Computer-Assisted Cognitive-Behavior Therapy for Depression in Primary Care:

Systematic Review and Meta-Analysis

Michael J. Wells, MD[a]; Jesse J. Owen, PhD[b,*]; Laura W. McCray, MD[c]; Laura B. Bishop, MD[d]; Tracy D. Eells, PhD[e]; Gregory K. Brown, PhD[f]; Derek Richards, PhD[g,h]; Michael E. Thase, MD[i,j]; and Jesse H. Wright, MD, PhD[e]

ABSTRACT

Objective: To examine evidence for the effectiveness of computer-assisted cognitive-behavior therapy (CCBT) for depression in primary care and assess the impact of therapist-supported CCBT versus self-guided CCBT.

Methods: A search for randomized studies of CCBT compared to control groups for treating depression in primary care settings was conducted using Ovid MEDLINE, PsycINFO, PubMed, and Scopus. We extracted the following information from the studies that met inclusion criteria: mean depression rating scale scores before and after treatment, number of patients, type of control group and CCBT program, therapist support time and method of support, and treatment completion rate. Meta-analyses compared differences between posttreatment mean scores in each condition, as well as mean scores at follow-up. Study quality and possible bias also were assessed.

Results: Eight studies of CCBT for depression in primary care met inclusion criteria. The overall effect size was $g = 0.258$, indicating a small but significant advantage for CCBT over control conditions. Therapist support was provided in 4 of the 8 studies. The effect size for therapist-supported CCBT was $g = 0.372$—a moderate effect. However, the effect size for self-guided CCBT was $g = 0.038$, indicating little effect.

Conclusions: Implementation of therapist-supported CCBT in primary care settings could enhance treatment efficiency, reduce cost, and improve access to effective treatment for depression. However, evidence to date suggests that self-guided CCBT offers no benefits over usual primary care.

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[a]Department of Family and Geriatric Medicine, University of Louisville School of Medicine, Louisville, Kentucky

[b]Department of Counseling Psychology, University of Denver, Denver, Colorado

[c]Family Medicine Residency Program, University of Vermont Medical Center, Burlington, Vermont

[d]Internal Medicine and Pediatrics Residency Program, University of Louisville School of Medicine, Louisville, Kentucky

[e]Department of Psychiatry and Behavioral Sciences, University of Louisville School of Medicine, Louisville, Kentucky

[f]Clinical Psychology in Psychiatry, Perelman School of Medicine of the University of Pennsylvania, Philadelphia, Pennsylvania

[g]E-mental Health Research Group, School of Psychology, Trinity College Dublin, University of Dublin, Dublin, Ireland

[h]SilverCloud Health, Dublin, Ireland

[i]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

[j]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, Pennsylvania

**Corresponding author:* Jesse J. Owen, PhD, Department of Counseling Psychology, University of Denver, Denver, CO 80208 (jesse.owen@du.edu).

Adequate treatment of depression remains a major challenge for primary care clinicians. With an 8.6% annual prevalence of major depressive disorder in the general population in the United States[1] and a heightened risk for depression in patients with medical illnesses such as diabetes, cardiovascular disease, and chronic obstructive pulmonary disease,[2] this illness is one of the more common problems encountered in primary care. The intense personal and familial suffering associated with depression and the large economic burden of over 200 billion dollars annually in the United States[3] underscore the need for development and dissemination of effective treatments.

The US Preventive Services Task Force[4] recommends that primary care doctors screen for depression in adults when resources are in place to "assure accurate diagnosis, effective treatment, and follow-up"; however, there can be many problems in service delivery, especially when psychotherapy is recommended. For example, there are a number of recognized barriers to implementation of cognitive-behavior therapy (CBT), a treatment that has been shown to be effective in a large number of outcome studies[5,6] in mental health populations. These obstacles include an insufficient number of trained therapists, costs of treatment, lack of transportation, and difficulty in scheduling and attending a large number of therapy sessions.[7–9] Thus, most primary care patients who could benefit from CBT do not participate in this form of treatment or receive any psychotherapy.[10] Integration of behavioral health into primary care can increase the frequency of psychotherapy contacts.[11,12] However, collaborative care with integrated behavioral health treatment is unavailable in most primary care practices,[13] and cost, transportation, and time constraints also are present in collaborative care delivery models.

Computer-assisted CBT (CCBT) has been developed as a way to reduce cost and improve access to evidence-based treatment for depression and other psychiatric disorders while providing data tracking and treatment management features not found in standard CBT.[14–16] Previous reviews and meta-analyses[17–20] of CCBT that focused largely on patient populations from mental health or community settings found evidence for effectiveness and acceptance of this form of treatment.

Clinical Points

- Computer-assisted cognitive-behavior therapy (CCBT) works best for depression if guided and supported by a clinician.
- Although primary care physicians could provide support for CCBT, it may be more practical to have mental health practitioners or care coordinators (either on site in the primary care practice or available by phone, internet, or telemedicine) guide patients in use of CCBT.
- CCBT offers opportunities for improving the efficiency of treatment for depression while maintaining effectiveness and reducing cost.

Medium-to-large effect sizes have been reported for CCBT of depression in such reviews and meta-analyses.[17–20] One previous meta-analysis[21] of all forms of CBT for depression or anxiety disorders in primary care included 4 studies of CCBT among a total sample of 29 randomized controlled trials. Three of the 4 CCBT studies in this meta-analysis[21] had effect sizes that indicated significantly better reduction in depression than control conditions. However, there have been no previous reviews and meta-analyses with a focus on studies of CCBT for depression in primary care.

METHODS

A computerized literature search was conducted using Ovid MEDLINE, PsycINFO, PubMed, and Scopus from their inception to July 18, 2016. In addition, the authors performed a manual search using other meta-analyses and published reports of CCBT.[17–20] The search keywords were *randomized controlled trials of computer-assisted cognitive-behavior therapy for depression* and *randomized controlled trials of mobile apps for cognitive-behavior therapy of depression*. Criteria for inclusion of studies were (1) randomized controlled trial with control group (ie, no treatment, wait list, attention control, or treatment as usual [TAU] other than standard face-to-face CBT); (2) subjects were depressed as measured by depression rating scales; (3) inclusion criteria specified for depression (ie, clinical diagnosis of depression, diagnosis with standardized assessment, eg, *DSM-IV*, Structured Clinical Interview for *DSM-IV* Axis I Disorders,[22] Mini International Neuropsychiatric Interview[23] [see Supplementary Appendix 1 for listing of full names of diagnostic instruments and measures] or assessment with validated measure for depressive symptoms and appropriate cutoff score, eg, 9-item Patient Health Questionnaire [PHQ-9],[24] Beck Depression Inventory [BDI],[25] Center for Epidemiologic Studies Depression Scale [CES-D][26]); (4) participants were 16 years of age or older; (5) involved use of a computer program or mobile app that covers core methods of CBT to deliver all or part of the treatment; (6) pre- and posttreatment mean scores with standard deviation using a standard depression rating scale (eg, PHQ-9, BDI, Hamilton Depression Rating Scale,[27] CES-D); and (7) participants were drawn from a primary care setting (family medicine and internal medicine).

Decisions on inclusion and exclusion were reached by consensus of 3 of the authors (D.R., M.E.T., and J.H.W.). Data were abstracted on pre- and posttreatment means and standard deviations on depression rating scales, means and standard deviations on depression rating scales for follow-up assessments (if available), numbers of subjects, type of control group, CCBT program utilized, completion rate, clinician support time, and type of clinician support. If these data were not in the published report, the corresponding author of the study was contacted to request data.

Study quality was assessed using the CLEAR NPT,[28] a checklist developed to evaluate reports of nonpharmacologic, randomized clinical trials. The CLEAR NPT includes 15 questions that address study characteristics such as the adequacy of the randomization process; description of the interventions; care provider experience or skill; measurement of adherence to treatment protocols; blinding of care providers, participants undergoing treatments, and outcome evaluators; consistency of follow-up assessments across all groups; and whether the data analysis used intent-to-treat principles. Two of the study authors (T.D.E. and G.K.B.) independently evaluated each study using the CLEAR NPT. Ratings were compared, and differences were reconciled through consensus.

Data Analysis

To determine the efficacy of CCBT versus control conditions, we calculated effect sizes with Hedges *g*, which is the difference in means at posttreatment or follow-up divided by the pooled standard deviation of both conditions and the estimate of variance. The primary measure of depression was used for these calculations.[29] Two studies[30,31] did not conduct follow-up assessments after completion of treatment, while 5 studies[32–36] had multiple follow-up assessments at varying times. A single study[37] had only 1 follow-up assessment. For the follow-up analysis, we aggregated all of the follow-up assessments per study. For some studies,[34,35] there were multiple comparisons (eg, multiple versions of CCBT vs control conditions), which were aggregated per study. We used random effects estimates to better generalize beyond the participants in these studies. The heterogeneity of the effects was examined with *Q*-tests and I^2 statistics. Comparison of effects of studies that used therapist-supported CCBT versus self-guided CCBT was planned in advance because of previous research[18] showing heterogeneity between these 2 types of studies and lower effect sizes for self-guided CCBT.

RESULTS

Of the 223 studies identified in the search, 215 were excluded, most commonly because the study was not a randomized controlled trial (60 studies). A list of reasons for exclusion is provided in Supplementary Appendix 1. We found 8[30–37] studies that were randomized controlled trials of CCBT for depression in primary care that met our study criteria. Study characteristics, other than means and SDs, are

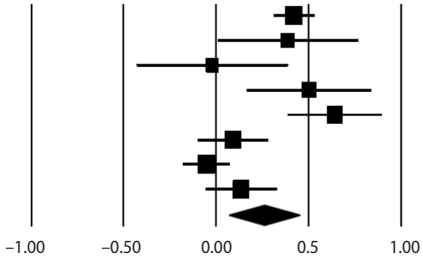
Table 1. Selected Characteristics of CCBT Studies for Depression in Primary Care

Authors	No. of Patients	Control	CCBT Program	Clinician Support Time	Completion Rate	Type of Therapist Support	Computer Program
Proudfoot et al, 2004[32]	274	TAU	Multimedia, 8 lessons, 9 weeks	NR	78%	NR	Beating the Blues
de Graaf et al, 2009[33]	303	TAU	Multimedia, 9 lessons, 12 weeks	0	36%–47%	None	Color Your Life
Hoifodt et al, 2013[37]	106	Wait list	Multimedia, 5 lessons, 7 weeks	90–180 min	60%	Face-to-face and e-mail	Mood Gym
Mohr et al, 2013[34]	101	Wait list	Multimedia, 18 lessons, 12 weeks	60–120 min	NR	Telephone coaching on adherence	Mood Manager and Telecoach
Kivi et al, 2014[30]	90	TAU	Multimedia, 7 lessons, 12 weeks	180 min	56%	Telephone and e-mail	Depressionshjälpen
Gilbody et al, 2015[35]	691	TAU	Multimedia, 8 lessons Beating the Blues or 6 lessons Mood Gym, 16 weeks	0	16%–18%	None	Beating the Blues and Mood Gym
Hallgren et al, 2015[31]	946	TAU and exercise	Multimedia, 13 lessons, 12 weeks	194 min	NR	E-mail and telephone	NR
Montero-Marin et al, 2016[36]	296	TAU	Multimedia, 10 lessons, 12 weeks	0	50%	No significant support	Smiling Is Fun

Abbreviations: CCBT = computer-assisted cognitive-behavior therapy, NR = not reported, TAU = treatment as usual.

Figure 1. Posttreatment Effect Sizes for Computer-Assisted Cognitive-Behavior Therapy (CCBT) Versus Control Conditions

Study	Hedges *g*	SE	Variance	95% CI	*z*	*P*
Hallgren et al[31,a]	0.422	0.057	0.003	0.311 to 0.534	7.410	<.001
Hoifodt et al[37,a]	0.389	0.195	0.038	0.007 to 0.770	1.996	.046
Kivi et al[30,a]	–0.019	0.209	0.044	–0.429 to 0.391	–0.092	.927
Mohr et al[34,a]	0.504	0.173	0.030	0.165 to 0.843	2.912	.004
Proudfoot et al[32,b]	0.643	0.130	0.017	0.388 to 0.898	4.941	<.001
de Graaf et al[33,c]	0.092	0.099	0.010	–0.102 to 0.286	0.927	.354
Gilbody et al[35,c]	–0.052	0.066	0.004	–0.181 to 0.076	–0.799	.424
Montero-Marin et al[36,c]	0.136	0.100	0.010	–0.060 to 0.332	1.363	.173
Total	0.258	0.097	0.009	0.068 to 0.449	2.654	.008



[a]Supported CBBT.
[b]Did not report support time.
[c]Not supported CCBT.

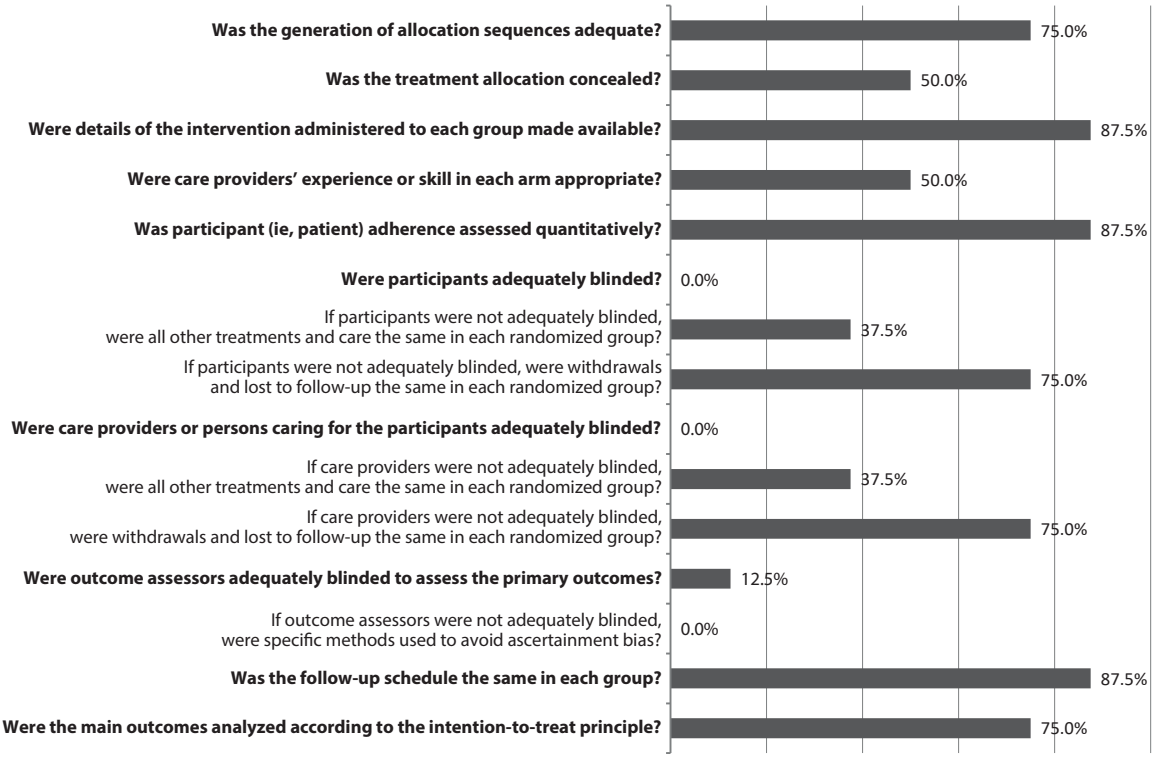
reported in Table 1. Three[33,35,36] of the 8 studies reported no therapist support time and thus were self-guided, 4 studies[30,34,36,37] utilized a blended method of a computer program plus therapist support (ranging from 60 to 194 minutes for the entire course of treatment), and 1 study[32] did not report support time. All studies used multimedia computer programs that integrated text with video or other multimedia elements and were delivered on personal computers or electronic notebooks. No studies used mobile delivery. Typically, CCBT was delivered in a series of lessons (5–18) over a time period of 7 to 16 weeks.

A forest plot for the posttreatment effects and 95% confidence intervals, along with numerical effect sizes for each study, is displayed in Figure 1. The random effects weighted mean effect size for CCBT versus TAU at posttreatment was $g = 0.258$ (SE = 0.097; 95% CI, 0.068–0.449; $P = .008$). As expected, there was significant heterogeneity in the effects ($Q_7 = 47.397$, $P < .001$, $I^2 = 85.23$), most likely influenced, in part, by inclusion of studies of self-guided CCBT. Examining the funnel plot for posttreatment effects, there was good symmetry, and, consistently, the Egger test of asymmetry was not significant (intercept = 0.65, SE = 2.34, $P = .78$); however, some caution should be taken with this test given the limited number of studies. A Duval and Tweedie trim and fill analysis yielded 1 study adjustment that only affected the overall g by 0.02. Collectively, these bias tests revealed no meaningful indications of bias in findings.

Six studies[32–37] included follow-up assessments ranging from 1 to 8 months after completion of treatment. In these studies, the random effects weighted mean effect size for CCBT versus control was $g = 0.400$ (SE = 0.103; 95% CI, 0.198–0.602; $P < .001$). Similar to posttreatment effects, there was significant heterogeneity in the effects ($Q_5 = 29.782$, $P < .001$, $I^2 = 83.21$).

For analysis of the influence of therapist support on outcome, we dichotomized the studies on the basis of whether patients received significant therapist support time ($k = 4$) or no (or negligible) therapist support time ($k = 3$). Therapist support was usually provided on a weekly basis throughout the active treatment period of 7 to 12

Figure 2. Percentage of Studies Meeting CLEAR NPT Quality Criteria[a]



[a]Based on Boutron et al.[28]
Abbreviation: CLEAR NPT = checklist to evaluate a report of a nonpharmacological trial.

weeks. Because a limited number of studies reported the therapist support time, and some studies did not calculate exact time spent in support (only the time scheduled for possible delivery), we did not attempt to examine the relationship between number of minutes of support and outcome. Two[35,36] of the studies placed in the no therapist support category offered minimal assistance. Gilbody et al[35] provided a mean of less than 7 minutes of technical support and no therapy support to patients in their study. Montero-Marin et al[36] provided a total of 17 e-mails to 13 patients out of 291 participants. The random effects weighted mean effect size for CCBT versus control at posttreatment for studies with therapist support time was $g = 0.372$ (SE = 0.086; 95% CI, 0.203–0.541; $P < .001$). In contrast, the random effects weighted mean effect size for CCBT versus control at posttreatment for studies without significant therapist support time was $g = 0.038$ (SE = 0.062; 95% CI, −0.083 to 0.160; $P = .535$). There was support for the homogeneity of these effects ($Q_3 = 4.50$, $P = .212$, $I^2 = 33.378$; $Q_2 = 3.08$, $P = .214$, $I^2 = 35.277$; CCBT versus control, respectively).

Study quality was evaluated with CLEAR NPT ratings that are shown in Figure 2. Design features such as appropriate randomization, adequate description of the interventions, reporting of participant adherence to treatment interventions, and following intent-to-treat principles in analyzing data were achieved by a majority of the studies. Some criteria that were not met, such as blinding participants and treatment providers to treatment conditions, are precluded from being realized by the nature of the interventions.

DISCUSSION

The findings of our review and meta-analysis indicate that CCBT has potential for improving delivery of effective psychotherapy in primary care settings. Studies that incorporated a modest amount of therapist support (60–194 minutes) had a mean effect size in the moderate range, indicating that CCBT was significantly better at relieving depression than usual care or a wait-list control. However, self-guided CCBT (3 of 7 studies reporting therapist support time) had a negligible effect size and thus was ineffective.

Meta-analyses[17–20] of larger samples of CCBT studies that included persons recruited on the internet, patients from mental health care delivery settings, and other non–primary care populations have found somewhat higher overall effect sizes for both guided and unguided CCBT. For example, Richards and Richardson[18] reported a mean effect size of $d = 0.56$ for all of the 19 studies in their meta-analysis. Therapist-supported studies in this meta-analysis[18] had a mean effect size of $d = 0.78$, while unsupported studies had a mean effect size of $d = 0.36$. In contrast, the effect sizes in our meta-analysis of primary care patients were lower. Although available data do not provide enough information

to discern why CCBT may be less effective in primary care patients, these influences could be implicated:

1. CCBT has been investigated less frequently in primary care than in other settings. Thus, less is known about how to effectively implement CCBT in primary care patients. It is possible that further research could help improve the delivery of CCBT in primary care.
2. Recruitment methods in many studies in non–primary care settings utilized the internet or advertisements, perhaps gathering a more highly motivated, better-educated, healthier, and computer-savvy group of participants than may be drawn from primary care practices. All but one[38] of the studies in our meta-analysis recruited from general practice (term used in European studies), family practice, or internal medicine settings. One trial[33] in the Netherlands used the internet to identify potential participants, but treatment was provided by their general practitioners.
3. It is likely that comorbid medical conditions are more common in primary care patients. These conditions could make it more difficult to participate in CCBT or benefit from it. None of the CCBT programs used to date in primary care have been tailored to persons who may have a significant physical illness.

Six[32–37] of the 8 studies in our meta-analysis provided follow-up data, an important indicator of the durability of treatment. Although the mean effect size was in the moderate range for follow-up assessments, there has not been enough research to conclude that CCBT for depression is a durable treatment in primary care settings. It would be ideal to have follow-up assessments at least a year posttreatment. However, funding is usually limited for extending evaluations to a year or longer.

The primary limitation of our review and meta-analysis is the small number of studies that have been conducted to date. However, research on CCBT has been expanding,[14,15,17–20] and additional studies in primary care are anticipated. Our research group is currently conducting an investigation of CCBT for depression in primary care using therapist support via telephone (NCT 02700009). An additional study (NCT 03068676) of CCBT for anxiety and depression in primary care is being conducted using graduate interns as supporters.

Quality assessments of studies also raise questions about research performed to date on CCBT for depression in primary care. Although some of the CLEAR NPT criteria (eg, care providers are blinded to treatment allocation; patients are blinded to treatment allocation; if care providers not blinded, other treatments are adequately controlled: if patients not blinded, other treatments are adequately controlled; assessments are performed by blind raters) are very difficult standards for practical studies of the effectiveness of CCBT in primary care settings, there is room for improvement in other CLEAR NPT criteria. Two[31,33] of the 8 studies did not use intent-to-treat principles for data analysis. Their reliance on data from treatment completers could have inflated effect sizes compared to investigations that employed more rigorous intent-to-treat analytic methods. Additional areas for enhanced study design include using best-practices randomization sequences, insuring that therapists are experienced in the delivery model, and employing outcome measures that do not rely solely on participant self-report.

Another limitation of the current review is that the optimal amount and type of therapist support (eg, face-to-face, telephone, e-mail) and predictors of outcome, other than therapist support, could not be determined. It would be helpful for future studies to report actual therapist support time and to give more detail on the methods of support. Only one[38] of the studies published a cost-benefit comparison. In this investigation, CCBT was more efficacious and cost-effective than usual treatment. Because studies[39,40] of patients treated in mental health settings have found economic advantages for CCBT, and CCBT requires considerably less therapist time than standard CBT, it is likely that CCBT would offer cost savings if widely disseminated in primary care.

Engagement in CCBT among primary care patients is another concern that has not been fully addressed to date. Will patients accept and complete this form of treatment compared to other approaches to treat depression? Two[33,36] of the 8 studies reported patient satisfaction, and both found high levels of acceptance of CCBT. Treatment satisfaction for CCBT typically has been high in studies in mental health settings,[14,18,39,40] and completion rates usually have been good in therapist-supported CCBT.[28,35,41,42] The overall completion rate in studies reviewed by Richards and Richardson[18] was 72%. However, more research is needed on acceptance of CCBT in primary care patients.

None of the 8 studies reviewed here used mobile delivery for the CBT computer program. A wide variety of CBT apps have been developed.[43] However, the quality, security, and efficacy of most apps have been questioned,[43] and CBT apps are typically designed for specific interventions such as relaxation or breathing training instead of delivery of a full program of CBT. Only a few mobile apps have been investigated as treatments for depression in randomized controlled trials.[44,45] It is possible that mobile delivery could provide greater flexibility and engagement if used as part of CCBT for depression.

Despite gaps in our current knowledge of CCBT for depression in primary care, there are indications that this method, if combined with therapist support, offers a way to engage greater numbers of patients in evidence-based psychotherapy, while improving the efficiency of treatment and reducing cost. Some of the important challenges for future research include detailing implementation strategies and improving the effectiveness of CCBT in primary care practice, delineation of the most effective ways of integrating human and computer elements of treatment, and realizing the potential for newer technologies as they become available.

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Potential conflicts of interest: **Dr Richards** is an employee of SilverCloud Health, developers of computerized psychological interventions for depression, anxiety, stress and comorbid long-term conditions. **Dr Thase** reports the following relationships during the course of this study. He was an advisory/consultant to Acadia, Alkermes, Allergan (Forest, Naurex), AstraZeneca, Cerecor, Eli Lilly, Johnson & Johnson (Janssen, Ortho-McNeil), Lundbeck, MedAvante, Merck, Mocksha8, Nestlé (PamLab), Neuronetics, Novartis, Otsuka, Pfizer, Shire, Sunovion, and Takeda. In addition to the National Institute of Mental Health, he received grant support from the Agency for Healthcare Research and Quality, Alkermes, Assurex, Avanir, Forest, Johnson & Johnson, Otsuka, and Takeda. Dr Thase received royalties from the American Psychiatric Press, Guilford Publications, Herald House, and W.W. Norton & Company, Inc. Dr Thase's spouse, Dr Diane Sloan, works for Peloton Advantage, which did business with Pfizer and AstraZeneca. **Dr Wright** is an author of the *Good Days Ahead* (GDA) program used in this investigation and has an equity interest in Empower Interactive and Mindstreet, developers and distributors of GDA. He receives no royalties or other payments from sales of this program. His conflict of interest is managed with an agreement with the University of Louisville. He receives book royalties from American Psychiatric Press, Inc, Guilford Press, and Simon and Schuster. Dr Wright receives grant support from the National Institutes of Health (Agency for Health Care Research and Quality). **Drs Wells**, **Owen**, **McCray**, **Bishop**, **Eells**, and **Brown** report no conflicts of interest related to the subject of this article.

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Supplementary material follows this article.

THE PRIMARY CARE COMPANION
FOR CNS DISORDERS

Supplementary Material

Article Title: Computer-Assisted Cognitive-Behavioral Therapy for Depression in Primary Care: Systematic Review and Meta-Analysis

Author(s): Michael J. Wells, MD; Jesse J. Owen, PhD; Laura W. McCray, MD; Laura B. Bishop, MD; Tracy D. Eells, PhD; Gregory K. Brown, PhD; Derek Richards, PhD; Michael E. Thase, MD; and Jesse H. Wright, MD, PhD

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List of Supplementary Material for the article

1. Supplementary Appendix 1

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Appendix 1

Diagnostic and Symptom Measures

Beck Depression Inventory (BDI)
Center for Epidemiologic Studies Depression Scale (CES-D)
Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (*DSM-4*)
Hamilton Rating Scale for Depression (HRSD)
Mini International Neuropsychiatric Interview (MINI)
Patient Health Questionnaire-9 (PHQ-9)
Structured Clinical Interview for DSM Disorders (SCID)

Reasons for Excluding Studies from Meta-analysis:

Studies found through computer search (Ovid Medline, PsychInfo, PubMed, Scopus) = 208
Studies found "manually" (through other meta-analysis, reviews, and other papers) = 15
Total number of studies in search = 223
Number of studies excluded = 215
Number of studies included = 8

Primary reason for exclusion:
- Not an RCT = 60
- RCT with active therapy as only control = 9
- Not on depressed subjects = 31
- No inclusion criteria for depression = 12
- Mixed sample including stress and anxiety, n= 2
- Not on adults (child and adolescent studies) = 13
- Didn't use computer-delivered therapy = 11
- Didn't use CBT = 4
- No pre-post means/SDs with standard depression rating scale = 11
- Duplicate (follow-up or other report on principal study found elsewhere in search) = 22
- Otherwise qualified for inclusion but study not performed in primary care setting = 40