta-analyses, and reviews were searched. Once both authors had completed their searches, the results were compared for reliability and comprehensiveness.

2.2. Study selection and data extraction

We selected studies that met the following criteria: participants met DSM-IV criteria for an anxiety disorder; randomized controlled or open studies for a specific anxiety disorder with at least one treatment condition being CBT in the absence of medication[1]; reported response rates. Our search resulted in 87 studies.

2.3. Measurement properties of response rate

The *measurement properties* included: (1) multiple measures, even if from the same modality (e.g., more than one self-report questionnaire; one self-report questionnaire and one behavioral measure; yes = 1, no = 0); (2) multiple modalities of measures (i.e., at least one measure from at least two of the following modalities: self, clinician, other report, behavioral data, or biological data; yes = 1, no = 0); (3) independent assessor, blinded to treatment condition (yes = 1, no = 0); (4) degree of change from baseline (yes = 1, no = 0); (5) reliable change index (RCI) (yes = 1, no = 0); (6) scores fell below a clinical cut-off (yes = 1, no = 0); (7) clinically significant change (yes = 1, no = 0); and (8) intent-to-treat [ITT] sample (yes = 1, no = 0). In addition, because response rates at follow-up were assessed at different intervals, the length of the follow-up period was also analyzed.

2.4. Control variables

Control variables included: (1) principal anxiety disorder treated in the study, consisting of social anxiety disorder (SAD), generalized anxiety disorder (GAD), panic disorder (PD), posttraumatic stress disorder (PTSD), obsessive–compulsive disorder (OCD), and specific phobia (SP) (principal anxiety disorder was coded using dummy variables); (2) the format of treatment, which was categorized as: individual CBT, group CBT,[2] phone/internet CBT, CBT in combination with other therapeutic strategies (e.g., "other" supportive listening, mindfulness, stress management), behavioral therapy (as defined by study authors as treatments using exposure only), and cognitive therapy (as defined by study authors as treatments without exposure components); (3) the number of participants in each treatment condition; (4) the number of

[1] For studies testing CBT versus medication, only the response rates for CBT in the absence of medication or pill placebo were analyzed. For CBT-only studies that allowed the inclusion of medicated patients, only studies that specified having a stabilization period prior to start were included in our analyses.

[2] Behavior therapy and cognitive therapy were delivered in a group format in one study each. These studies were categorized under their type of therapy rather than as group therapy.

treatment sessions; (5) attrition percentage; 6) targeted age population (adult, senior); and (7) whether the study was published or not. Child and adolescent studies were excluded because of their small sample size.

2.5. Reliability

Measurement, treatment, and study properties were rated by two raters for each study. The first author conducted ratings for all studies, and the second, third, and sixth authors each conducted ratings on 33% of the studies to assess reliability. Any inconsistency between the two raters was resolved through group consensus.

2.6. Data analysis

The studies extracted included a wide range of methods for determining response rate (e.g., reduction from baseline alone as well as in combination with a clinical cut-off) and design properties (e.g., one versus multiple CBT conditions). Consequently, some studies contributed only one data point to the analysis, whereas others contributed several data points. Multilevel modeling (MLM), using HLM 7.0, was chosen to account for (1) the hierarchical structure of the data (e.g., multiple treatment conditions and multiple outcome measures nested within studies), (2) the varying number of reported response rates based on different methods within studies, and (3) the multiple simultaneous predictors of outcomes at every level of the data (e.g., multiple properties of response and study properties). The simultaneous inclusion of all predictors is critical to understanding whether certain properties are truly related to outcome or merely associated with outcome through their relation with other properties. Because the number of participants in the respective treatment conditions varied greatly (from 10 to 146), the data were weighted by the number of participants.[3] We used the natural log of sample size for weighting (range: 2.30 to 4.98, Mean = 3.42, Median = 3.40, SD = .56, Skewness = .20) rather than the raw sample size to mitigate the influence of large N studies. Full maximum likelihood estimation was used.

The initial analyses included only the intercept in order to ascertain the overall mean response rate and to determine if there was significant homogeneity in response rate between studies. We then investigated how our variables of interest impacted response rate (controlling for the various control variables). Predictors were entered simultaneously in the MLM equations to determine the effects of each predictor controlling for all other predictors. *Measurement properties* included the 8 methodological features for operationalizing response rate: more than one measure used, more than one modality used, an independent assessor, degree of change from baseline, a reliable change index, a clinical cut-off, clinically significant change, and ITT vs. completer samples. Length of follow-up interval was also examined as a characteristic of the follow-up response rate index. Because clinically significant change is statistically equivalent to the interaction of RCI and a clinical cutoff (the value of the interaction is 1 when RCI and clinical cutoff are 1, just like clinically significant change), RCI and clinical cutoff were centered at their means before forming the interaction. Thus, the interpretation of the main effects of these variables is their average effect across the sample.

To account for variability in treatment and study characteristics across studies, we included control variables, namely: the principal disorder treated, the format of CBT, the number of participants in a condition (log transformed because it was highly skewed), the number of treatment sessions, attrition rate (%) for the response rate measure, targeted age population, and whether the study was published vs. unpublished.

Two analyses were performed, one predicting response rate at post-treatment, and one predicting response rate at follow-up.

3. Results

Our review identified a total of 87 studies, which provided a total of 208 response rates. Eighty-four of the studies (96.5%) reported response rates at post-treatment (providing 194 response rates); 53 studies (60.9%) reported response rates at follow-up (173 response rates). The number of response rates (data points) per study ranged from 1 (in 30 out of the 87 studies) to 14 (in 1 study; Mean = 2.05, Median = 2.0). Number of treatment sessions ranged from 1 to 28 (Mean = 11.3, Median = 12), and attrition ranged from 0 to 53% (Mean = 15.6%, Median = 14.0%). Most response rates were based on intent-to-treat samples (63.0%). The most common form of treatment was individual CBT (38.9%). The means, standard deviations, and ranges of scores for the targeted study variables and response rate measures are reported in Table 1.[4]

3.1. Predictors of response rate at post-treatment

The overall mean (weighted) response rate at post-treatment was 49.5% (range: 0–100%). The response rates for the different anxiety disorders are listed in Table 1. The variance in response rates across studies was significant, χ^2 (83) = 174.2, $p < .001$, indicating that response rate was heterogeneous across studies and that there was substantial variability that could be explained by our MLM model.

3.1.1. Measurement properties as predictors of short-term outcome

The measurement properties of response rate were not highly related to one another. Of the 21 inter-correlations, most (13) were nonsignificant, only three were greater than .30, and only one was greater than .50 (i.e., multiple measures and multiple modalities, $r = .78$, $p < .001$).

Our full MLM model (including the measurement properties and control variables as predictors) accounted for 54.6% of the overall variability in response rate across the 194 reported post-treatment response rates. Controlling for all other properties, studies using two or more measures to operationalize response rate had a 16% lower rate of "response" than studies that used one measure only, $b = -15.8$, 95% CI: [−27.7, −3.8], $t(94) = -2.59$, $p = .011$. Also associated with worse outcome were studies using intent-to-treat versus completer analyses (about 8% less), $b = -7.91$, 95% CI: [−14.9, −0.9], $t(94) = -2.21$, $p = .029$. Use of multiple modalities (p = .390), degree of change from baseline ($p = .604$), reliable change index ($p = .113$), and clinical cut-off ($p = .797$) were not related to outcomes. However, the interaction of the use of a reliable change index *and* a clinical cut-off (clinically significant change), was significant, $b = -28.0$, 95% CI: [−44.5, −14.5], $t(94) = 4.08$, $p < .001$. In studies using both indices in combination, response rates were 28% lower than the sum of the effects of each factor individually. In contrast, studies that used independent assessors yielded 12% better outcomes, $b = 12.4$, 95% CI: [5.9, 19.0], $t(94) = 3.71$, $p < .001$.

3.1.2. Total number of properties

We also investigated whether the *total number of properties used to determine response rate* (out of the 8 properties) was related to outcome (e.g., does use of multiple measures plus independent assessors plus clinical cut offs affect outcome relative to multiple measures alone). Because the "number of properties met" was multi-collinear with the 8 response rate properties, we deleted the individual response rate properties and reran the analyses using total number of properties

[3] Sample size weighting, rather than inverse variance weighting, was chosen because there were 4 cases in which the inverse variance was either infinity (because response rate was either 0 or 100) or over 1000 (because response rates were either very small or very large). Using inverse variance weighted analyses (imposing an upper limit on the inverse variance) or unweighted analyses did not result in different outcomes.

[4] The response rates reported in Table 1 are the raw, unadjusted, unweighted response rates reported by each study. Rates may differ from rates derived from the model which adjusted for sample size and controlled for the other predictors.

Table 1
Prevalence and response rate associated with each property.

Variable	% of studies or mean (SD)[a] of the property or characteristic	Response rate post-treatment[b]	Response rate follow-up[b]
Measurement properties of response rate			
More than one measure[c]	21.6%	43.5% vs. 50.7%	49.8% vs. 51.3%
Multiple modalities[c]	14.4%	42.5% vs. 50.3%	48.5% vs. 51.6%
Independent assessor[c]	45.2%	52.4% vs. 46.3%	55.9% vs. 46.6%
Change from baseline[c]	90.9%	49.6% vs. 43.9%	51.1% vs. 50.0%
Reliable change index[c]	31.1%	44.5% vs. 51.1%	44.4% vs. 53.5%
Use a clinical cut-off[c]	70.7%	46.7% vs. 54.4%	50.5% vs. 52.1%
Intent to treat[c]	63.0%	49.0% vs. 49.3%	52.7% vs. 47.8%
Treatment properties			
Individual CBT	38.9%	48.8%	49.9%
Group CBT	21.6%	44.5%	44.7%
Phone/teleconference/internet	14.9%	53.8%	62.1%
Combined CBT[d]	6.7%	54.3%	58.0%
Behavior therapy	11.5%	50.9%	44.5%
Cognitive therapy	6.3%	47.5%	49.6%
N for the condition	36.1 (23.3)	N/A	N/A
Number of sessions	11.3 (4.6)	N/A	N/A
Attrition rate	15.6% (12.2%)	N/A	N/A
Study properties			
Social anxiety disorder	11.5%	45.3%	55.5%
Generalized anxiety disorder	21.8%	47.0%	47.7%
Panic disorder	31.0%	53.2%	59.3%
Posttraumatic stress disorder	11.5%	59.0%	62.6%
Obsessive compulsive disorder	21.8%	43.3%	35.6%
Specific phobia	2.3%	52.7%	N/A
Adult	90.8%	49.6%	51.5%
Late-life	9.2%	44.9%	46.3%
Published[c]	95.4%	49.7% vs. 35.0%	N/A
Short term follow-up (1–3 months)	24.9%	N/A	43.7%
Medium term follow-up (6 months)	43.9%	N/A	53.9%
Long term follow-up (9–15 months)	22.5%	N/A	51.0%
Very long follow-up (22–84 months)	8.7%	N/A	56.1%

[a] Percent of the treatment conditions or studies possessing the property. Response rate properties are not mutually exclusive; therefore, their percentages do not add up to 100.
[b] Response rates reported here are the raw, unadjusted, unweighted response rates, not controlling for differences between studies on any of the other variables.
[c] For dichotomous predictors, mean response rate is listed for those conditions with the characteristic (e.g., intent to treat) vs. those without the characteristic (e.g., not intent to treat).
[d] CBT combined with placebo/parent involvement/mindfulness/stress management.

(possible range: 0–8; observed range 1–8, Mean: 3.67, Median: 4.0) as a predictor of response rate, but still controlling for the control variables. Number of properties was negatively related to outcome at post-treatment, $b = -2.85$, 95% CI: [−5.6, −0.1], $t(101) = 2.00$, $p = .048$, such that the response rate generally decreased about 3% per property.

3.1.3. Control variables

In the primary analysis (that included measurement properties and the control variables), results for the control variables indicated that larger sample sizes were related to lower outcomes, $b = -10.97$, 95% CI: [−16.7, −5.3], $t(94) = -3.75$, $p < .001$, as were higher rates of attrition, $b = -.40$, 95% CI: [−.69, −.11], $t(94) = -2.67$, $p = .009$. Control variables that were not significantly related to response rate were: principal anxiety disorder (SAD, GAD, PD, PTSD, OCD, SP, $p = .416$), treatment format (individual CBT, group CBT, phone/internet CBT, CBT + other, behavioral therapy, and cognitive therapy, $p = .623$), number of sessions in the treatment protocol ($p = .066$), published vs. unpublished studies ($p = .084$), and age of targeted population (adult vs. late-life; $p = .804$).

3.2. Predictors of response rate at follow-up

Analyses of follow-up data were conducted in the same manner as those for the post-treatment data. However, the timing of the follow-up assessment varied greatly among studies, from 1 month to 84 months. Thus, length of follow-up was added as a predictor of response rate at follow-up. Because it was unknown how it would affect response rate, length of follow-up was not assumed to be linearly related to outcome. Rather, it was coded into four categories, and response rates in these categories were allowed to vary unconstrained. The categories were: short-term follow-up (1–3 months, n = 43 data points), medium-term follow-up (6 months, n = 76), long-term (9–15 months, n = 39), and very long-term (22–84 months, n = 15), which were dummy coded with the short-term follow-up as the reference category.

Of the 87 studies included in our investigation, 61% (53) reported response rates (173 total) at one or more follow-up intervals. An initial analysis showed that the overall mean response rate at follow-up was 53.6% (range: 0–100%). Variance in response rates across studies was significant, $\chi^2(52) = 183.9$, $p < .001$, indicating that the response rate at follow-up was heterogeneous across studies.

3.2.1. Measurement properties as predictors of long-term outcome

Our full MLM predictor model accounted for 69.1% of the overall variability in response rate across the 173 reported post-treatment response rates. Consistent with the results at post-treatment, at follow-up, ITT samples were related to a 13% lower response rate than completer samples, $b = -12.6$, 95% CI: [−21.1, −4.1], $t(101) = 2.89$, $p = .005$, as was the use of two or more measures (by 15%), albeit this result did not reach conventional levels of significance, $b = -15.1$, 95% CI: [−32.6, 2.4], $t(101) = 1.69$, $p = .093$. Also consistent with post-treatment data, an independent assessor was associated with a 16% better outcome, $b = 15.6$, 95% CI: [7.1, 24.1], $t(101) = 3.60$, $p < .001$. None of the other measurement properties were significantly related to outcome at follow-up.

Longer follow-up periods (6 months+) were generally associated with higher response rates than shorter (1–3 months) follow-ups. Specifically, response rates for medium-term follow-ups (6 months) were slightly, but not-significantly, higher (8.5%) than for short-term follow-ups (1–3 months), $b = 8.5$, 95% CI: [−0.3, 17.3], $t(101) = 1.90$, $p = .060$. Long (9–15 months) and very long-term (22–84 months) follow-up response rates were significantly higher than short-term follow-ups, $b = 12.8$, 95% CI: [3.3, 22.3], $t(101) = 2.64$, $p = .010$, and $b = 15.2$, 95% CI: [2.7, 27.7], $t(101) = 2.38$, $p = .019$.

3.2.2. Total number of properties

The number of properties used to determine response rate (out of the 8 properties) was not a significant predictor of outcome at follow-up ($p = .123$).

3.2.3. Control variables

Results for the control variables at follow-up were comparable (but not identical) to their effects at post-treatment. Both larger sample sizes and higher attrition rates were related to significantly lower long-term outcomes, $b = -18.0$, 95% CI: [-25.1, −10.9], $t(101) = -4.97$, $p < .001$ and $b = -.52$, 95% CI: [−0.9, −0.2], $t(101) = -2.92$, $p = .004$, respectively. Unlike post-treatment, follow-up outcome did vary by principal diagnosis, χ^2 (4) = 9.99, $p = .041$. Treatments for PTSD and PD had 20% higher response rates than treatments for OCD (the disorder with the lowest follow-up response rate), $b = 20.3$, 95% CI: [3.8, 36.8], $t(47) = -2.41$, $p = .020$, and $b = 20.2$, 95% CI: [5.9, 34.5], $t(47) = -2.76$, $p = .008$, respectively. However, treatment outcomes for GAD, $b = 7.7$, 95% CI: [−8.0, 23.4], $t(47) = 0.96$, $p = .340$ and SAD, $b = 17.3$, 95% CI: [−0.3, 35.9], $t(47) = -1.93$, $p = .059$, did not significantly differ from those for OCD. Mean follow-up response rates for each disorder are displayed in Table 1.

Control variables that were not related to response rate at follow-up were: number of treatment sessions ($p = .179$) and age of target population ($p = .526$). None of the unpublished studies included a follow-up.

4. Discussion

Response rates serve as an invaluable tool for judging the clinical effectiveness of treatments beyond the statistical significance offered by meta-analytic effect sizes. However, research and cross-study comparisons have been hampered by lack of standardization of the measures and methods used to operationalize response rate. The focus of this review was to determine how currently used variations in methods to define response to CBT for anxiety disorders influence the reported outcomes. To accomplish this, all randomized-controlled and open trials from 2000-2014 reporting response rates for a form of CBT for anxiety disorders were examined. The overall response rate across all anxiety disorders was lower than expected, with post-treatment rates averaging 49.5% and long-term rates averaging 53.6%. Post-treatment rates for specific anxiety disorders were 0%–86% for OCD, 10%–97% for PD, 3%–86% for GAD, 4%–80% for SAD, 8%–100% for SP, and 28%–88% for PTSD. Long-term rates were 0%–64% for OCD, 1%–100% for PD, 3%–86% for GAD, 19%–89% for SAD, and 13%–93% for PTSD (none of the SP studies reported long-term response rates). The response rates varied substantially from study to study. Our models were able to account for a substantial proportion of this variability, explaining almost 55% of the post-treatment variability, and about 69% of the variability at follow-up in reported response rates.

In line with our expectations, several of the measurement properties were related to outcome. In particular, intent-to-treat samples yielded lower post-treatment and follow-up response rates than completer samples (by 8% and 13%, respectively). One possible reason is that participants who are not responding well to treatment terminate treatment prematurely. In support, we found that higher rates of attrition were associated with lower response rates at post and follow-up, which suggests that more participants drop from studies in which treatment is less effective (i.e., lower response rates). Thus, we encourage researchers to report response rates for intent-to-treat samples in order to avoid possible inflation of estimates. Earlier methods for deriving intent-to-treat response rates included carrying forward the last observation point. However, this approach may underestimate response rates because individuals whose last observation point is carried forward are not exposed to the full treatment (Hamer & Simpson, 2009). Hamer and Simpson (2009) suggest mixed effects models, which include the full intent-to-treat sample, and which can provide unbiased estimates of outcomes in the presence of missing data, if that data is missing at random. However, data is not always missing at random. Thus, the most accurate estimates are likely to come from mixed models that include the entire sample and which model missing data is missing not at random (Enders, 2011).

In addition, response rates were generally lower (16% less at post and 15% less at follow-up) when using more than one measure to define response rate. Multiple measures of the same construct enhance reliability of the construct and reduce the criticism of method variance (Campbell & Fiske, 1959), and multiple measures are important for constructs that are complex, like response to treatment. For these reasons, we recommend using multiple measures to define response rate. Although using multiple measures is likely to lower response rates, doing so may more accurately assesses full, instead of partial, response to treatment, and therefore reduce overestimates of response rates. As indicated by our findings, using measures from multiple modalities (e.g., self-report and behavioral observation) does not itself influence response rate. Nonetheless, assessment across multiple modalities captures the multifaceted nature of anxiety disorders that spans self-report, cognitive, behavioral, and (neuro)physiological features (see Craske et al., 2009) that would be missed by reliance on a single modality of assessment. As noted by Strauss and Smith (2009), individual variation on a single score lacks meaning when examining constructs with multiple dimensions. At the same time, we recognize the difficulties multimodality measurement can pose such as discordant or desynchronous scores across modalities (Rachman & Hodgson, 1974). Techniques such as multivariate mixed models (see, for example, Hox, 2010) or SEM (using a complex measurement model to investigate multiple possible latent outcomes) may be helpful to address such situations.

Neither change from baseline nor clinical cut-offs, as independent measurement properties, was associated with outcome. However, as hypothesized, clinically significant change (the combination of a reliable change index *and* a clinical cut-off) was associated with lower response rates (by −28%). Note that this effect represents the interactive, synergistic effect of the combination of reliable change and a clinical cutoff, so the effect (−28%) indicates how the combination of these two factors impact response rate over and above (and in addition to) the sum of the separate main effects of these two factors. The combination of these two indices addresses the limitations of each by itself, those being that some individuals may achieve reliable change but remain clinically anxious because of high baseline levels of anxiety, whereas others may have improved only slightly due to low baseline levels of anxiety. For these reasons, we recommend the clinically significant change method (Jacobson & Truax, 1991) to insure that participants achieve both substantial reductions in symptoms *and* levels of post-treatment outcome that are subclinical, even though so doing lowers response rates. Using both indices also complies with our prior recommendation to use multiple measures for defining response rate.

Based on data from a prior meta-analysis (Wood et al., 2008) in which lack of blinding was associated with exaggerated effect estimates for subjective outcomes in clinical trials, we expected higher response rates for unblinded studies. In contrast, we found that response rates determined by independent assessors were higher at post-treatment (12%) and follow-up (16%). The current results could reflect more conservative judgment on the part of clients or clinicians compared to independent raters. In accord, there is some evidence that participant ratings of improvement, albeit with internet-based CBT, are more conservative

than independent assessor ratings (Cuijpers, van Straten, Bohmeijer, Hollon, & Andersson, 2010). Alternatively, independent assessors may be able to more objectively judge a client's current state independent of their histories, which may lead them to recognize response faster than do clients or clinicians. Regardless of the reasons for higher response rates when using independent assessors, we recommend use of blinded assessors given their independent and thereby potentially less biased perspective (CONSORT, 2010).

Due to the variability between studies in treatment and study characteristics, we controlled for the impact of a number of treatment and study characteristics on rate of response. Providing these controls should decrease Type II error by accounting for variance that otherwise would be included in the error term, while at the same time minimizing Type I error by controlling for third variables that might be related to our variables of interest. While we will not discuss in detail all the results for the control variables, one finding is particularly interesting. Notably, the format in which CBT was delivered, whether alone or in combination with other therapeutic strategies, whether defined solely as behavior therapy or as cognitive therapy, or whether delivered individually or in groups, did not relate significantly to response rates.

In addition to the empirical, methodological, and applied contributions, this study contains limitations that should be considered in future research. The present investigation only included studies published since 2000. This was done purposefully in order to rely upon studies using more standardized forms of CBT and more sophisticated research methods. However, this approach limited the number of studies, which limited power especially for follow-up analyses. Second, as there are no established best practices for determination of response rates, we reviewed the literature and selected likely properties that would be of interest. This selection is not exhaustive and other determinants of response rate could be considered. Further, because there are no established guidelines for objectively determining overall response rate, it is impossible to conclude whether the various measurement properties of response rate actually biased the results compared to what they should have been. Additionally, our recommendations for measuring response rate lack prospective validity. In order to test the validity of our recommendations, a future study could compare individuals who are classified as responders using our recommended methods for establishing response rate with individuals who are classified using less stringent methods for establishing response rate in terms of their long-term status.

The current findings highlight the importance of an agreed upon set of criteria for judging whether an individual is a responder or not to treatment. Such consensus is necessary for cross-study summaries and comparisons, which in turn are necessary for clinical decision making regarding the potential benefits of CBT for given individuals. Furthermore, as agreement develops on the manner in which clinically meaningful change is calculated, it may be practical for individual clinicians as well as larger practices to adopt standardized methods to calculate effectiveness of a treatment. This will help clinicians and practices determine their effectiveness and compare their response rates to general benchmarks. This form of feedback might ultimately result in greater personal and professional accountability for the success of interventions.

Consistent with prior recommendations (Campbell & Fiske, 1959; CONSORT, 2010; Hamer & Simpson, 2009; Jacobson & Truax, 1991; Maassen, 2004; Strauss & Smith, 2009; Wood et al., 2008), we recommend the following measures to best assess treatment response: (1) a clinically significant change index to demonstrate both significant improvement during treatment and achievement of normative functioning, (2) an intent-to-treat, mixed model analysis to reflect response rates for the targeted population rather than the rate for completers only (who may have a more favorable response than non-completers), (3) use of independent assessors to provide a less biased estimate of outcome, (4) use of multiple measures, and (5) preferably ones that include more than one modality (i.e., self-report, behavioral observation, physiological recording) to enhance construct validity and capture the complex nature of treatment response and the multifaceted nature of anxiety disorders. Although some of these methods may lower estimated response rates (i.e., a clinically significant change index, multiple measures and an intent-to-treat sample), others would not (i.e., independent assessor and multiple modalities). That being said, inclusion of all five of the recommended properties for measuring response rate will likely reduce response rate estimates. Nonetheless, the lower response rate may lead to a more accurate estimate of the true success of our currently existing CBT treatments.

Authors' disclosures

Statement 1: role of funding sources

There was no funding provided for this study.

Statement 2: contributors

All authors worked together to design and write the study. The first and fifth authors conducted extensive literature searches. The first author conducted ratings for all studies, and the second, third, and sixth authors each conducted ratings on 33% of the studies to assess reliability. The fourth author conducted the statistical analysis. All authors contributed to and have approved the final manuscript.

Statement 3: conflict of interest

All authors declare that they have no conflicts of interest.

Appendix A

Excluded studies:

Abramowitz, J. S., Moore, E. L., Braddock, A. E., & Harrington, D. L. (2009). Self-help cognitive–behavioral therapy with minimal therapist contact for social phobia: A controlled trial. *Journal of Behavior Therapy and Experimental Psychiatry*, *40*(1), 98–105.

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