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Cognitive behavioral therapy for primary care depression and anxiety: a secondary meta-analytic review using robust variance estimation in meta-regression

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Abstract Cognitive-behavioral therapy (CBT) is well supported for treating depressive and anxiety disorders. Trials of CBT for anxiety and depression in primary care have increased over the past decade, yet only one meta-analysis, published in 2015, examined this topic and the scope of that review is relatively narrow. This study conducted a systematic review and meta-analysis of primary care based CBT for depression and anxiety. A search of seven electronic databases, six professional websites, and reference lists from articles meeting inclusion criteria was conducted for studies published between 1900 and November 2018. Fifty-seven eligible studies (including 10,701 participants; 221 effect sizes) of randomized controlled trials were eligible and included for meta-analysis using robust variance estimation in meta-regression. Outcome indicators were depression and anxiety measures. An overall significant treatment effect, $d = 0.400$, 95% CI (0.235, 0.566), $p < 0.001$, of CBT for depression and anxiety disorders in primary care was identified. Subgroup analyses indicated significant treatment effect for: (1) depressive ($d = 0.425$, $p < 0.001$) and anxiety ($d = 0.393$, $p < 0.01$) outcomes, (2) studies conducted inside primary care ($d = 0.412$, $p < 0.001$), (3) studies using individual-based CBT ($d = 0.412$, $p < 0.001$), (4) studies without primary care physician involvement ($d = 0.395$, $p < 0.001$), and (5) studies using both tele-health ($d = 0.563$, $p < 0.001$) and in-person CBT ($d = 0.363$, $p < 0.001$). The percentage of White participants, treatment composition (CBT only versus CBT + other approaches), and treatment duration were significant moderators. Implications for clinical practice are discussed based on both moderator and subgroup analysis results.

Keywords Cognitive behavioral therapy · Primary care · Depression · Anxiety · Meta-analysis

Introduction

Depression and anxiety disorders are among the most prevalent mental health problems globally (Baxter et al., 2013; Steel et al., 2014). The total estimated number of people with depression increased by 18.5% between 2005 and 2015 (Vos et al., 2016), and as many as 33.7% of the world's population experiences an anxiety disorder during their lifetime (Bandelow & Michaelis, 2015). Untreated depression and anxiety disorders are associated with substantial functional impairments across multiple domains, including social and family relationships and employment (Aderka et al., 2012, Rizvi et al., 2015). Both depressive and anxiety disorders are among the top 10 causes of disease burden worldwide, with depression being the second and anxiety being the fifth highest causes of years lost due to disability (Walker et al., 2015). Unfortunately, over half of those who live with depression and anxiety don't receive any treatment and even fewer receive guideline concordant care, such as empirically supported interventions with

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minimal dosage needed to achieve effectiveness (ADAA, 2018). This treatment access disparity is in part due to the lack of assessment and treatment for depression and anxiety in primary care settings.

The primary care setting provides an accessible, acceptable venue for addressing a wide range of health concerns, which has driven the worldwide importance of understanding the role of primary care in mental health care. Primary care is often the first contact point for mental health problems in many countries worldwide (Patel et al., 2013; Petterson et al., 2014; Starfield, 2009). Evidence from the United States suggests more than half of primary care visits relate to depression- or anxiety-associated somatic complaints (Culpepper et al., 2008). As individuals may not recognize symptoms as mental health-related, primary care is typically the first place where mental health needs are detected and identified (Serrano-Blanco et al., 2010). However, primary care settings also provide less stigmatized environments than specialty mental health settings; therefore, individuals with awareness of their mental health needs are more likely to disclose concerns and symptoms to their primary care physicians (Corrigan et al., 2014). Given the high prevalence of mental health-related primary care visits and potential advantages of treating depression and anxiety in primary care settings, previous literature (e.g., Asarnow et al., 2015; Smith et al., 2012) has highlighted the importance of developing and implementing empirically supported interventions for depression and anxiety in primary care.

Substantial literature indicates that cognitive behavioral therapy (CBT) is an effective psychosocial treatment for depression and anxiety disorders in primary care and other treatment settings. In fact, CBT is arguably one of the most well-researched psychosocial treatments, with the number of studies focused on CBT continuing to grow. In their 2006 study, Butler and colleagues identified 16 meta-analyses of CBT. By 2012, Hofmann and colleagues identified 269 meta-analytic studies focusing on CBT. To date, several hundred meta-analyses of CBT report its effectiveness for both depressive (Cuijpers et al., 2013) and anxiety disorders (Hofmann & Smits, 2008), including major depressive disorder (Cuijpers et al., 2010), dysthymia (Driessen & Hollon, 2010), unipolar depression (Hans & Hiller, 2013), comorbid depression and physical conditions (Beltman et al., 2010), generalized anxiety disorder (Gould et al., 1997) social phobia (Gould et al., 1997), and panic disorder with or without agoraphobia (Norton & Price, 2007). More importantly, effectiveness research suggests the versatility of CBT, with robust support for CBT for depression and anxiety across developmental stages, from younger children, adolescents (Reinecke et al., 1998) to older adults (Gould et al., 2012). Additionally, support for CBT's effectiveness is demonstrated across various patient populations, such as those living with chronic pain (Morley et al., 1999), diabetes (Gary et al., 2003) and insomnia (Trauer et al., 2015).

The extensive literature on CBT's effectiveness in treating depression and anxiety suggests that it deserves continued study in primary care settings. In the last decade there have been two large scale randomized controlled trials (Craske et al., 2009; Roy-Byrne et al., 2010a, b) supporting the effectiveness of computer-assisted CBT in primary settings for anxiety disorders. Additionally, Twomey and colleagues (2015) conducted a meta-analysis of CBT for anxiety and depression in primary care. This meta-analysis found that CBT was effective for anxiety and depression in primary care but the results favored anxiety disorders. Several limitations also exist in the scope and methods of Twomey and colleagues' (2015) meta-analysis that prevent their review from providing a comprehensive assessment of CBT interventions in primary care. For example, the search strategy utilized in this review only included four electronic databases, which likely resulted in a relatively small number of studies (n = 29) meeting inclusion criteria. The small sample size did not allow the authors to conduct important moderator analyses to determine factors associated with greater treatment effects (Twomey et al., 2015). Three other meta-analyses (Cuijpers et al., 2009; Bortollotti et al., 2008; Cape et al., 2010) also included several studies that tested CBT within primary care. These studies found mixed effects for the effectiveness of psychological therapies on depression and anxiety; however, based on these studies' search strategies, all three studies were unlikely to be systematic reviews and had relatively small sample sizes (N = 10–34).

Based on the limitations of other reviews of CBT in primary care, an updated and more comprehensive systematic review and meta-analysis of CBT for depression and anxiety in primary care settings is indicated. The aims of this new review are to evaluate the effectiveness of CBT interventions that are delivered in primary care settings for depression and anxiety. This current review will also examine modalities of CBT interventions in primary care to better inform implementation (e.g., technology assisted CBT versus in-person CBT; or individual CBT versus group CBT).

This secondary meta-analysis study systematically reviews and conducts a meta-analysis to evaluate the effectiveness of CBT for primary care depression and anxiety. The current study includes all studies of CBT for depression and anxiety disorders in primary care identified as part of a larger published systematic review (Zhang et al., 2019) of the effectiveness of four empirically supported interventions in primary care: (1) cognitive behavioral therapy, (2) problem solving therapy, (3) motivational interviewing, and (4) solution-focused brief therapy. The

current study focuses on CBT studies separately for the following reasons: (1) CBT is among the most well-researched psychotherapeutic interventions for depression and anxiety and there are a sufficient number of empirical investigations of CBT for depression and anxiety in primary care to warrant a stand-alone meta-analysis; (2) a separate investigation of CBT allows us to answers important questions related to real world practice that cannot be addressed when examining CBT along with other interventions (e.g., what is the average length of CBT sessions?; Are longer CBT session associated with greater treatment effect?); and (3) the current review includes an update of the original search strategy and original dataset, described in the Methods section, which resulted in the inclusion of additional studies. This results in an up-to-date review of articles testing CBT for depression and anxiety disorders in primary care setting that makes an important and unique contribution to the literature. Given the increased sample size, compared to other meta-analyses examining CBT in primary care, this study uses an advanced meta-analytic method that produces better estimation of an overall treatment effect across all eligible studies. A greater number of studies meeting inclusion criteria and the use of advanced meta-analytic methods in this study also allow for moderator analysis to identify factors (e.g., treatment length, modality) associated with greater treatment effect.

Methods

Search procedure and selection criteria

The search and selection procedure used to identify all CBT studies conducted in primary care settings between 1900 and November of 2018 are described below. Although CBT was developed in the 1960s, the search parameters included articles 1900 through 2018 to ensure the other three interventions included in the original systematic review were adequately captured. Three search strategies were used to identify published and unpublished studies, dissertations, and grey literature: (1) electronic database search, (2) manual search of professional and/or academic websites (for published and grey literature), and (3) manual search of reference lists from articles meeting inclusion criteria. Seven electronic databases and six professional and/or academic websites were systematically searched (see "Appendix"). Within each database and website, search terms included three sets of key words: (1) cognitive behavioral therapy ("cognitive behavior therapy" or "cognitive-behavior therapy" or "cognitive therapy" or "CBT"); (2) depressive and/or anxiety disorders ("depression" or "depressive" or "anxiety" or "panic" or "phobia"); and (3) primary care setting ("primarycare" or "primary care" or "PCP" or "family medicine" or "family doctor"). These key words were used for title and abstract search.

To be eligible for inclusion in this meta-analytic review, studies had to be: 1) randomized controlled trials (RCT) of CBT; 2) conducted in a primary care-based setting; and 3) targeting depressive and/or anxiety as primary outcomes. Primary care-based delivery was operationalized in this study as: (1) CBT provided inside a primary care setting by a health care provider, through a technological platform, or via a combination of both, or (2) CBT delivered outside a primary care setting by a health care provider, through a technological platform, or via a combination of both, but directly connected with or prescribed by a primary care health care provider. All modalities of CBT studies (e.g., technology-assisted; in-person; individual; group) were included in the current study. Assessment of whether studies utilized CBT was based on authors' self-identification of the intervention as CBT.

Data collection and extraction

At least two independent reviewers screened and reviewed all articles for inclusion eligibility and for data extraction. Reviewers' decisions were blind to each other during screening and coding. If there was lack of consensus during the screening and coding processes, the two reviewers would discuss and resolve the conflict. If the two reviewers were unable to achieve consensus, a third reviewer reviewed the disputed study and made an independent judgement. Issues requiring a third reviewer were discussed with the research team to reach a final decision. A detailed coding sheet is available upon reasonable request to the corresponding author. The following information was extracted from all studies meeting inclusion criteria: sample demographics (e.g., age, gender, race, educational background), research design (e.g., comparison/control group (e.g., treatment as usual; wait list), measurements used to assess primary outcome variables, and characteristics of CBT delivery (e.g., provider; providers' training, treatment length, intervention delivery setting). The final inter-rater agreement rate among the independent reviewers was 87%, indicating satisfactory inter-rater reliability.

Publication bias and quality of study assessment

Publication bias was tested by inspecting the funnel plot by plotting observed treatment effect size estimates against their standard errors. The quality of studies included in this review was assessed using both the Oxford Quality Scoring System (Jadad et al., 1996) and the Cochrane Collabora-

tion's tool for assessing risk of bias in randomized trials (Higgins et al., 2011).

Meta-analytic procedures

All measures of depressive and/or anxiety disorders were first converted to Hedges's *g* to indicate the difference in standardized units between participants in the treatment and control group (Cooper et al., 2009). Given all reported outcomes were continuous measures, we calculated the standardized mean differences between the treatment and control group. Following Cooper et al.s' (2009) suggestion we further bias corrected the *g* statistic using a J function to obtain an unbiased estimation of the treatment effect size, noted as *d* in this review. Heterogeneity statistic was assessed using multi-level modeling.

To synthesize effect size estimates and to investigate potential moderators for sources of heterogeneity across studies, this review used meta-regression with robust variance estimation (RVE) (Hedges et al., 2010; Tipton & Pustejovsky, 2015). An intercept only meta-regression model provides the point estimate of a pooled estimate of effect sizes across studies. Through adding covariate(s) to the meta-regression model we investigated if any covariates moderate treatment effect sizes. Meta-regression with RVE is a preferred method for this review's data because it effectively handles the statistical dependence created by multiple effect size estimates from the same study without minimal loss of statistical information from eligible studies. Additionally, this method produces robust results across both random and fixed effect models (Hedges et al., 2010).

Data analysis used R software (R Core Team, 2013). The "metafor" package and the "rma.mv" function were used to assess between study and between effect size heterogeneity. The "robumeta" and "clubSandwich" package, and the "robu" function were used to conduct meta-regression with robust variance estimation for overall treatment effect and moderator analyses.

Results

Search results and study characteristics

Figure 1 presents the literature search and selection process for this meta-analysis (including both the original and updated search). In the original search, conducted in April 2017, yielded an initial pool of 752 records (after duplications removed). Of those 752 records, 78 studies were eligible for full-text review and 47 studies met inclusion criteria for this meta-analytic review. The updated search, conducted in November 2018, identified an additional 10 studies meeting inclusion criteria, resulting in a final analytical sample of 57 studies. The 57 studies contained 221 effect size estimates and included a total of 10,701 participants. Participants' average age was 45.24 years old (*SD* = 15.01) and the majority were female (70.35%) and White (65.20%). Although two-thirds of studies examined CBT delivered inside primary care (n = 38; 66.7%), about one-quarter (n = 14) examined CBT delivered outside primary care (PCP referred), and almost 10% (n = 5; 8.8%) used a mixture of both inside and outside primary care when delivering CBT. Most studies (n = 42, 73.7%) examined CBT independently; however, 15 studies (26.3%) used CBT as a primary intervention but added adjunct therapeutic techniques (e.g., motivational interviewing). The vast majority of studies of CBT for depression and anxiety in primary care included in this review delivered individual treatment (n = 49, 86.0%), whereas 7 studies (12.3%) delivered group-based CBT and 1 study (1.8%) delivered CBT for couples. Individual CBT interventions averaged 47.74 min per session (SD = 9.98) with participants attending an average of 8.7 sessions over 12.07 weeks. Group CBT interventions averaged 101 min per session (SD = 32.48) with participants attending an average of 8.14 sessions over 9 weeks. Thirty-six (63.2%) studies examined in-person CBT while 21 studies (36.8%) investigated technology assisted CBT.

Forty-four studies (77.2%) focused on depression as the primary outcome and 13 studies (22.8%) studies examined anxiety as the primary outcome. Almost 85% of studies (n = 48) used treatment as usual or another active intervention as comparison, with only about 15% of studies (n = 9) comparing CBT with medication only (n = 5; 8.7%) or wait list control (n = 4; 7.0%) conditions. Study characteristics are presented in Table 1.

Heterogeneity statistics were calculated using the "metafor" package in R with the "rma.mv" function. Both the between study variability ($\sigma^2 = .315$, $p < 0.001$) and between effect size variability ($\sigma^2 = .057$, $p < 0.01$) were statistically significant, indicating significant heterogeneity among studies and effect size estimates. The multi-level analysis also obtained a statistically significant Q statistic, $Q(df = 200) = 2485.87$, $p < 0.001$, suggesting significant between effect size variability (while accounting for the clustering nature of the data).

Quality of studies and risk of bias

Using the Jadad Scale (Table 2) for randomized controlled trials, the 57 studies had an average rating of 3.30 (SD = 1.18) out of 5.0, indicating an overall acceptable study quality across included trials. In general, studies included in this review were satisfactorily rated in mentioning randomization (57/57), appropriate randomization (41/57) and

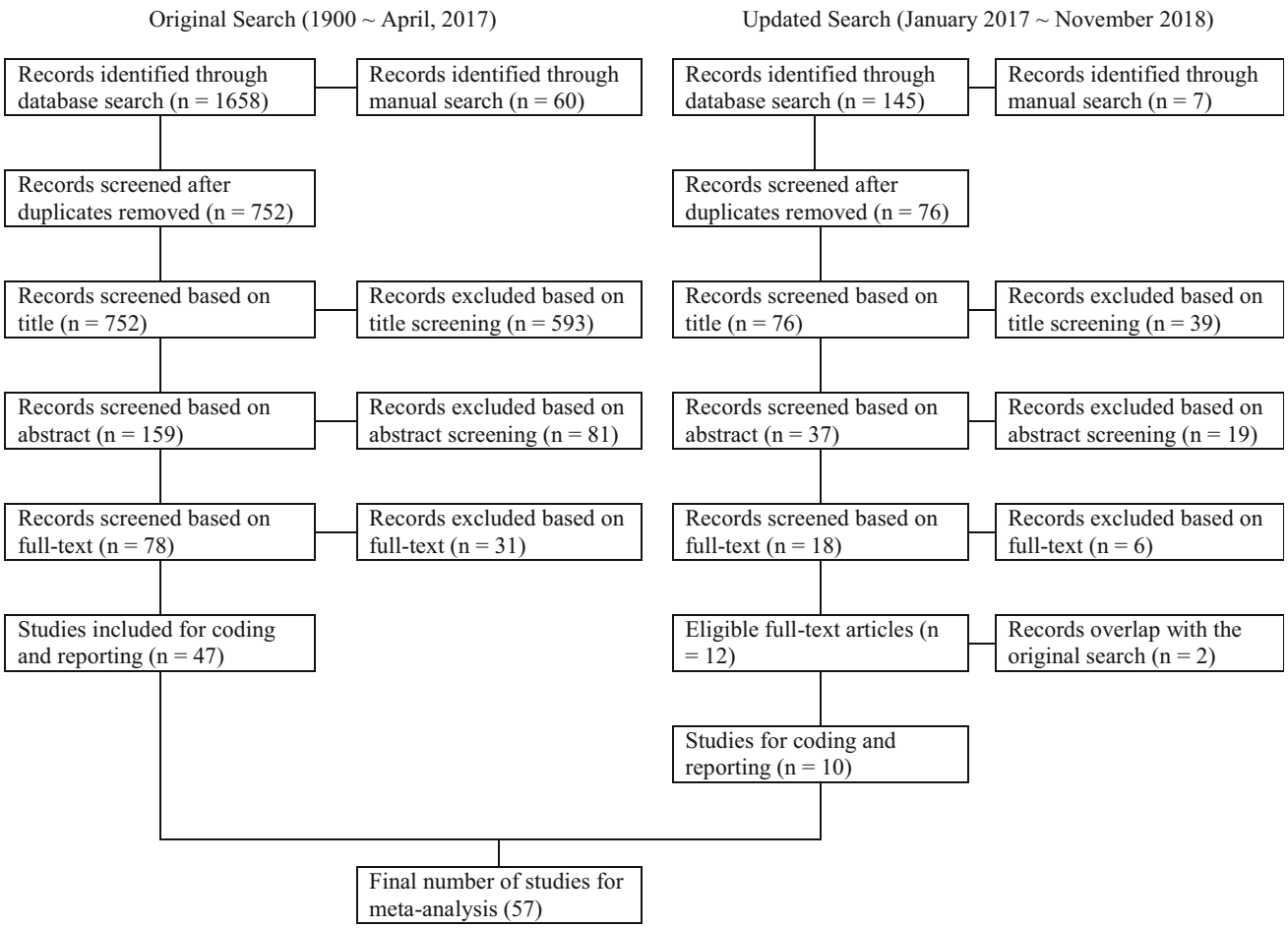

Fig. 1 PRISMA Chart

accounting for all participants (44/57). However, they were not satisfactory using appropriate blinding (11/57) if blinding was used at all (35/57). Using the Cochrane Collaboration's tool for assessing risk of bias (Table 3), studies were satisfactorily rated in random sequence generation (57/57), no selective reporting (54/57) and handling incomplete outcome data (45/57). Risk of bias existed among studies in allocation concealment (22/57), blinding of outcome data (23/57) and blinding of participants and personnel (9/57).

Publication bias

Publication bias was assessed using both funnel plot and the Vevea and Woods (2005) sensitivity analysis. By plotting effect size estimates against their corresponding standard errors, the plot is reasonably symmetric which indicates absence of publication bias. The Vevea and Woods (2005) sensitivity analysis, which statistically investigates publication bias, further confirms absence of publication bias. As indicated in Fig. 2 there exists no visible difference between the observed and the theoretical effect size which further supports absence of publication bias.

Meta-analytic results

Across the 57 trials (containing 221 effect sizes) included in this meta-analysis, the pooled treatment effect size of CBT for depression or anxiety disorders in primary care was $d = 0.40$, 95% CI [0.235, 0.566], $p < 0.001$. Subgroup analysis indicated that CBT had a moderate treatment effect size for depressive ($d = 0.425$, $p < 0.001$) and anxiety outcomes ($d = 0.393$, $p < 0.01$). Significant pooled CBT effect sizes were observed in studies that delivered CBT inside ($d = 0.412$, $p < 0.001$) but not outside ($d = 0.371$, $p = 0.108$) primary care. Studies using individual-based CBT reported a moderate and significant treatment effect ($d = 0.399$, $p < 0.001$) while studies using group-based CBT reported an overall nonsignificant treatment effect ($d = 0.391$, $p = 0.07$). Both tele-health based ($d = 0.563$, $p < 0.001$) and not tele-health based

Table 1 Study characteristics of cognitive-behavioral therapy

Author	Sample[†]	Demographics[††]	Control[†††]	Provider and PCP's role in CBT (if applicable)	Treatment dosage	Diagnostic criteria	Outcome measures	Setting and disorders[††††]
Asarnow et al. (2005)	T = 211 C = 207	17.2 years old, 22% male, 12.7% White	TAU	PhD or master's level psychotherapists with a mental health or nursing background with 1 day training., PCP no involvement	Adapted CBT manual 5 sessions each session being 50 min	CIDI-12 CES-D	CES-D MCS-12	PC, depression
Biesheuvel-Leliefeld et al. (2017)	T = 124 C = 124	48.7 years old, 30.2% male, Race NR	TAU	Mental health nurses and psychologists (N = 24) trained. PCP no involvement	Manualized preventive CT self-help with support for 8 weeks each session being 60 min	SCID/DSM-IV	QIDS-sr FDSQ-A	PC, depression
Buntrock et al. (2016)	T = 202 C = 204	45.04 years old, 26.1% male, 83.5% White	TAU	Guided an online program. Psychologist supervised graduate students and healthcare professionals.	30 min sessions lasting for a mean duration of 6 weeks	CES-D DSM-IV	CES-D HADS Anxiety BADS-SF PSWQ	NIPC, depression
Cape et al. (2016)	T = 19 C = 120	42.2 years old, 40.2% male, 66.1% White	TAU	Two recent graduates with a bachelor's in psychology	90-min group treatment sessions for 5 weeks.	Identified concern about sleeping	PHQ-9 GAD-7	PC, depression and insomnia
Carmody et al. (2013)	T = 50 C = 51	67.5 years old, 97% male, 68.4% White	EDU	4 practitioners with a masters degrees who have received training and experience	20 weeks with 12 sessions over the phone	MINI	BDI-II	NIPC, chronic pain and depression
Carta et al. (2012)	T = 42 C = 42	42.5 years old, 34.4% male, Race NR	TAU	Psychologists (N = 2) trained. No PCP involvement. TAU was provided	6 months with 12 sessions	DSM-IV-TR	BDI WHOQOL CGI	PC, depression
Clarke et al. (2005)	T = 77 C = 75	15.3 years old, 22.5% male, Race NR	MED	Therapists were trained in CBT. No reported information education level or demographics	An average of 5.3 sessions (5–9 offered) with each session lasting 60 min	K-SADS-PL DSM-IV	CES-D HDRS CBCL-D YSR-I	PC, depression
Clarke et al. (2017)	T = 106 C = 106	14.6 years old, 31.6% male, 72.2 White	TAU	Master's degree and several years of experience delivering CBT at minimum	2 4-session modules with length of sessions unspecified	DSM-IV-TR	CDRS-R CES-D	PC, depression
Conradi et al. (2008)	T = 41 C1 = 104 C2 = 63	Demographic information NR (short report)	TAU	NR	10–12 CBT sessions	NR	BDI	PC, depression
Cramer et al. (2011)	T = 52 C = 21	42.5 years old, 0% male, 87.7% White	TAU	Not mental health professionals who were trained as facilitators. PCP no involvement	CBT and PST group intervention over 10 weeks with 12 sessions total and 2 booster sessions at the end	PHQ-9	PHQ-9 BAI	PC, depression

Table 1 continued

Author	Sample†	Demographics††	Control†††	Provider and PCP's role in CBT (if applicable)	Treatment dosage	Diagnostic criteria	Outcome measures	Setting and disorders††††
Craske et al. (2011)	T = 503 C = 501	43.2 years old, 28.88% male, 56.57% White	TAU	Professionals included social workers (N = 6), nurses (N = 5), master's psychologist (N = 2), and doc. Psychologist (N = 1). PCP no involvement	8 individual and online modules running from 8 to 10 weeks. The length of sessions were not reported	DSM-IV	GADSS PDSS-SR SPIN PCL-C	Combined, anxiety
Cully et al. (2017)	T = 180 C = 122	65.52 years old, 94.4% male, 67.9% White	TAU	Mental health providers and advanced trainees (6 psychologist, 2 social workers, 2 physician assistants, 6 psychology fellows and 3 psychology interns)	6 weekly/biweekly sessions and two telephone "booster" sessions over 4 months	BAI PHQ-9	BAI PHQ-9	PC, depression and anxiety
de Graaf et al. (2009)	T1 = 100 T2 = 100 C = 103	44.9 years old, 43.2% male, Race NR	TAU	Computer-based program	8 sessions with each session lasting 30 min online. A 9th booster session at the end	DSM-III-R BDI-II CIDI	BDI-II	NIPC, depression
Dwight-Johnson et al. (2011)	T = 50 C = 51	39.8 years old, 22% male, Race NR	TAU	Part-time MSW therapists (N = 5). No PCP involvement	8 sessions lasting 45–50 min. 2–4 booster sessions at the end	PHQ-9 MDQ	SCL-D PHQ-9	NIPC, depression
Eriksson et al. (2017)	T = 52 C = 38	36.26 years old, 30% male, Race NR	TAU	Internet-delivered cognitive behavioral therapy. 10 therapists supported the clients (licensed psychologist or psychotherapist)	7 sessions across 10 weeks with technology assisted delivery	DSM-IV MADRS-S	BDI-II MADRS-S	PC, depression
Gilbody et al. (2015)	T1 = 210 T2 = 242 C = 239	39.9 years old, 33.0% male, Race NR	TAU	Computer-based program	T1: 15-min intro session with 8 sessions lasting 50 min T2: http://moodgym.anu.edu.au	PHQ-9	PHQ-9	NIPC, depression
Goodyer et al. (2017)	T = 154 C = 156	15.6 years old, 25.0% male, 85.0% White	TAU	Providers were NHS staff from a range of professional backgrounds, clinical and counseling psychologist, nurses, and occupational therapist	Maximum of 20 sessions, delivered weekly, tapering to every 2 weeks as needed, plus up to four family sessions	DSM-IV	MFQ RCMAS	PC, depression
Hange et al. (2017)	T = 46 C = 31	77 years old, 32% male, Race NR	TAU	Online CBT program	12 weeks with seven modules. Each session lasting 35 min on average	MINI MADRS-S	MADRS-S	NIPC, depression

Table 1 continued

Author	Sample†	Demographics††	Control†††	Provider and PCP's role in CBT (if applicable)	Treatment dosage	Diagnostic criteria	Outcome measures	Setting and disorders††††
Hegerl et al. (2010)	T = 61 C1 = 83 C2 = 83 C3 = 59	46.4 years old, 31.8% male, Race NR	MED PLC TAU	NR	10 weeks of group sessions. Each session lasting 90 min	HAMD DSM-IV	HAMD IDS	PC, depression
Høifødt et al. (2013)	T = 52 C = 54	36.1 years old, 27.4% male, Race NR	W/NT	Online modules with therapists' background not reported PCP no involvement	Online CBT MoodGYM version with 5 modules. Personal therapeutic support and email support was provided	BDI-II	BDI-II BAI HADS	Combined, depression
Jones et al. (2018)	T = 37 C = 35	43.98 years old, 31.9% male	TAU	3 therapists certified by the British Association for Behavioural and cognitive Psychotherapies	Individual sessions up to 10 sessions, other information NR	DSM-IV(SCID) HADS-A	HAM-A STAI	Combined, anxiety and bipolar
Kessler et al. (2009)	T = 149 C = 148	34.9 years old, 32% male, Race NR	TAU	Psychologists trained in CBT. No PCP involvement	10 sessions with each session lasting 55 min	BDI ICD-10	BDI	NIPC, depression
King, Marston, and Bower (2014)	T = 58 C1 = 49 C2 = 23	34.9 years old, 25% male, 89.3% White	TAU PCM	Accredited professionals (counselors and psychologist). No PCP involvement	12 weekly sessions with each session lasting 50 min	ICD-10 BDI	BDI BSI	PC, depression
Kivi et al. (2014)	T = 45 C = 47	36.6 years old, (SD = 11.3) 34% male, Race NR	TAU	Licensed professional at a doctoral level. No PCP involvement	Online therapy containing 7 modules over 8–12 weeks. Contact with therapists weekly	MINI DSM-IV	BDI-II MADRS-S BAI	NIPC, depression
Kuyken et al. (2015)	T = 212 C = 212	52.0 years old, 23.3% male, 99% White	MED	NR. No information reported on the providers	Eight group sessions lasting 2.25 h each	DSM-IV	Depression-free-days BDI GRID-HAMD	PC, depression
Lagomasino et al. (2016)	T = 196 C = 204	49.6 years old, 17% male, 4.0% White	TAU	3 bilingual master's-level social workers with no previous mental health experiences functioned as depression care specialist. One week training	12-week CBT intervention. Other information NR	PRIME-MD PHQ-9	PHQ-9	PC, depression
Laidlaw et al. (2008)	T = 21 C = 23	74 years old, 27.5% male, Race NR	TAU	Masters and doctoral level professionals. No PCP involvement	8 sessions of CBT on average	DSM-IV SADS-L HDRS BDI-II	HRSD BDI-II GDS BHS PSWQ WHOQOL	PC, late life depression

Table 1 continued

Author	Sample†	Demographics††	Control†††	Provider and PCP's role in CBT (if applicable)	Treatment dosage	Diagnostic criteria	Outcome measures	Setting and disorders††††
Lamers et al. (2010)	T = 96 C = 91	71 years old, 60% male, Race NR	TAU	Registered nurses provided services. PCP involvement through training the providers	2–10 individual sessions over the course of 3 months. Each session lasted 60 min	PHQ-9, MINI, HDRS	BDI post SCL-A post BDI 9 month SCL-A 9 month	NIPC, depression and COPD
Löbner et al. (2018)	T = 320 C = 327	43.9 years old, 31.5% male, Race NR	TAU	Internet-based, self-management program designed to prevent and alleviate symptoms of depression	5 interactive modules delivered in a specific order. Other information NR	ICD-10 PHQ-9	BDI-II PHQ-9	PC, depression
Longchoopol et al. (2018)	T = 30 C = 30	70.5 years old, 0% male, 0% White	TAU	The study PI facilitated the group sessions. No PCP involvement	12 group-administered sessions of 45–60 min each. 3 times per week over 4 weeks	PHQ-9	PHQ-9	PC, depression
Ludman et al. (2007)	T = 198 C = 195	44.4 years old, 24.1% male, 77.4% White	TAU	Psychotherapists at a master's level with at least 1 year of experience. PCP prescribed anti-depressant	Eight sessions with 2–4 booster sessions over 1 year. Each sessions lasting 30–40 min	HSCL DSM-IV	HSCL PHQ-9	NIPC, depression
Martin et al. (2015)	T = 36 C = 30	40.6 years old, 25.75% male, Race NR	TAU	Clinical psychologist provided services. No PCP involvement	12 weekly individual face-to-face sessions lasting 50 min	CIDI-LT (depression and anxiety)	BDI-II BAI PHQ-9	PC, headache and depression
Milgrom et al. (2011)	T = 23 T_2 = 22 C = 23	31.5 years old, 0% male, 86.76% White	TAU	Psychologist T1 Nurse T2 with PCP control. PCP involved with the treatment condition	6 individual face-to-face sessions over the course of 6 weeks. The length of the sessions was not reported	EPDS	BDI-II DASS	PC, postnatal depression
Morrell et al. (2009)	T = 271 C = 147	30.9 years old, 0% male, Race NR	TAU	Providers trained. No PCP involvement	8 weekly individual session. Each session lasting 60 min	EPDS SF-12	EPDS STAI	PC, postnatal depression
Naeem, Waheed, Gobbi, Ayub, and Kingdon (2011)	T = 17 C = 17	32.9 years old 26.5% male, Race NR	MED	Psychiatrist (N = 1) and psychologists (N = 2) were the providers	9 sessions of CBT. Session length was not reported	ICD-10-DCR	HADS anxiety HADS depression BSI	PC, depression
Newby et al. (2013)	T = 49 C = 60	44.3 years old, 22.2% male, Race NR	W/NT	Online CBT program with therapist assistance. No PCP involvement	6 sessions. The length of the sessions was not reported	ICD-10 PHQ-9 GAD-7	PHQ-9 GAD-7 BDI-II	NIPC, anxiety and depression
Nordgren et al. (2014)	T = 50 C = 50	35.4 years old, 37% male, Race NR	W/NT	Internet module with therapist involvement. No PCP involvement	13 internet modules across an estimated 13 weeks	DSM-IV (Anxiety)	CORE-OM BAI MADRS-S	NIPC, anxiety

Table 1 continued

Author	Sample†	Demographics††	Control†††	Provider and PCP's role in CBT (if applicable)	Treatment dosage	Diagnostic criteria	Outcome measures	Setting and disorders††††
Pigeon, Funderburk, Bishop, and Crean (2017)	T = 13 C = 14	58.46 years old, 89% male, 77.48% White	TAU	Psychology student with graduate level training. No PCP involvement	Four weekly over the phone sessions Session 1 lasted 40 min, session 2 lasted 20 min and session 3 lasted 30 min and sessions 4 lasted 20 min	PHQ-2 PHQ-9 ISI	PHQ-9	Combined, insomnia and depression
Power et al. (1989)	T = 10 C1 = 10 C2 = 11	34.2 years old, 12.9% male, Race NR	MED PLC	Psychologist served as the provider. PCP involvement through two additional assessment appointments	4 sessions each lasting 50 min with 2–15 PC sessions occurring over the course of 6 weeks	Initial GP and psychologist assessor evaluation	HRSA	PC, anxiety
Power and Freeman (2012)	T = 65 T_2 = 64 C = 28	36.1 years old, 38.2% male, Race NR	TAU	Therapists with clinical training. No PCP involvement	12–16 sessions aligning with Beck's manual	SCID-R	BDI-II	PC, anxiety
Proudfoot et al. (2003)	T = 89 C = 78	44.6 years old, 26.3% male, 74.9% White	TAU	Computer-based program. No PCP involvement	8 therapy sessions with each session lasting 50 min	ICD-10	BDI BAI	NIPC, anxiety and depression
Proudfoot et al. (2004)	T = 146 C = 128	43.5 years old, 26.3% male, 80.3% White	TAU	Computer-based program. No PCP involvement	8 therapy sessions with each session lasting 50 min	GHQ-12 CIS-R	BDI BAI	NIPC, anxiety and depression
Roy-Byrne et al. (2010a, b)	T = 503 C = 501	43.5 years old, 28.9% male, 56.6% White	TAU	Social workers (N = 6), nurses (N = 5), master's psychologist (N = 2), and doctoral level Psychologist (N = 1). PCP involvement through offering medication	Individual online modules lasting from 8 to 10 weeks. The length of session was not reported	DSM-IV OASIS	BSI-12 PHQ-8	PC, anxiety
Sandlund et al. (2018)	T = 90 C = 75	54.0 years old, 27.3% male, Race NR	TAU	District nurses (N = 8) received 16-h training and other information NR	Seven 2-h sessions over the course of 10 weeks: 6 weekly sessions and one follow-up session 4 weeks later	DSM-IV, sleep disorders	MAFDRS-S	PC, depression and insomnia
Scogin et al. (2018)	T = 22 C = 18	Age NR, 10% male, 57.7% White	TAU	Research psychotherapists were advanced (3rd yr and beyond) graduate students specializing in clinical geropsychology or health psychology in a doctoral program	Refined 10-session manualized protocol based on treatment of geriatric depression. 25 min of each treatment session	SLUMS	HAM-D	PC, depression and insomnia

Table 1 continued

Author	Sample†	Demographics††	Control†††	Provider and PCP's role in CBT (if applicable)	Treatment dosage	Diagnostic criteria	Outcome measures	Setting and disorders††††
Scott et al. (1997)	T = 24 C = 24	41 years old, 33.3% male, Race NR	TAU	Therapist with graduate level training in cognitive therapy. No PCP involvement	6 weeks of CBT with each session lasting 30 min	DSM-III-R	BDI HRSD	PC, depression
Serfaty et al. (2009)	T1 = 70 C1 = 67 C2 = 67	74.1 years old 20.6% male, 75.5% White	TC*** TAU	Accredited professional with 5 years of experience using CBT. No PCP involvement	6–8 sessions with potential for up to 12 sessions	GMSHES BDI-II	BDI-II BAI-II	PC, depression
Sharp and Power (1998)	T = 92 C = 57	Demographic information not reported	MED PLC	Provider information NR. No PCP involvement	9 sessions with each session lasting 30–60 min	DSM-III-R	HAM-A SRT FQ-AG	PC, panic disorder
Sharp et al. (2004)**	T1 = 20 (CBT_G) T2 = 31 (CBT_I) C = 19	37.7 years old Gender NR Race NR	W/NT	NR	12 weekly group sessions with each session lasting 1 h. Additionally 12 individual weekly sessions each session lasting 1 h	DSM-IV HAS MADRS	HAM-A SRT MADRS FQ-AG	PC, panic disorder and agoraphobia
Stanley et al. (2003)	T = 6 C = 6	70.6 years old, 16.7% male, 50% White	TAU	No information about therapists was provided	CBT with PST components. 8 weekly sessions	PRIME-MD MMSE DSM-IV (SCID-I/P)	PSWQ BAI BDI SCID-GAD	PC, anxiety—GAD
Stanley et al. (2009)	N = 134	64 years old, 21.6% male, 70.2% White	TAU	Masters level professionals with 2 years of experience (N = 3), pre-doctoral with 3 years of experience (N = 1) and bachelors with 5 years of experience (N = 1). No PCP involvement	Individual face-to-face 7.4 sessions over 12 weeks. The length of the sessions was not reported	MINI DSM-IV	PSWQ GADSS SIGH-A BDI-II	PC, anxiety
Stanley et al. (2014)	T = 76 T_2 = 74 C = 73	66.9 years old, 46.64% male, 78.92% White	TAU	Psychologist	Individual face-to-face and telephone therapy. Maximum of 10 sessions over 6 months. The length of the sessions was not reported	DSM-IV (GAD)	PSWQ-A GADSS STAI-T SIGH-A PHQ-8	PC, older adults GAD
Sundquist et al. (2017)	T = 105 C = 110	41.5 years old, 20.5% male, Race NR	ALT*****	No information about therapists was provided	6.3 individual CBT session, other information NR	ICD-10 MADRS-S HADS-A HADS-D PHQ-9	SCL-D6 SCL-ASS8	PC, depression and anxiety

Table 1 continued

Author	Sample[†]	Demographics[††]	Control[†††]	Provider and PCP's role in CBT (if applicable)	Treatment dosage	Diagnostic criteria	Outcome measures	Setting and disorders[††††]
Ward et al. (2000)	T = 63 C1 = 67 C2 = 67	36.7 years old, 22.8% male, 89.8% White	TAU TAU2	Counselors (N = 6) and psychologists (N = 3)	Six sessions with a maximum of 12 appointments. Each session lasted 50 min	ICD-10	BDI BSI	PC, depression
Wiles et al. (2013)	T = 234 C = 235	49.6 years old, 27.72% male, 97.87% White	TAU	Psychotherapist education was not reported	12–18 face-to-face sessions over the course of 6.3 months with each session lasting 50–60 min	BDI-II ICD-10	BDI-II PHQ-9 GAD-7 Panic score	PC, depression
Wiles et al. (2016)	T = 234 C = 235	49.6 years old, 27.72% male, 97.87% White	TAU	Psychotherapist education was not reported	Individual, in person, 12–18 sessions and 50–60 min per session over 6.3 months	BDI-II ICD-10	BDI-II PHQ-9 GAD-7	PC, treatment-resistant depression
Williams et al. (2013)	T = 141 C = 140	41.7 years old, 31.7% male, Race NR	TAU	Internet-based CBT	3–4 sessions each lasting 40 min with potential for one additional session	BDI-II	BDI-II	NIPC, depression

[†]Sample size: T = Treatment, T2 = Treatment 2 if applicable, C = Control

[††]Demographic: NR = Not Reported

[†††]Control: TAU = Treatment as usual, W/NT = Waitlist or no treatment, MED = Medication, EDU = Psycho-education, PLC = Placebo, PCM: Primary care management

[††††]PC = Primary care setting, NIPC = Not in primary care

*If does not meet DSM criteria but CES-D cut off score, still included in the trial. **Treatment 1 = group CBT and treatment 2 = individual CBT. ***TC = TAU + talking control. ****Diazepam = 22, Placebo = 19, Cognitive-behaviour therapy = 21, Diazepam + Cognitive-behaviour therapy = 21, Placebo + Cognitive-behaviour therapy = 18. *****ALT: alternative intervention

ASI Anxiety Severity Index, *BADS-SF* Behavioral Activation for Depression Scale—Short Form, *BAI* Beck Anxiety Inventory, *BAI-II* Beck Anxiety Inventory II, *BDI* Beck Depression Inventory, *BDI-II* Beck Depression Inventory II, *BSI* Brief Symptoms Inventory, *BSI-12* Brief Symptoms Inventory, 12 items, *CDRS-R* Children's Depression Rating Scale—Revised, *CES-D* Center for Epidemiology Scale—Depression, *CGI* Clinical Global Impression, *CIDI-(LT)* Composite International Diagnostic Interview (Life Time Version), *CIS-R* Clinical Interview Schedule—Revised, *CORE-OM* The Clinical Outcomes in Routine Evaluation Outcome Measure, *DASS* Depression and Anxiety Stress Scale, *EPDS* Edinburgh Postnatal Depression Scale, *FDSQ-A* Four-Dimensional Symptom Questionnaire—Anxiety, *FQ-AG* agoraphobia subscale of the Fear Questionnaire *GADSS* Generalized Anxiety Disorder Severity Scale, *GAD-7* Generalized Anxiety Disorder 7-item, *GHQ-12* General Health Questionnaire, *GMSHES* Geriatric Mental State and History and Etiology Schedule, *GRID-HAMD* Interview version of the Hamilton Depression Rating Scale, *HADS* Hospital Anxiety and Depression Scale, *HADS-A* Hospital Anxiety and Depression Scale—Anxiety, *HAM-A* Hamilton Anxiety Rating Scale, *HAMD* Hamilton Depression Rating Scale, *HAS* Hamilton Anxiety Scale, *HDRS* Hamilton Depression Rating Scale, *HRSA* Hamilton Rating Scale for Anxiety, *HRSD* Hamilton Rating Scale for Depression, *ICD-10-DCR* ICD-10 Diagnostic Criteria for Research, *IDS* Inventory for Depressive Symptomatology, *ISI* Insomnia Severity Index, *MADRS* Montgomery–Åsberg Depression Rating Scale, *MADRS-S* Montgomery–Åsberg Depression Rating Scale—Self Reported, *MFQ* Mood and Feelings Questionnaire, *MINI* Mini International Neuropsychiatric Interview, *MMSE* Mini–Mental State Examination *OASIS* Overall Anxiety Severity and Impairment Scale, *PHQ-2* Patient Health Questionnaire -2, *PHQ-8* Patient Health Questionnaire—8, *PHQ-9* Patient Health Questionnaire, 9-item, *PCL-C* PTSD Checklist—Civilian Version, *PDSS-SR* Panic Disorder Severity Scale—Self-report, *PRIME-MD* Primary Care Evaluation of Mental Disorders, *PSWQ* Penn State Worry Questionnaire, *PSWQ-A* Penn State Worry Questionnaire—Abbreviated, *QIDS-sr* Quick Inventory of Depressive Symptomatology—Self Report, *RCMAS* Revised Children's Manifest Anxiety Scale, *SCID-R* Structured Clinical Interview for DSM-IV, Research version, *SCL* Hopkins Symptom Checklist, *SCL-90, ASS8* Symptom Distress Checklist, Specific Anxiety, *SCL-90, DS* Symptom Distress Checklist, Depression Severity, *SCID/DSM-IV* Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II), *SF-12* SF-36 Health Survey 12-item version, *SOI* Severity of Illness [for generalized anxiety disorder], *SRT* patient-rated Symptom Rating Test, *STAI* State-Trait Anxiety Inventory, *STAI-T* The trait subscale of the Spielberger State-Trait Anxiety Inventory, *SIGH-A* Structured Interview Guide for the Hamilton Anxiety Scale, *SLUMS* Saint Louis University Mental Status Examination (SLUMS), *WHOQOL* the Quality of the Life Questionnaire of the World Health Organization

Table 2 Quality rating using Jadad Scale for reporting randomized controlled trials

	Randomization		Blinding		An account of all patients	Total score
	Mentioned randomization	Appropriate randomization	Mentioned blinding	Appropriate blinding	All patients' fate stated	
Asarnow et al. (2005)	1	1	0	0	1	3
Biesheuvel-Leliefeld et al. (2017)	1	1	1	0	1	4
Buntrock et al. (2016)	1	1	1	1	1	5
Cape et al. (2016)	1	1	1	0	1	4
Carmody et al. (2013)	1	0	0	0	1	2
Carta et al. (2012)	1	0	1	0	0	2
Clarke et al. (2005)	1	0	1	0	0	2
Clarke et al. (2017)	1	1	1	0	1	4
Conradi et al. (2008)	1	0	0	0	0	1
Cramer et al. (2011)	1	1	1	0	1	4
Craske et al. (2011)	1	1	1	1	1	5
Cully et al. (2017)	1	1	0	0	1	3
De Graaf et al. (2009)	1	0	0	0	1	2
Dwight-Johnson et al. (2011)	1	0	1	0	0	2
Eriksson et al. (2017)	1	1	0	0	1	3
Gilbody et al. (2015)	1	1	1	0	1	4
Goodyer et al. (2017)	1	1	1	1	1	5
Hange et al. (2017)	1	1	0	0	1	3
Hegerl et al. (2010)	1	1	1	1	1	5
Høifødt et al. (2013)	1	1	1	0	1	4
Jones et al. (2018)	1	1	1	1	1	5
Kessler et al. (2009)	1	1	0	0	1	3
King et al. (2014)	1	1	1	0	1	4
Kivi et al. (2014)	1	1	1	0	1	4
Kuyken et al. (2015)	1	1	1	0	1	4
Lagomasino et al. (2016)	1	1	0	0	1	3
Laidlaw et al. (2008)	1	1	1	1	1	5
Lamers et al. (2010)	1	1	1	0	1	4
Löbner et al. (2018)	1	1	1	1	1	5
Longchoopol et al. (2018)	1	1	0	0	1	3
Ludman et al. (2007)	1	0	1	0	1	3
Martin et al. (2015)	1	0	0	0	1	2
Milgrom et al. (2011)	1	0	1	0	0	2
Morrell et al. (2009)	1	1	1	0	1	4
Naeem et al. (2011)	1	0	1	0	1	3
Newby et al. (2013)	1	0	1	0	0	2
Nordgren et al. (2014)	1	1	0	0	1	3
Pigeon et al. (2017)	1	1	0	0	1	3
Power et al. (1989)	1	0	0	0	0	1
Power and Freeman (2012)	1	1	1	1	0	4
Proudfoot et al. (2003)	1	1	0	0	0	2
Proudfoot et al. (2004)	1	1	0	0	1	3
Roy-Byrne et al. (2010a, b)	1	1	1	1	1	5
Sandlund et al. (2018)	1	1	1	0	1	4
Scogin et al. (2018)	1	1	1	1	1	5
Scott et al. (1997)	1	0	0	0	0	1

Table 2 continued

	Randomization		Blinding		An account of all patients	Total score
	Mentioned randomization	Appropriate randomization	Mentioned blinding	Appropriate blinding	All patients' fate stated	
Serfaty et al. (2009)	1	1	1	0	0	3
Sharp and Power (1998)	1	0	0	0	0	1
Sharp et al. (2004)	1	1	0	0	1	3
Stanley et al. (2003)	1	0	0	0	0	1
Stanley et al. (2009)	1	1	1	0	1	4
Stanley et al. (2014)	1	0	1	0	1	3
Sundquist et al. (2017)	1	1	1	0	1	4
Ward et al. (2000)	1	1	0	0	1	3
Wiles et al. (2013)	1	1	1	0	1	4
Wiles et al. (2016)	1	1	1	0	1	4
Williams et al. (2013)	1	1	0	1	1	4
Total Score	57	41	35	11	44	Mean = 3.30

($d = 0.363$, $p < 0.001$) CBT studies reported statistically significant treatment effects. Interestingly, only non-primary care physician (PCP) involved CBT studies were statistically significant ($d = 0.395$, $p < 0.001$) while those PCP involved CBT trials reported an overall nonsignificant effect size ($d = 0.612$, $p = 0.154$). Both high- (Jadad score > 3) and low-quality (Jadad score ≤ 3) studies reported statistically significant overall treatment effect with $d = 0.302$, $p < 0.05$ and $d = 0.500$, $p < 0.001$ respectively. The above results are presented in Table 4. While subgroup analysis indicates if an overall significant treatment effect was observed among a subgroup of studies, it does not reflect if the difference between subgroups is statistically significant. Therefore, we further conducted moderator analyses to reflect the between subgroup differences.

Moderator analysis results

Moderator analysis (see Table 5) indicated that race (%White) significantly moderates CBT trials' effect sizes, $b = -0.016$, 95% CI [-0.024, -0.009], $p < 0.001$. Each 1% increase in a study's Caucasian participants, is associated with a 0.016 standard deviation decrease in treatment effect sizes. Treatment duration (in weeks) is negatively associated with treatment effect sizes, $b = -0.018$, 95% CI [-0.036, -0.001], $p < 0.05$. An additional week of CBT is associated 0.018 standard deviation decrease in treatment effect. Interestingly, multimodal CBT trials that used CBT as the primary intervention but added additional therapeutic techniques like motivation interviewing reported an overall significantly greater treatment effect than trials of CBT alone, $b = -0.431$, CI [-0.666, -0.196], $p < 0.05$. On average, trials of CBT alone were 0.431 standard deviations lower than multi-modal CBT trials in treatment effect sizes. Study quality (Jadad score ≤ 3 versus Jadad score > 3) did not moderate treatment effect size estimates.

Discussion

Depression and anxiety disorders remain a significant public health concern; yet, the majority of individuals experiencing symptoms of anxiety and depression do not receive treatment. Even fewer individuals have access to CBT, which is the most well-researched and effective psychosocial treatment for depression and anxiety. Primary care settings have emerged as preferred settings for addressing mental health needs, and service delivery innovations, such as technology-assisted delivery of mental health treatment and integrated healthcare models, have further encouraged the incorporation of mental health treatment in primary care. However, to date, there has not been a systematic review of CBT for depression and anxiety in primary care. This systematic review and meta-analysis addresses this gap with results supporting the clinical value of providing CBT for depression and anxiety in primary care. This study also informs the implementation of CBT for depression and anxiety in primary care, providing preliminary evidence on delivery strategies that may result in better clinical outcomes.

This meta-analysis of CBT for depression and anxiety disorders in primary care adds to the robust literature suggesting CBT is effective for these disorders (Hofmann

Table 3 Cochrane collaboration's tool for assessing risk of bias

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome data	Incomplete outcome data	Selective reporting
Asarnow et al. (2005)	+	–	–	–	+	+
Biesheuvel-Leliefeld et al. (2017)	+	+	+	+	+	+
Buntrock et al. (2016)	+	+	?	+	+	+
Cape et al. (2016)	+	?	–	+	+	+
Carmody et al. (2013)	+	?	–	–	–	+
Carta et al. (2012)	+	–	–	+	?	+
Clarke et al. (2005)	+	?	–	+	+	+
Clarke et al. (2017)	+	–	–	+	+	+
Conradi et al. (2008)	+	–	–	–	?	–
Cramer et al. (2011)	+	–	–	+	–	+
Craske et al. (2011)	+	+	?	–	+	+
Cully et al. (2017)	+	–	–	–	+	+
De Graaf et al. (2009)	+	–	–	–	+	+
Dwight-Johnson et al. (2011)	+	–	–	–	+	+
Eriksson et al. (2017)	+	?	–	–	+	+
Gilbody et al. (2015)	+	+	–	–	+	+
Goodyer et al. (2017)	+	+	+	+	+	+
Hange et al. (2017)	+	+	–	–	+	+
Hegerl et al. (2010)	+	+	–	+	+	+
Høifødt et al. (2013)	+	–	+	+	+	+
Jones et al. (2018)	+	+	+	+	+	+
Kessler et al. (2009)	+	+	?	?	+	+
King et al. (2014)	+	–	–	–	+	+
Kivi et al. (2014)	+	+	+	?	+	+
Kuyken et al. (2015)	+	+	–	+	+	+
Lagomasino et al. (2016)	+	?	–	–	+	+
Laidlaw et al. (2008)	+	+	?	+	–	+
Lamers et al. (2010)	+	+	–	–	+	+
Löbner et al. (2018)	+	+	?	?	+	+
Longchoopol et al. (2018)	+	+	?	?	+	+
Ludman et al. (2007)	+	–	–	+	+	+
Martin et al. (2015)	+	–	–	–	?	+
Milgrom et al. (2011)	+	?	–	–	+	+
Morrell et al. (2009)	+	?	–	+	+	+
Naeem et al. (2011)	+	?	?	+	+	+
Newby et al. (2013)	+	–	–	–	+	+
Nordgren et al. (2014)	+	?	?	?	+	+
Pigeon et al. (2017)	+	–	?	–	+	+
Power et al. (1989)	+	–	–	?	?	+
Power and Freeman (2012)	+	?	+	+	+	?
Proudfoot et al. (2003)	+	+	–	–	+	+
Proudfoot et al. (2004)	+	?	–	–	?	+
Roy-Byrne et al. (2010a, b)	+	+	+	+	+	+

Table 3 continued

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome data	Incomplete outcome data	Selective reporting
Sandlund et al. (2018)	+	+	+	–	+	+
Scogin et al. (2018)	+	?	+	+	+	+
Scott et al. (1997)	+	–	–	–	–	?
Serfaty et al. (2009)	+	?	–	+	+	+
Sharp and Power (1998)	+	–	–	–	–	+
Sharp et al. (2004)	+	?	–	+	+	+
Stanley et al. (2003)	+	–	–	–	–	+
Stanley et al. (2009)	+	+	–	?	+	+
Stanley et al. (2014)	+	+	–	–	+	+
Sundquist et al. (2017)	+	?	–	+	+	+
Ward et al. (2000)	+	+	–	–	–	+
Wiles et al. (2013)	+	–	–	?	+	+
Wiles et al. (2016)	+	–	–	?	+	+
Williams et al. (2013)	+	+	–	+	+	+
	57 + s	22 + s	9 + s	23 + s	45 + s	54 + s

"+" low risk of bias; "−" high risk of bias; "?" unclear risk of bias

et al., 2012; Twomey et al., 2015) and that CBT can be successfully delivered across a variety of settings (e.g., Himle et al., 2014). This review included 23 of the 29 studies in Twomey and colleagues' (2015) review and has added an additional 34 studies. The 6 studies that were included in the Twomey review but excluded for this study were due to differences in the operationalization of CBT intervention and primary care-based interventions.

Results across the 57 randomized controlled trials (RCTs) included in this review suggest an average medium and statistically significant treatment effect of CBT on both depression and anxiety in primary care. Studies included in this review were limited to RCTs, which are the most scientifically rigorous group research designs used to evaluate treatment effectiveness. For this reason, we have relative confidence in these findings in relation to the potential sources of biases that have been identified in the study designs that may preclude some confidence in these results. The most significant biases identified on the Cochrane Risk of Bias measure, for example, is the lack of blinding of participants and assessors. Future studies need to give further attention to these procedures in order to improve research designs and methodological rigor of studies in this area.

The overall treatment effect size (d = 0.40) of CBT for depression and anxiety disorders in primary care settings is lower compared to CBT's effect size for these disorders in other settings. For example, studies of CBT delivered in outpatient mental health settings have found relatively higher treatment effect sizes for depression among adults (d = 0.83) (Beltman et al., 2010) and for anxiety among children (d = 0.94). One possible explanation for the lower overall treatment effect size found in this review may be that most evidence-based CBT protocols for depression and anxiety disorders include more than 10 treatment sessions (Beck, 2011), whereas studies included in this review included CBT protocols with an average of 8 sessions.

In addition, it is important to note that findings indicate CBT is equally effective for the treatment of depression and anxiety disorders in primary care, as treatment outcome (depression versus anxiety) was not a significant moderator. While the effect size of CBT for depression was slightly higher than anxiety outcomes, this difference was minimal and statistically nonsignificant (difference in d = 0.05). However, it should be noted that only 13 out of 57 trials in this review examined anxiety as the primary outcome. Therefore, CBT's effectiveness for anxiety disorders in primary care remains preliminary. These findings differ from previous reviews showing greater effect sizes of CBT interventions for anxiety disorders than for depression (Cape et al., 2010; Twomey et al., 2015). Difference in results may be due to different statistical procedures used. The current review included multiple effect sizes from one study whereas many previous reviews only included one effect size per study (e.g., Cape et al., 2010). Nevertheless, previous studies (Butler at el., 2006; Ebert et al., 2015; Hofmann & Smith, 2008) have suggested that there is a need for more CBT trials focused explicitly on anxiety disorders as the primary outcome.

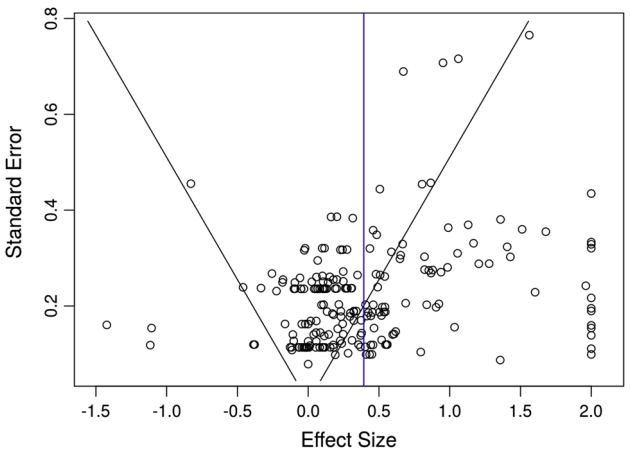

Fig. 2 Funnel plot and Vevea and Wood sensitivity analysis for publication bias

Further, our findings add support to a growing body of literature on the effectiveness of technology-assisted CBT (e.g., Rooksby et al., 2015; Spurgeon & Wright, 2010). Among studies included in this review, subgroup and moderator analyses indicated that technology-assisted CBT and in-person CBT are associated with significant overall treatment effect size in treating depression and anxiety in primary care, and the difference between the two subgroups were statistically nonsignificant. These results echo findings reported by Twomey and colleagues (2015) who found "*good preliminary evidence … for … computerized/online CBT and guided self-help CBT*" (p. 13). These findings are not surprising given technology-based interventions are intentionally designed to reduce barriers in mental health treatment particularly related to stigma and accessibility (Price et al., 2014; Wagner et al., 2015), two major factors that contribute mental health services being sought in primary care. Therefore, technology-assisted CBT in primary care offers a delivery method that can reach an equivalent treatment effect, if not better, than in-person CBT, and is likely more acceptable and accessible to clients. Technology-assisted CBT may also reduce structural barriers, such as provider availability, that likely make it challenging to deliver face-to-face CBT in primary care.

Results of this review also indicate that studies in which CBT was not delivered by a physician reported an overall significant treatment effect compared to studies in which CBT was delivered by a physician, where there was an overall *nonsignificant* treatment effect; although, the difference in effect size was not statistically significant. This may be a result of low statistical power as only 4 studies (with 9 effect sizes) included physician-involved CBT interventions. However, non-physician-involved CBT was predominantly delivered by mental health providers who

Table 4 Overall and sub-group meta-analysis

	Estimate	t (df)	K/N	95% CI	*p* value
Overall treatment effect	0.400	5.00 (22.9)	57/221	[0.235, 0.566]	$p < 0.001$***
Outcome type					
Depressive outcomes	0.425	5.00 (30.4)	51/110	[0.252, 0.599]	$p < 0.001$***
Anxiety outcomes	0.393	3.64 (10.2)	31/109	[0.153, 0.634]	$p < 0.01$**
Setting of delivery					
Inside primary care	0.412	4.75 (17.8)	39/155	[0.230, 0.594]	$p < 0.001$***
Outside primary care	0.371	1.94 (5.2)	18/66	[− 0.115, 0.857]	$p = 0.108$
Treatment modality					
Individual based	0.399	4.62 (19.5)	50/200	[0.218, 0.579]	$p < 0.001$***
Non-individual based	0.391	2.17 (6.01)	8/21	[− 0.050, 0.831]	$p = 0.07$
PCP involvement					
PCP involved	0.612	2.01 (2.54)	4/9	[− 0.463, 1.690]	$p = 0.154$
Non-PCP involved	0.395	4.39 (20.0)	50/188	[0.207, 0.583]	$p < 0.001$***
Tele-health or not					
Tele-health based	0.563	3.32 (15.8)	21/50	[0.203, 0.923]	$p < 0.001$***
Not tele-health based	0.363	4.24 (13.7)	35/169	[0.179, 0.547]	$p < 0.001$***
Study quality					
High quality (Jadad > 3)	0.302	2.57 (9.62)	21/116	[0.038, 0.565]	$p < 0.05$
Low quality (Jadad ≤ 3)	0.500	7.65 (14.4)	30/105	[0.360, 0.640]	$p < 0.001$***

if df < 4, a lower *p* value ($p < 0.01$) should be used for statistical inference

K number of studies, *N* number of effect size estimates

***$p < 0.001$, **$p < 0.01$

Table 5 Univariate meta-regression models with robust variance estimation

	N/K[a]	β [95% CI]	p value
Depression (*ref:* Anxiety)	221/57	0.050 [− 0.167, 0.268]	$p = 0.635$
Age (*centered at 43.65 years*)	200/54	0.007 [− 0.001, 0.016]	$p = 0.635$
Gender (*% female*)	193/54	0.001 [− 0.008, 0.010]	$p = 0.714$
Race (*% White*)	127/30	− 0.016 [− 0.024, − 0.009]	$p < 0.001$
Marital Status (*% married*)	122/33	0.008 [− 0.016, 0.017]	$p = 0.092$
Control (*ref:* low intensity)	221/57	− 0.226 [− 0.490, 0.039]	$p = 0.083$
Setting (*ref:* not in primary care)	221/57	0.038 [− 0.411, 0.487]	$p = 0.856$
Modality (*ref:* group)	221/57	− 0.025 [− 0.566, 0.516]	$p = 0.916$
Composition (*ref:* multi-modal)	221/47	− 0.431 [− 0.666, − 0.196]	$p < 0.01$
Minutes per session	110/36	0.001 [− 0.007, 0.007]	$p = 0.902$
Number of sessions	221/57	− 0.023 [− 0.059, 0.012]	$p = 0.100$
Duration (weeks)	213/54	− 0.018 [− 0.036, − 0.001]	$p < 0.05$
Dosage	110/36	− 0.001 [− 0.003, 0.002]	$p = 0.881$
Tele-health (*ref:* No tele-health)	219/56	0.183 [− 0.208, 0.575]	$p = 0.344$
PCP involvement	197/54	0.245 [− 0.840, 1.330]	$p = 0.520$
Study quality (*ref:* low quality score[b])	221/57	− 0.191 [− 0.471, 0.089]	$p = 0.295$

Individual coefficients should be interpreted as the only predictor/IV in the meta-regression analysis. All degrees of freedom greater than 4, so statistical significance should be interpreted at 0.05 level

[a]N stands for number of effect size estimates, K stands for number of studies, n.s. stands for not significant. n.s. stands for "not significant"

[b]Low quality score refers to studies with a Jadad scale score of 3 or lower

are likely to have received some CBT trainings, whereas most primary care physicians do not typically receive training in CBT or psychotherapy as part of their professional education. Also, in reality, primary care physicians are not likely to deliver CBT during their daily practice for a couple of reasons like: time constraints, professional expectations among others (e.g., Zhang et al., 2018). The differences in professional education and training focused on CBT may also account for the difference in observed outcomes. In fact, an influential study by Johnsen and Friborg (2015) found the treatment effect of CBT as a behavioral anti-depressant is declining over the years. According to Johnsen and Friborg (2015), one potential reason for this decrease is that although more and more therapists are using CBT in practice, not all are sufficiently equipped with the degree of experience and receipt of formal training necessary to deliver CBT with high fidelity. Although this finding should not discourage primary care physicians from delivering CBT, it does indicate that integrated health care models, in which interdisciplinary teams of physical, mental, and behavioral providers share decision making and care delivery via active, ongoing collaboration (Blount et al., 2007), may be particularly relevant to facilitate CBT delivery in primary care.

A significant and unique contribution of this study is the examination of CBT format. CBT format (i.e., individual- or group-based CBT) and modality (i.e., CBT only versus CBT with adjunct techniques) were significant moderators of CBT's effectiveness for depression and anxiety treatment in primary care. Interestingly, a significant overall treatment effect was only observed among the subgroup of individual-based CBT studies (not among group-based CBT studies), even though the difference was not statistically significant. Findings also suggest multi-modal CBT studies overall reported a significantly greater treatment effect than studies with CBT only intervention for primary care depression and anxiety. Both findings are consistent with the existing CBT and broader mental health literature. For instance, previous literature suggests that individual-based CBT may be more consistent with patients' expectations for primary care, and therefore a more acceptable intervention format. As indicated by previous literature (Funk, 2008; Shim & Rust, 2013), patients of primary care may attach greater stigma to mental health challenges than those who regularly visit specialty mental health outpatient clinics. It is likely that a primary care patient may be more uncomfortable disclosing or discussing their mental health needs with others. Thus, it is possible that a primary care patient may show greater resistance to a group-based intervention than an individual-based approach. It is also important to acknowledge that regular primary care visits are analogous to individual-based sessions, with patients typically having one-on-one visits with primary care physicians in an exam room. Therefore, it may be the case that individual-based CBT is more consistent with the expected delivery style of treat-

ment within a primary care setting. That said, only a small number of studies (n = 7) used group-based CBT, with an overall effect size reporting a $p = 0.07$. Considering the small sample size, thus low statistical power, it is reasonable to suspect that group-based CBT may report an overall statistically significant treatment effect in the future as more studies are available. Group-based interventions may be a more viable option for primary care settings with limited resources, given that more clients can be treated in less time. As a result, there is a need for more research on the effectiveness of group-based CBT for depression and anxiety in primary care as well as implementation research exploring the acceptability of a group-based intervention among patients and providers.

Interestingly, multi-modal CBT studies on average reported significantly greater treatment effect than studies delivering CBT alone. Many of the multi-modal CBT studies included in this review augmented standard CBT with motivational interviewing. There is a very strong line of research suggesting the use of CBT in conjunction with motivational interviewing (Merlo et al., 2010; Westra & Dozois, 2006; Westra et al., 2009) offers an ideal way to prepare and motivate clients for treatment engagement and future change efforts. When clients are equipped with greater motivation and readiness, higher CBT treatment effects are expected (Riper et al., 2014). However, it is also important to note the use and effectiveness of multi-modal CBT within the context of the evolution of the field. Over the past decade, the field has been experiencing an ongoing transformation from the second wave of CBT (Beck's Cognitive Therapy) to a third wave that incorporates other therapeutic components into Beck's CBT model, or in some cases modifies Beck's model (Kahl et al., 2012). Third wave approaches, such as the acceptance and commitment therapy (ACT), dialectical behavior therapy (DBT), functional analytic psychotherapy, metacognitive therapy, and several others (Hayes & Hofmann, 2017) have been added to modalities that include traditional (first and second generation) CBT approaches. This has resulted in useful methods that work more effectively across various disorders and patient populations.

Although CBT trials for depression and anxiety disorders in primary care reported an overall significant and moderate treatment effect, it is important to critically reflect upon the existing literature and acknowledge a few deficiencies. Among studies included in this meta-analysis, there was limited racial and ethnic diversity among participants, with the majority identifying as White (65%). Therefore, the transferability of CBT's effectiveness in primary care among racial and ethnic minority populations remains an open question. Although a couple of studies specifically focused on testing the effect of CBT on depression and anxiety among racial and ethnic minority populations (Chavira et al., 2014; Miranda et al., 2005), there is a critical need for future research in this area that includes more diverse samples and/or focuses solely on the experiences of racial and ethnic minority populations. Further, individual CBT interventions remain relatively long (47.74 min per session) and require a great time commitment for patients in primary care and providers delivering the interventions (average of 8.14 sessions across 12.07 weeks). Given the substantial time commitments for both patients and providers, the ability for primary care settings to sustain delivery of CBT outside of the research context is not yet understood. Moreover, the feasibility and acceptability of delivering CBT at this intensity and duration within real world practice settings remains unclear, though literature on this important topic is growing (e.g., Sawchuk et al., 2018). It is imperative for future research to examine the implementation of CBT in primary care in order to better understand barriers and facilitators to providing CBT in this setting, as well as identify and test implementation strategies that will increase uptake and encourage adoption of CBT in primary care.

Limitations

It is important to acknowledge the limitations of this study, as well as those inherent to systematic reviews and meta-analysis. First, despite a rigorous process for searching and reviewing the literature, there is always a possibility that not all available studies that met the inclusion criteria were in fact included, which may, though unlikely, change the overall finding. It is also possible that a studies were missed because we did not specifically search for the British variation of search terms (e.g., behaviour) or the term "general practice" to reflect primary care settings. However, we believe that given our extensive, systematic search strategy, we were likely to accurately and comprehensively capture existing studies in this area. Second, although we adopted an advanced meta-analytic method for effect size estimation and moderator analysis, due to the nature of the data structure, some models suffered from low statistical power given the relatively small number of studies and effect sizes included in this review. Therefore, it is possible that some of the nonsignificant findings may be due to low power and should be interpreted cautiously. This limitation cannot be addressed until more studies of CBT for depression and anxiety in primary care are conducted. Third, many studies included in this review had high risk of bias, which should be considered when interpreting findings. Specifically, significant subgroup analyses are known to be instable and can change with only a few studies added or removed. Fourth, while this review included two independent reviewers who engaged in a process of blind

review and coding, results of this study remain susceptible to human error. Finally, this study only included randomized controlled trials which impacts our findings external validity as results from quasi-experimental design and non-experimental design studies are not considered.

These limitations notwithstanding, this study is, to our knowledge, the first comprehensive meta-analysis of CBT for depression and anxiety in primary care. Given the high prevalence of these disorders and the emergence of primary care as the de facto mental health system in the United States, it is essential to understand if evidence-based practices, such as CBT, can be effectively delivered in these settings in order to address mental health treatment access disparities. This study suggests that CBT for depression and anxiety in primary care is, in fact, effective, identifying an overall statistically significant and moderate treatment effect size. Additionally, this study provides preliminary information on potential treatment-related moderators suggesting that individual-based CBT, CBT augmented with motivational intervention, and CBT delivered by non-physicians may result in better outcomes for clients in primary care. Finally, results of this study point towards the need for future research to examine the effect of CBT for depression and anxiety in various primary care settings and among racial and ethnic minority populations, as well as implementation research focused on identifying and testing strategies to increase the uptake of CBT in primary care. As research in this area progresses, future studies should also examine the long-term effect of CBT in primary care and control for ancillary variables in meta-regression models.

Conclusion

This comprehensive meta-analysis shows that CBT is effective for depression and anxiety in primary care and addresses the mixed effects that have been found in other smaller studies in the field. Results from the current study also have a number of implications for how to deliver the CBT interventions within primary care. CBT interventions may get better results when provided by non-physician providers, when delivered in individual sessions, and when combined with Motivational Interviewing. Technology-assisted CBT and in-person CBT are equally effective for treating depression and anxiety disorders in primary care; this finding has implications for accessibility of CBT treatment and the engagement of patients. Future research priorities should include bolstering the number of studies testing CBT for anxiety disorders in primary care and studying CBT in primary care with more diverse samples that include ethnic minority populations, as well as identifying barriers and facilitators to intervention implementation and developing and testing implementation strategies to increase adoption and uptake of CBT for depression and anxiety disorders within primary care settings.

Compliance with ethical standards

Conflict of interest Anao Zhang, Lindsay A. Borhneimer, Addie Weaver, Cynthia Franklin, Audrey Hang Hai, Samantha Guz, Li Shen have no conflict of interest to declare.

Human and animal rights and Informed consent All procedures followed were in accordance with ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

Appendix: Search strategies

The seven electronic databases included in this study are:

1. Academic Search Complete (ASC);
2. PsycINFO;
3. Cumulative Index of Nursing and Allied Health Literature (CINAHL);
4. PUBMED;
5. Medline;
6. The Cochrane library/database of systematic reviews and controlled trials;
7. ProQuest Dissertations and Theses Global.

The six professional websites included in this study were:

1. Academy of Cognitive Therapy (www.academyofct.org).
2. The IMPACT evidence-based depression care (www.impact-uw.org).
3. Motivational Interviewing Network of Trainers (http://www.motivationalinterviewing.org).
4. Solution-focused Brief Therapy Association (www.sfbta.org).
5. European Brief Therapy Association (www.ebta.eu).
6. Anxiety and Depression Association of America (www.adaa.org).

To search for dissertation, we used EBSCO Open Dissertations.

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