APPENDIX A. SEARCH STRATEGIES

Table A-1. Search strategy for PubMed (August 30, 2013)

Set #	Terms	Results
1	"Behavior Therapy"[Mesh] OR ((behavior[tiab] OR behaviour[tiab]) AND (therapy [tiab] OR therapies[tiab)) OR Aversive[tiab] OR Biofeedback[tiab] OR Feedback[tiab] OR Neurofeedback[tiab] OR Desensitization[tiab] OR Virtual Reality[tiab] OR Exposure[tiab] OR Relaxation[tiab] OR Meditation[tiab] OR chronotherapy[tiab] OR commitment[tiab] OR dialectical[tiab] OR "Cognitive Therapy"[Mesh] OR ((cognitive[tiab] OR cognition[tiab]) AND (therapy[tiab] OR therapies[tiab])) OR "Psychotherapy, Brief"[Mesh] OR ((brief[tiab] OR short-term[tiab]) AND (psychotherapy[tiab] OR psychotherapies[tiab]))	**784265**
2	"Depressive Disorder"[Mesh] OR "Dysthymic Disorder"[Mesh] OR "Adjustment Disorders"[Mesh] OR "Stress Disorders, Post-Traumatic"[Mesh] OR Dysthymia[tiab] OR Minor Depression[tiab] OR Adjustment disorder[tiab] OR ptsd[tiab] OR generalized anxiety disorder[tiab] OR Depression[Mesh] OR Anxiety[Mesh:noexp] OR "Anxiety Disorders"[Mesh:noexp] OR "Panic Disorder"[Mesh] OR "Obsessive-Compulsive Disorder"[Mesh] OR anxiety disorder nos[tiab] OR mixed anxiety[tiab] OR subthreshold depression[tiab] OR minor depression[tiab] OR subsyndromal depression[tiab] OR panic[Mesh]	**213813**
3	(Computer-assisted Psychotherapy[tiab] OR Computerized Cognitive Behavioral Therapy[tiab] OR Low Intensity[tiab]) OR ("Internet"[Mesh] OR internet[tiab] OR web[tiab] OR social-media[tiab] OR "Therapy, Computer-Assisted"[Mesh]) OR (online[tiab] OR computer[tiab] OR computers[tiab] OR computerized[tiab] OR mobile[tiab] OR smartphone[tiab] OR smartphones[tiab] OR tablet[tiab] OR tablets[tiab] OR self-paced[tiab] OR computers[Mesh])	**456239**
4	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR control[tiab] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp])	**3151494**
5	#1 AND #2 AND #3 AND #4 Filters: Publication date from 1990/01/01 to 2013/12/31; English	**442**

APPENDIX B. CRITERIA USED IN RISK OF BIAS ASSESSMENT

Guidance on Assessing Risk of Bias for Randomized Controlled Trials

General instructions: (1) Rate each risk of bias item listed below as Low risk/ High risk/ Unclear risk (refer to Cochrane guidance to inform judgements). Add comments to justify ratings.
(2) After considering each quality item, give the study an overall rating of "Low risk," "Moderate risk," or "High risk" (see below).

Rating of individual items

* Indicates items contained in Cochrane Risk of Bias Tool.

1. **Selection bias:**
   a. *Randomization adequate (Adequate methods include random number table, computer-generated randomization, minimization without a random element.) **Low risk/ High risk/ Unclear risk**
   b. *Allocation concealment (Adequate methods include pharmacy-controlled randomization, numbered sealed envelopes, central allocation.) **Low risk/ High risk/ Unclear risk**
   c. Baseline characteristics (Consider whether there were systematic differences observed in baseline characteristics and prognostic factors between groups, and if important differences were observed, if the analyses controlled for these differences.) **Low risk/ High risk/ Unclear risk**

2. **Performance bias:**
   a. *Concurrent interventions or unintended exposures (Consider concurrent intervention or an unintended exposure (e.g., crossovers; contamination – some control group gets the intervention) that might bias results) **Low risk/ High risk/ Unclear risk**
   b. Protocol variation (Consider whether variation from the protocol compromised the conclusions of the study.) **Low risk/ High risk/ Unclear risk**

3. **Detection bias:**
   a. *Subjects blinded (Consider measures used to blind subjects to treatment assignment and any data presented on effectiveness of these measures.) **Low risk/ High risk/ Unclear risk**
   b. *Outcome assessors blinded, hard outcomes (Outcome assessors blind to treatment assignment for "hard outcomes" such as mortality.) **Low risk/ High risk/ Unclear risk**
   c. *Outcome assessors blinded, soft outcomes (Outcome assessors blind to treatment assignment for "soft outcomes" such as symptoms.) **Low risk/ High risk/ Unclear risk**
   d. Measurement bias (Reliability and validity of measures used.) **Low risk/ High risk/ Unclear risk**

4. **Attrition bias:**
   a. *Incomplete outcome data (Consider whether incomplete outcome data were adequately addressed, including systematic differences in attrition between groups [differential attrition]; overall loss to followup [overall attrition]; and whether an "intention-to-treat"

[ITT; all eligible patients that were randomized are included in analysis] analysis was performed.) (Note: mixed models and survival analyses are, in general, ITT.) **Low risk/ High risk/ Unclear risk**

5. **Reporting bias:**
   a. *Selective outcomes reporting (Consider whether there is any suggestion of selective outcome reporting; e.g., systematic differences between planned and reported findings.) **Low risk/ High risk/ Unclear risk**

Overall study rating

Please assign each study an overall quality rating of "Low risk," "High risk," or "Unclear risk" based on the following definitions:

A "**Low risk**" study has the least bias, and results are considered valid. A low risk study uses a valid approach to allocate patients to alternative treatments; has a low dropout rate; and uses appropriate means to prevent bias, measure outcomes, and analyze and report results. [Items 1a and 1c; 2a; 3b and 3c; and 4a are all rated low risk]

A "**Moderate risk**" study is susceptible to some bias but probably not enough to invalidate the results. The study may be missing information, making it difficult to assess limitations and potential problems (unclear risk). As the moderate risk category is broad, studies with this rating vary in their strengths and weaknesses. [Most, but not all of the following items are rated low risk: Items 1a and 1c; 2a; 3b and 3c; and 4a]

A "**High risk**" rating indicates significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; have large amounts of missing information; or have discrepancies in reporting. The results of a high risk study are at least as likely to reflect flaws in the study design as to indicate true differences between the compared interventions. [At least one-half of the individual quality items are rated high risk or unclear risk]

Conflict of interest (recorded but not used as part of Risk of Bias Assessment)

Was there the absence of potential important conflict of interest? The focus here is financial conflict of interest. If no financial conflict of interest (e.g., if funded by government or foundation and authors do not have financial relationships with drug/device manufacturer), then answer "Yes." **Yes /No /Unclear**

APPENDIX C. PEER REVIEW COMMENTS

Reviewer	Comment	Response
Question 1: Are the objectives, scope, and methods for this review clearly described?		
1	Yes.	Thank you.
2	Yes, the objectives, scope and methods were clearly described.	Thank you.
3	Overall, the objectives, scope, and methods are clear, and it appears that the investigators' approach was thorough and descriptive. Below are some specific comments that hopefully will be helpful in finalizing the report. 1. Many studies excluded patients with severe symptoms – this is an important limitation given that the mean baseline scores on symptom measures of Veterans receiving CBT and other evidence-based psychotherapies are typically in the severe range. This may affect the generalizability of the findings to the Veteran patient population. At minimum, recommend that this be emphasized and included as a limitation in the executive summary. 2. Similarly, studies examined generally included few older individuals (who represent the majority of the Veteran patient population) and seemingly included primarily individuals with significant interest and experience using computers and/or the Internet. While this is appropriately noted in the discussion of the findings, I think the implications of this should be further emphasized. In fact, it appears that no one truly older individual, using the conventional definition for this age group (65+), was included in any of the studies. 3. In addition, examinations of CBT with Veterans, specifically, have shown that the therapeutic alliance (emphasized in in-person VA CBT protocols) is significantly related to outcome – and this relationship is even greater among older Veterans. This seems at least worthy of mention. 4. There is limited mention of to what extent and how the quality of studies was considered. Were only studies of certain quality included and how many studies were excluded? 5. Psychotropic medication was allowed in 75 percent of the studies examined – if individuals were newer to treatment and not receiving psychotropic medication for some time, improvements could have been due to the psychotropic medication. Were studies excluded if this potential confound was not addressed? If not, this should be noted as a limitation 6. I do not recommend combining studies examining PTSD and anxiety disorder and reporting the effect size across these studies.	1. We agree that this issue is important for applicability to the Veteran population. We have given this point greater prominence (see pages 56-58). We think that CBT delivered via computer might be well suited to patients seen in primary care, who typically have mild to moderate severity. We agree that the evidence does not directly address patients with severe symptoms and that these patients might be served better by a clinic-based therapist in case of the need for crisis intervention. 2. We agree that this is an important issue related to applicability of the findings. Older adults may respond differentially to treatment compared with younger adults and may have different facility with or different response to computerized CBT. We have emphasized the absence of studies in older adults in the Executive Summary and Discussion. 3. This is an important consideration, and we think our analysis of the level of human support for cCBT is relevant to this question. As a result, we have added some discussion of the potentially important role of therapeutic alliance to the section of the Clinical and Policy Implications that addresses cCBT support. 4. Otherwise eligible studies were included without regard to the quality rating. Quality ratings are detailed in Appendix B and provided for each study in Appendix D. Quality rating (Risk of Bias) is included in the qualitative description of the studies and considered explicitly in the SOE rating (see Methods section). 5. With the literature from the updated search added, this falls to 70 percent. The reviewer makes a good point; however, all studies that allow for concurrent medication required that patients be on a stable dose for a period of time prior to study enrollment or the patients were excluded. This clarification has been added. 6. We did not combine studies to compute a summary estimate of effect for studies examining PTSD and anxiety disorders. We combined major depressive disorder and depressive symptoms.

Reviewer	Comment	Response
3 (continued)	7. The method of calculating the SMD by dividing the result by the pooled standard deviations of the two groups is considered by some to be a less conservative method for calculating the effect size.	7. We acknowledge that there are different approaches to calculating the SMD, including approaches that correct for small sample sizes. We conducted a sensitivity analysis and found little impact on the estimates (≤0.01SMD) across methods.
4	Yes. The authors prepared a very clear and comprehensive review of the topic.	Thank you.
Question 2: Is there any indication of bias in our synthesis of the evidence?		
1	No. The systematic review was clearly well done and free of bias, following all standards in existence regarding transparency in review.	Thank you.
2	Yes, bias was examined and was minimal	Thank you.
3	No.	Thank you.
4	No.	Thank you.
Question 3: Are there any published or unpublished studies that we may have overlooked?		
1	No. The internet based and computer based projects are all well represented. You will need to do a new review in a few years to include apps and mobile mental health games (once data from the Harnessing Technologies RFA are published).	Thank you for the suggestion.
2	Yes. The authors refer to additional studies that will be included in the manuscript and it was not clear why these studies were not included in the current report or at least at a minimum, discussion provided as to whether these studies influence outcomes reported in anyway	All but one of the additional eight studies referred to were published in 2013 and found when we updated the literature search on August 30, 2013. We have rerun all analyses and updated all outcomes affected by these new studies.
3	No. None identified.	Thank you.
4	No.	Thank you.
Question 4: Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.		
1	The review as comprehensive, I have no other comments	Thank you.
2	May highlight in the review articles that specifically included veterans. In general, the report was clearly written, justifications for decisions were sound, and the report addresses an important topic. Page 34 – 35 the x axis changes from figure 7 to figure 8. Helpful to ensure that the labels are consistent for all graphs Worth considering for the paper, the role of adherence. Did interventions that have higher rates of intervention adherence result in better outcomes? What aspects of treatment intervention adherence were helpful?	Our review of the literature found only one article specifically addressing Veterans. This is given special emphasis in the report. We chose the X axis such that the effect estimate and 95% CI for most studies is included. This means the X axis is ± 2.0 for almost all graphs but in selected cases had to be modified to meet our graphical display criteria. We conducted a meta-regression analysis for the subset of studies reporting proportion of patients completing all modules. There was no association with the estimate of treatment effect. With regard to the relationship between the treatment intervention and adherence, there was not sufficient detail or number of studies reporting these characteristics to evaluate this association.

Reviewer	Comment	Response
3	1. Electronic CBT (eCBT) is not typically the standard term used for referring to computerized CBT. This is more commonly referred to as "computer-assisted", "computer-administered", "computerized", "computer-based", etc. Further, "eCBT" is the name of a specific, proprietary phone app for CBT for depression.	1. We have revised the report to use the term computerized CBT (cCBT).
	2. The low completion rate observed appears to be significantly lower than that for in-person CBT (e.g., Eftekhari et al., 2013; Karlin et al., 2012).	2. We agree and have noted in the summary of evidence that the adherence rates were relatively low compared with those observed for in-person therapy. In addition, improved adherence/completion was identified as a future direction for cCBT.
	3. "Mental health disorders" should read "mental disorders."	3. We have made the correction.
	4. I appreciate the investigators' focus on the relationship between eCBT support and patient outcomes. The issue of therapist support has been an important one in this area, as it has appeared that level of therapist supported is positively associated with outcomes and adherence. As noted by the investigators, the "supported" category included a broad range of support types, making it difficult to fully examine this question. Additional, systematic research examining this issue would be worthwhile. However, the current investigation appears to confirm previous findings.	4. Acknowledged; thank you for your comment.
	5. It would likely be useful to report the adherence/completion rate by condition cluster, in addition to or place of the overall rate across diagnostic areas. Looking at the rates reported for each individual study, there appears to be very wide variability. Is there evidence of why this was? Presumably, this may be related to level of therapist involvement, as some previous research had suggested. Thank you for the opportunity to review this report.	5. Thank you for this suggestion. We found the proportion completing all modules does vary by condition cluster. We have added this information to the results and discussion of adherence. There were not sufficient studies reporting adherence to the control group within condition clusters to examine an association between therapist support and adherence.
4	Very minor comments: 1. There was a possible typo on page 24, should be 218 excluded rather than 220 to get numbers to add up	1. We have updated and corrected the numbers in the literature flow.
	2. In cases when there were multiple measures in the same study, the authors chose to calculate the mean effect from all instruments (Page 21). While this sounds reasonable to me, I wonder if the authors chose the same approach if a study pre-specified a primary outcome.	2. We compared the authors' prespecified primary measure(s) to the outcome measures included in our analyses. In almost all instances there was perfect agreement.

Reviewer	Comment	Response
Optional Dissemination and Implementation Questions		
Question 5: Are there any clinical performance measures, programs, quality improvement measures, patient care services, or conferences that will be directly affected by this report? If so, please provide detail.		
1	All I am aware of is the National Center for PTSD and their work around mobile mental health – they would benefit from this report. Worthwhile at some point to do a review for older adults and technology interventions, given the aging of the veteran population	Thank you for the suggestion.
2	If issues related to IT and confidentiality are addressed in the VA, the report may be able to influence policy by providing electronic CBT to veterans to address the continued lack of adequate mental health providers	Thank you for the suggestion about IT. This has been discussed in a little more detail in the revised discussion section.
3	No comments	Thank you.
4	No comments	Thank you.
Question 6: Please provide any recommendations on how this report can be revised to more directly address or assist implementation needs.		
1	Maybe more on how these data affect older populations.	Thank you for the suggestion.
2	Further clarify what the recommendations the VA can use to implement electronic CBT. A recommendation for a comparator may be examining outcomes of individuals who can select receiving cognitive behavioral interventions via life person, or computer based. In reality, this is likely the way these programs would likely be introduced. Consider providing more comment on the resources and staffing of the use of ECBT? If there are a limited of mental health clinicians, is using computer based CBI a way to offset these challenges?	Thank you, we have provided further explanation in the Discussion section of the report.
3	No comments	Thank you.
4	No comments	Thank you.
Question 7: Please provide us with contact details of any additional individuals/stakeholders who should be made aware of this report.		
1	David Mohr at NorthWestern	Thank you for the suggestion.
2	No comments	Thank you.
3	No comments	Thank you.
4	No comments	Thank you.

APPENDIX D. STUDY CHARACTERISTICS TABLES

Table D-1. Detailed study characteristics of cCBT interventions

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
Major depressive disorder (11 trials)						
Andersson, 2005[1]	Europe (Sweden) Newspaper advertisement Government 117	Total: 36.14 (NR) Grand mean: 75% NR No	MDD CIDI-SF Allowed, not managed	EOT: 10 wk (mean) Followup: 26 wk BDI BAI MADRS Quality of life Adherence Therapist productivity	2 cCBT Attention control (online discussion group)	RCT Fair
Berger, 2011[2]	Europe (Switzerland and Germany) Advertisement and website University affiliated 76	Grand mean: 38.8 (NA) Grand mean: 69.7% NR No	MDD, dysthymia BDI-II >13 Allowed, not managed	EOT: 10 wk; Followup: 26 wk BDI WHOQOL-BREF Adherence Therapist productivity	3 cCBT (guided) cCBT (unguided) Waitlist	RCT Good
Carlbring, 2013[3]	Europe (Sweden) Advertisement: website, newspaper Government 80	Total: 44.4 (13.5) Total: 82.5% NR No	MDD MADRS SCID Allowed, not managed	EOT: 8 wk Followup: 13 wk BDI-II BAI MADRS HRQOL	2 cCBT (BA) Waitlist	RCT Good
Choi, 2012[4]	Australia Mass media Government 63	Grand mean: 39.2 (NA) Grand mean: 80.5% Asian: 100% No	MDD NR Allowed, not managed	EOT: 8 wk Followup: 26 wk BDI (Chinese version) PHQ-9 (Chinese version) HRQOL: SDS ≥50% reduction in BDI Adherence	2 cCBT Waitlist	RCT Fair
Johansson, 2012[5]	Europe (Sweden) Newspaper advertisement, waitlist from prior study Government 121	Total: 45 (12.1) Total: 71.1% NR No	MDD MADRS >14 and <36 Allowed, not managed	EOT: 10 wk Followup: 6 mo BDI-1 MADRS BAI QOLI	3 Standard cCBT Tailored cCBT Attention control	RCT Fair

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
Kessler, 2009[6]	Europe (UK) Within 3 primary care centers Government 297	Grand mean: 34.95 (NA) Grand mean: 68% NR No	New episode of depression BDI ≥14 Allowed, not managed	EOT: 16 wk Followup: 34.8 wk HRQOL: SF-12 EQ5D BDI Reduction to BDI <10	2 IPCRESS study TAU	Cluster RCT Fair
Perini, 2009[7]	Australia Web University affiliated 48	Grand mean: 49.3 (NA) Grand mean: 76% NR No	MDD PHQ-9 >5 Allowed, not managed	EOT: 8 wk No followup BDI-II PHQ-9 Adherence Therapist productivity	2 cCBT Waitlist	RCT Fair
Titov, 2010[8]	Australia Website Government 141	Grand mean: 43.3 (NA) Grand mean: 73.3% NR No	MDD PHQ-9 Allowed, not managed	EOT: 9 wk Followup: 17.4 wk PHQ-9 BDI-II Adherence Therapist productivity	3 cCBT (clinician assisted) cCBT (technician assisted) Waitlist	RCT Good
Vernmark, 2010[9]	Europe (Sweden) University campus mail and newspaper; radio interview Government 88	Grand mean: 36.6 (NA) Grand mean: 68.2% NR No	MDD MADRS-S >14 Allowed, not managed	EOT: 8 wk Followup: 26 wk Quality of life inventory BID BAI MADRS-SR SCID (no depression diagnosis); value reflects N without depression Therapist productivity	3 cCBT (supported) cCBT (self-help) Waitlist	RCT Good
Williams, 2013[10]	Australia Website Government 297	Grand mean: 44.81 (NA) Grand mean: 76% NR No	MDD MINI NR	EOT: 11 wk No followup BDI-II PHQ-9 K10 AST-D SST STAI-T HRQoL	2 CBM + cCBT Waitlist	RCT Fair
Wright, 2005[11]	US (Kentucky) Advertisement, referral University affiliated 45	Grand mean: 40.2 (NA) Grand mean: 75.5% NR No	MDD, dysthymia BDI ≥14 Not allowed	EOT: 8 wk Followup: 26 wk HADS BDI Cognitive therapy awareness Adherence Therapist productivity	3 cCBT Standard CBT Waitlist	RCT Fair

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
Depressive symptoms (15 trials)						
Clarke, 2002[12]	US (Oregon) Mailing to HMO members Kaiser HMO 299	Grand mean: 43.9 (NA) Grand mean: 75.5% White: 94.5% No	MDD, minor depression NR Allowed, not managed	EOT: 17 wk Followup: 34.8 wk CES-D	2 cCBT Waitlist	RCT Good
de Graaf, 2009[13]	Europe (Netherlands) Mailed invitation to complete online screening questionnaire Government 303	Grand mean: 44.9 (NA) Grand mean: 55.7% NR No	Significant depressive symptoms BDI-II >16 Not allowed	EOT: 13 wk Followup: 52.1 wk SF-36 BDI-II BDI decrease ≥9 points WSAS Adherence	3 cCBT + TAU cCBT (no support) TAU	RCT Fair
Farrer, 2011[14]	Australia Callers to lifeline telephone counseling service Government 188	Grand mean: 41.0 (NA) Grand mean: 82.7% NR No	Significant depressive symptoms K10 ≥22 NR	EOT: 6 wk Followup: 26 wk CES-D CES-D <16 Adherence	3 cCBT (supported) cCBT (not supported) TAU	RCT Fair
Glozier, 2013[15]	Australia Recruited from cohort study University affiliated 562	Grand mean: 58.0 (NA) Grand mean: 61.4% NR No	Depression symptoms (mild to moderate) PHQ-9 >8 Allowed, not managed	EOT: 12 wk No followup PHQ-9 GAD-7 WHODAS	2 cCBT Attention control	RCT Good
Griffiths, 2012[16]	Australia Mailing to general population Government 355	Grand mean: 43.7 (NR) Grand mean: 70.0% NR No	Depressive symptoms K10 >22 NR	EOT: 13 wk Followup: 52.1 wk CES-D <16 Adherence	3 cCBT cCBT + internet support Attention control	RCT Fair
Hickie, 2010[17]	Australia Primary care Government 83	Grand mean: 33.4 (NA) Grand mean: 71.5% NR No	Significant depressive symptoms K10 >19 Not allowed	EOT: 8 wk Followup: 52.1 wk K10 <16	2 cCBT TAU	Cluster RCT Poor

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
Levin, 2011[18]	US (Oregon) Primary care Kaiser HMO 191	Grand mean: 43.5 (NA) Grand mean: 77% Grand mean: White: 90.15% Black: 2.2% Hispanic: 3.1% Asian: 0.5% Other: 4.1% No	Significant depressive symptoms NR Allowed, not managed	6 wk 26 wk SCID CES-D STAI S-STAI	2 cCBT (supported) TAU	RCT Good
Lintvedt, 2013[19]	Europe (Norway) University (mailed questionnaire to all students) University affiliated 163	28.2 (7.4) 76.7% NR No	Depressive symptoms 62.8% "unmet need for help" NR	8 wk No followup K10 screening CES-D ATQ Treatment depression literacy	2 Informational website + cCBT Waitlist/TAU	RCT Fair
McKinnon, 2008[20]	Australia Community (mailed questionnaire to participants from electoral roll) University affiliated 525	Grand mean: 36.0 (NA) Grand mean: 72.5% NR No	Significant depressive symptoms K10 ≥22 NR	EOT:6 wk Followup:52 wk CES-D ATQ	3 cCBT Information control (Blue Pages) Attention control	RCT Fair
Moritz, 2012[21]	Western Europe (Germany) Online advertising University affiliated 210	Grand mean: 38.6 (NA) Grand mean: 78.6% NR No	Depressive symptoms NR Allowed, not managed	EOT: 8 wk No followup BDI-II DAS WHOQOL	2 cCBT Waitlist	RCT Fair
Spek, 2007[22]	Europe (Netherlands) Mail; newspaper and letter of invitation to all older adults in the city Government 301	Grand mean: 54.7 (NA) Grand mean: 63.4% NR No	Minor depression Edinburgh depression scale >12 NR	10 wk 52.1 wk BDI-II Adherence	3 cCBT Group CBT Waitlist	RCT Good
van Bastelaar, 2008[23]	Europe (Netherlands) Web/mail: Open-access study website University medical center 255	Total: 50.0 (12.0) Total: 61% White: 89% Yes	MDD, dysthymia, minor depression, or significant depressive symptoms and type 1 or type 2 diabetes mellitus CES-D ≥16 Allowed, not managed	12 wk No followup Perceived health status: SF-12 CES-D PAID (diabetes-specific emotional distress) Adherence	2 cCBT Waitlist	RCT Poor

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
van der Zanden, 2012[24]	Europe (Netherlands) Advertisement: promotional material in physician's office and educational institutions and websites Mental health clinics 244	Total: 20.9 (2.2) Total 84.4% NR No	Significant depressive symptoms CES-D: 10 to 45 NR	EOT: 12 wk Followup: 6 mo CES-D HADS Adherence	2 cCBT Waitlist	RCT Fair
Wagner, 2013[25]	Europe (Germany, Switzerland) Advertisements in newspapers, local facilities, university websites Government 62	Grand mean: 38.0 Grand mean: 65% NR Yes: gender	Depressive symptoms BDI-II Grand mean: 23.2 Allowed, not managed	EOT: 8 wk Followup: 3 mo BDI-II BSI SCL anxiety subscale ATQ	2 cCBT Face-to-face	RCT Fair
Warmerdam, 2008[26]	Europe (Netherlands) Website, newspaper advertisement Government 263	Grand mean: 45.0 (NA) Grand mean: 71.1% NR No	Significant depressive symptoms CES-D ≥16 NR	EOT: 8 wk No followup EQ5D CES-D HADS Clinically significant change Adherence Therapist productivity Cost	3 cCBT PST Waitlist	RCT Fair
Mixed depression and anxiety (3 trials)						
Newby, 2013[27]	Australia Previous interest, internet advertising University affiliated 109	44.30(12.2) 77.8% NR Yes	GAD and/or MDD MINI Allowed, not managed	EOT: 10 wk Followup: 3 mo PHQ-9 GAD-7 WHODAS-II Adherence	2 cCBT Waitlist	RCT Good
Proudfoot, 2003[28]	Europe (UK) Primary care Government 274	Grand mean: 43.5 (NA) Grand mean: 73.8% Grand mean: White: 80% Black: 3.6% Asian: 1.95% Other: 4.75% No	Minor depression, significant depressive symptoms, GAD, panic disorder, anxiety NOS, significant anxiety symptoms, and phobia GHQ-12 ≥4 CIS-R ≥12 Not allowed	EOT: 9 wk Followup: 26 wk WSAS BDI BAI Hospitalization Cost	2 cCBT TAU	RCT Fair

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
Proudfoot, 2004[29]	Europe (UK) Primary care General practice in London and southeast England 167	Grand mean: 44.7 (NA) Grand mean: 73.7% Grand mean: White: 88% Black: 5% Asian: 3.5% Other: 4% No	Significant depressive symptoms, anxiety NOS, significant anxiety symptoms, and other (anxious and/or depressed) GHQ-12 ≥4 CIS-R (PROQSY) ≥12 Not allowed	EOT: 89 wk Followup: 26 wk WSAS BDI BAI	2 cCBT TAU	RCT Fair
Generalized anxiety disorder (4 trials)						
Andersson, 2012[30]	Europe (Sweden) Advertisement (website, newspaper) Not described 81	Grand mean: 42 (NA) Grand mean: 76% NR No	GAD NR Allowed, not managed	EOT: 8 wk Followup: 21 to 22 wk QOLI BDI-II PSWQ BAI (0-63) Adherence	2 cCBT Waitlist	RCT Good
Paxling, 2011[31]	Europe (Sweden) Advertisement in newspaper, website Academic clinics 89	Grand mean: 39.3 (NA) Grand mean: 80% NR No	GAD PSWQ >53 GAD-Q-IV >5.7 Allowed, not managed	EOT: 8 wk Followup: 52.1 wk QOLI BDI PSWQ BAI Adherence	2 cCBT Waitlist	RCT Fair
Robinson, 2010[32]	Australia Website www.virtualclinic.org.au NR 150	Grand mean:47(NA) Grand mean: 68.4% NR Yes: marital status, age	GAD NR Allowed, not managed	EOT: 11 wk Followup: 13 wk PHQ-9 PSWQ GAD-7 Therapist productivity	3 cCBT (clinician) cCBT (technician) Waitlist	RCT Good
Titov, 2009[33]	Australia Website www.virtualclinic.org.au Government 48	Total: 44.0 (12.98) Total: 75% NR No	GAD GAD section of MINI to determine if patient met DSM-IV criteria for GAD Allowed, not managed	EOT: 10 wk No followup SDS PHQ-9 PSWQ GAD-7	2 cCBT Waitlist	RCT Fair

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
Panic disorder (10 trials)						
Bergstrom, 2010[34]	Europe (Sweden) Primary care, self-referral Government 113	Grand mean: 34.2 (NA) Grand mean: 61.5% NR No	Panic disorder DSM-IV criteria for panic disorder with or without agoraphobia on MINI Allowed, not managed	EOT: 10 wk Followup: 26 wk SDS MADRS ASI PDSS Response on PDSS ≥40% Cost	2 cCBT Group CBT	RCT Good
Carlbring, 2001[35]	Europe (Sweden) Website and mail advertisement Government 31	Total: 34 (7.5); range (21 to 51) Total: 70.7% NR No	Panic disorder No Allowed, not managed	6 to 14 wk postrandomization QOLI BDI BAI MADRAS-SR Therapist productivity	2 cCBT Waitlist	RCT Poor
Carlbring, 2005[36]	Europe (Sweden) Waitlist of participants from Carlbring, 2001, study Government 49	Grand mean: 35.0 (NA) Grand mean: 71.5% NR No	Panic disorder No Allowed, not managed	EOT: 10 wk Followup: 52 wk QOLI MADRS-SR BDI BAI ACQ Adherence	2 cCBT Face-to-face CBT	RCT Fair
Carlbring, 2006[37]	Europe (Sweden) Waitlist of people who had expressed interest in participating in internet-administered self-help program on panic disorder Government 60	Total: 36.7 (10.0) Total: 60% NR No	Panic disorder DSM-IV criteria for panic disorder Allowed, not managed	EOT: 10 wk Followup: 9 mo QOLI MADRS BDI BAI Body sensations Questionnaire Adherence	2 cCBT Waitlist	RCT Good
Kenardy, 2003[38]	Europe (Scotland) and Australia Primary care and mental health specialty University affiliated 121	Total: 36.8 (10.0) Total: 75.5% NR Yes: education	Panic disorder No Allowed, not managed	EOT: 3 wk Followup: 26 wk Composite panic-anxiety measure STAI-Trait Change on STAI-Trait Cost	3 cCBT Face-to-face Waitlist	RCT Fair

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
Kiropoulos, 2008[39]	Australia Website, advertisement Government 86	Total Age: 39.0 (11.13) Grand mean: 72.5% NR No	Panic disorder No Allowed, not managed	EOT: 12 wk No followup WHO QOL DASS ADIS clinician overall panic disorder rating PDSS Adherence Therapist productivity	2 cCBT Face-to-face	RCT Good
Klein, 2006[40]	Australia Website, mail advertisement Government 55	Range: 18 to 70 years Total: 81% NR NR	Panic disorder No Allowed, not managed	EOT: 12 wk Followup: 3 mo HRQOL "health rating" DASS depression PDSS (interview) BVS Panic disorder clinician ratings Adherence Therapist productivity Cost	2 cCBT Information control	RCT Fair
Richards, 2006[41]	Australia Website, advertisement Government 32	Grand mean: 36.9 (NA) Grand mean: 30.7% NR Yes: gender	Panic disorder 2 points greater than any secondary diagnosis on the clinician's 9-point severity rating scale in the ADIS-IV Allowed, not managed	EOT: 8 wk Followup: 13 wk QOL (psychological) DASS (depression) PDSS ACQ Therapist productivity GP visits pre-post	3 cCBT cCBT + stress management Information control	RCT Poor
Silfvernagel, 2012[42]	Europe (Sweden) Information on web; recruited via email Not specified 57	Grand mean: 32.4 (NA) Grand mean: 64.8% NR Yes: gender	Panic symptoms with significant comorbid depressive or anxiety symptoms No Allowed, not managed	EOT: 8 wk Followup: 60 wk QOLI MADRS-S PDSS BAI PDSS score decrease by ≥40% Adherence (# of patients completed sessions) Therapist productivity	2 cCBT Waitlist	RCT Fair
Wims, 2010[43]	Australia Website University affiliated 141	Grand mean: 42.3 (NA) Grand mean: 76% NR No	Panic disorder No Allowed, not managed	EOT: 9 wk Followup: 13 wk SDS PHQ-9 ACQ PDSS Adherence Therapist productivity	2 cCBT Waitlist	RCT Good

Study	Location Recruitment Setting Organization Total N	Age in Years (SD) % Female % Race/ethnicity Baseline differences?	Target Condition Baseline Severity Medications	Study Duration Outcomes Reported	Number of Arms Intervention Comparator	Design Quality
PTSD (2 trials)						
Litz, 2007[44]	US Advertisement on website U.S. Department of Defense 45	Grand mean: 39.2 (NA) Grand mean: 22% Black: 77.5% No	PTSD NR Allowed, not managed	EOT: 8 wk Followup: 6 mo PTSD-SS BDI-II BAI	2 cCBT Internet support group	RCT Fair
Spence, 2011[45]	Australia Website www.virtualclinic.org.au, email newsletter from www.beyondblue.org.au, mail advertisement, local newspaper NR 44	Grand mean: 42.5 (NA) Grand mean: 81.5% NR No	PTSD No Allowed, not managed	EOT: 8 wk Followup: 13 wk PHQ-9 PCL-C GAD-7 SDS Therapist productivity	2 cCBT Waitlist	RCT Fair
Anxiety symptoms (2 trials)						
Kenardy, 2006[46]	Australia Psychology class Academic clinics 83	Total: 20.7 (6.29) Total: 78.3% NR NR	Significant anxiety symptoms Anxiety sensitivity >24 Not allowed	EOT: 6 wk Followup: 26 wk CES-D ASI BSQ Adherence	2 cCBT Waitlist	RCT Poor
Ruwaard, 2010[47]	Europe (Netherlands) Website, mail advertisement Government 58	Grand mean: 38.5 (NA) Grand mean: 73% NR Yes: gender	Greater than or equal to subsyndromal panic disorder NR Allowed, not managed	EOT: 13 wk (variable) Followup: 156 wk DASS-Depression PDSS-SR PDSS-SR Responder (<8) BSQ Therapist productivity	2 cCBT Waitlist	RCT Fair

Table D-2. Program components of cCBT interventions

Study Program Name cCBT Level	Behavior Activation	Cognitive Restructuring	Exposure	Interpersonal Skills Assertiveness	Lifestyle Factors	Problem Solving	Relapse Prevention	Relaxation Training	Other Components
Major depressive disorder: 11 trials, 15 arms									
Andersson, 2005[1] No name cCBT-S	Yes	Yes	No	NR	Yes	NR	Yes	NR	NR
Berger, 2011[2] DEPREXIS Arm 1: cCBT-S Arm 2: cCBT-NS	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	Arm 1: Psychoeducation, dreamwork, emotional work Arm 2: NA
Carlbring, 2013[3] Depressionshjälpen cCBT-S	Yes	Yes	No	NR	Yes	NR	Yes	NR	Acceptance and commitment therapy—mindfulness
Choi, 2012[4] SADNESS (adapted to Chinese) cCBT-LS	Yes	Yes	No	Yes	Yes	Yes	NR	NR	NR
Johansson, 2012[5] No name Arm 1: cCBT-S Arm 2: cCBT-S	Yes	Yes	No	NR	Yes	Yes (Tailored only)	Yes	Yes (Tailored only)	Arm 1: Tailored sleep management, mindfulness, Arm 2: Panic, social anxiety, worrying stress
Kessler, 2009[6] No name cCBT-LS	55 minutes of instant messaging for 10 sessions	NA	No	NA	NA	NA	NA	NA	NR
Perini, 2009[7] SADNESS cCBT-S	Yes	Yes	No	Yes	Yes	Yes	NR	NR	NR
Titov, 2010[8] SADNESS Arm 1: cCBT-LS Arm 2: cCBT-LS	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	Arm 1: Topics that came up on discussion forum Arm 2: Program script only
Vernmark, 2010[9] No name Arm 1: cCBT-S Arm 2: cCBT-S	Yes	Yes	No	NR	Yes	NR	Yes	NR	Arm 1: Goal setting Arm 2: Topics that came up while tailoring to the individual patient

Study Program Name cCBT Level	Behavior Activation	Cognitive Restructuring	Exposure	Interpersonal Skills Assertiveness	Lifestyle Factors	Problem Solving	Relapse Prevention	Relaxation Training	Other Components
Williams, 2013[10] CBM +Sadness CBT-LS	Yes	Yes	No	Yes	Yes	Yes	NR	NR	Cognitive bias modification
Wright, 2005[11] No name cCBT-AT	Yes	Yes x 3	No	NR	Yes	Yes	Yes	NR	Task breakdown
Depressive symptoms: 15 trials, 19 arms									
Clarke, 2002[12] Overcoming Depression via the Internet cCBT-NS	NR	Yes	No	NR	NR	NR	NR	NR	Skills training, psychoeducation
de Graaf, 2009[13] CYL[a] + treatment as usual Arm 1: cCBT-NS Arm 2: cCBT-NS	NR	NR	No	Yes	NR	Yes	NR	NR	Arm 1: Stress management, planning Arm 2: NA
Farrer, 2011[14] MoodGYM Arm 1: cCBT-LS Arm 2: cCBT-NS	Yes	Yes	No	Yes	NR	Yes	NR	Yes	Arm 1: Psychoeducation Arm 2: NA
Glozier, 2013[15] E-couch cCBT-NS	NR	Yes	No	Yes	Yes	NR	NR	NR	Psychoeducation based on Blue Pages
Griffiths, 2012[16] E-couch Arm 1: cCBT-NS Arm 2: cCBT-NS	NR	NR	No	Yes	Yes	NR	NR	Yes	Arm 1: Psychoeducation, internet support group Arm 2: Psychoeducation
Hickie, 2010[17] MoodGYM cCBT-NS	Yes	Yes	No	Yes	NR	Yes	NR	Yes	Psychoeducation
Levin, 2011[18] Wellness Workshop[a] cCBT-NS	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	NA

Study Program Name cCBT Level	Behavior Activation	Cognitive Restructuring	Exposure	Interpersonal Skills Assertiveness	Lifestyle Factors	Problem Solving	Relapse Prevention	Relaxation Training	Other Components
Lintvedt, 2013[19] MoodGYM + Blue Pages cCBT-NS	Yes	Yes	No	Yes	Yes	NR	NR	Yes	Psychoeducation
McKinnon, 2008 #290[20] MoodGYM cCBT-S	Yes	Yes	No	Yes	NR	Yes	NR	Yes	Psychoeducation
Moritz, 2012[21] Deprexis cCBT-NS	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	Arm 1: Psychoeducation, dreamwork, emotional work Arm 2: NA
Spek, 2007[22] No name[a] cCBT-NS	Yes	Yes	No	Yes	NR	NR	NR	Yes	Psychoeducation
van Bastelaar, 2008[23] CYL-DM[a] cCBT-S	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	Adapted specifically for patients with diabetes
van der Zanden, 2012[24] Master Your Mood[a] cCBT-LS	Yes	Yes	No	Yes	NR	NR	Yes	NR	Psychoeducation
Wagner, 2013[25] No name cCBT-S	Yes	Yes	No	Yes	NR	NR	Yes	NR	Psychoeducation
Warmerdam, 2008[26] No named programs Arm 1: cCBT-S[a] Arm 2: cCBT-S	Arm 1: Yes Arm 2: No	Yes	No	Yes	NR	Arm 1: NR Arm 2: Yes	Yes	NR	Arm 1: Psychoeducation, based on classic CBT[a] Arm 2:Based on classic problem-solving therapy
Mixed depression and anxiety: 3 trials, 3 arms									
Newby, 2013[27] Worry and Sadness Program cCBT-LS	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Psychoeducation
Proudfoot, 2003[28] Beating the Blues cCBT-NS	Yes	Yes x 3	No	NR	Yes	Yes	Yes	NR	Introduction is psychoeducation, goal-setting planning; task breakdown

Study Program Name cCBT Level	Behavior Activation	Cognitive Restructuring	Exposure	Interpersonal Skills Assertiveness	Lifestyle Factors	Problem Solving	Relapse Prevention	Relaxation Training	Other Components
Proudfoot, 2004[29] Beating the Blues cCBT-LS	Yes	Yes x 3	No	NR	Yes	Yes	Yes	NR	Introduction is psychoeducation, goal-setting planning; task breakdown
Generalized anxiety disorder: 4 trials, 5 arms									
Andersson, 2012[30] No name cCBT-S	NR	Yes	Yes	Yes	Yes	Yes	NR	Yes	Psychoeducation, worry exposure
Paxling, 2011[31] No name cCBT-S	NR	Yes	Yes	Yes	Yes	Yes	NR	Yes	Psychoeducation, worry exposure
Robinson, 2010[32] Worry program Arm 1: cCBT-LS (clinician) Arm 2: cCBT-LS (technician)	NR	Yes	Yes	Yes	Yes	Yes	NR	Yes	Arm 1: Psychoeducation, worry exposure, online discussion forum Arm 2: Same, but no forum
Titov, 2009[33] Worry program cCBT-LS	NR	Yes	Yes	Yes	Yes	Yes	NR	Yes	Psychoeducation, worry exposure
Panic disorder: 10 trials, 11 arms									
Bergstrom, 2010[34] No name cCBT-S	NR	Yes	Yes	NR	NR	NR	Yes	NR	Psychoeducation, panic exposure
Carlbring, 2001[35] No name cCBT-S	NR	Yes	Yes	Yes	NR	NR	Yes	Yes (breathing)	Psychoeducation, panic exposure
Carlbring, 2005[36] No name cCBT-S	NR	Yes	Yes	Yes	NR	NR	Yes	Yes (breathing)	Psychoeducation, panic exposure
Carlbring, 2006[37] No name cCBT-LS	NR	Yes	Yes	Yes	NR	NR	Yes	Yes (breathing)	Psychoeducation, panic exposure
Kenardy, 2003[38] No name cCBT-AT	NR	Yes	Yes	NR	NR	NR	NR	Yes (breathing)	Goal-setting, panic exposure

Study Program Name cCBT Level	Behavior Activation	Cognitive Restructuring	Exposure	Interpersonal Skills Assertiveness	Lifestyle Factors	Problem Solving	Relapse Prevention	Relaxation Training	Other Components
Kiropoulos, 2008[39] Panic Online cCBT-S	NR	Yes	Yes	NR	NR	NR	Yes	Yes	Psychoeducation, panic exposure
Klein, 2006[40] Panic Online cCBT-S	NR	Yes	Yes	NR	NR	NR	Yes	Yes	Psychoeducation, panic exposure
Richards, 2006[41] Panic Online Arm 1: cCBT-S Arm 2: cCBT-S	NR	Yes	Yes	Arm1: NR Arm 2: Yes in stress modules	Arm1: NR Arm 2: Yes in stress modules	NR	Yes	Yes	Arm 1: Psychoeducation, panic exposure Arm 2: Same + 6 modules on stress management
Silfvernagel, 2012[42] No name cCBT-S	NR	NR	Yes	NR	NR	NR	Yes	NR	Psychoeducation, panic exposure
Wims, 2010[43] Panic Program cCBT-S	NR	Yes	Yes	NR	NR	NR	Yes	NR	Psychoeducation, de-arousal, panic exposure
PTSD: 2 trials, 2 arms									
Litz, 2007[44] DE-STRESS cCBT-LS	Yes	NR	Yes	NR	NR	NR	Yes	Yes	Planning, trauma exposure, stress management
Spence, 2011[45] No name cCBT-LS	Yes	Yes	Yes	Yes	Yes	Managing panic attacks	Yes	NR	De-arousal, trauma exposure
Anxiety symptoms: 2 trials, 2 arms									
Kenardy, 2006[46] Anxiety Prevention Program cCBT-S	NR	Yes	Yes	NR	NR	NR	Yes	Yes	Psychoeducation, anxiety exposure
Ruwaard, 2010[47] Interapy cCBT-S	NR	Yes	Yes	NR	NR	NR	Yes	Yes	Psychoeducation, awareness, anxiety exposure

[a] Interventions that are loosely based on Lewinsohn's model of depression: Lewinsohn PM, Youngren MA, Grosscup SJ. Reinforcement and depression. In RA Dupue (Ed*.),* The psychobiology of depressive disorders: Implications for the effects of stress (pp. 291-316). New York: Academic Press, 1979.

Table D-3. General characteristics of cCBT interventions

Study Comparison and Arm (if applicable)	Recruitment	Clinical Context	Program Name	Setting	Technical Support	Duration (Weeks)	Module Number	Planned Contacts
Major depressive disorder: 11 trials, 15 arms								
Andersson, 2005[1] cCBT-S vs. AC	Advertisements in newspapers	Not established, but AC was moderated online group	No name	Nonclinical	NR	8-10	5	≥6
Berger, 2009[2] Arm 1: cCBT-S vs. cCBT-NS Arm 2:cCBT-NS vs. WL	Advertisement and website	No established clinical relationship	Deprexis®	Nonclinical	NR	10	10	10
Carlbring, 2013[3] cCBT-S vs. WL	Advertisement and website	No established clinical relationship	*Depression-shjälpen*	Nonclinical	Yes	8	7	7
Choi, 2012[4] cCBT-LS vs. WL	Mass media (unspecified)	No established clinical relationship	Sadness (adapted to Chinese)	Nonclinical	NR	8	6	6
Johansson, 2012[5] Arm 1: cCBT-S (standard) Arm 2: cCBT-S (tailored) vs. AC	Advertisements in newspaper (waiting list)	No established clinical relationship	No name	Nonclinical	Yes	10	8 (standard) 8-10 (tailored)	10
Kessler, 2009[6] cCBT-LS vs. TAU	Primary care	Yes, medical home	No name	Nonclinical	NR	16	10	10
Perini, 2009[7] cCBT-S vs. WL	Website	No established clinical relationship	Sadness	Nonclinical	NR	8	6	6
Titov, 2010[8] Arm 1: cCBT-LS (clinician) vs. cCBT-LS (technician) Arm 2: cCBT-LS (either) vs. WL	Website virtualclinic.org.au	No established clinical relationship	Sadness	Nonclinical	NR	8	6	≥6
Vernmark, 2010[9] Arm 1: cCBT-S vs. cCBT-NS Arm 2: cCBT-S vs. WL	University mail newspaper and radio	No established clinical relationship	No name	Nonclinical	Yes	8	7	Variable, minimum 8
Williams, 2013[10] cCBT-LS vs. WL	Website	No established relationship	CBM + Sadness	Non clinical	Yes	11 (1 CBM, 10 CBT)	CBM=7 sessions CBT=6 modules	NR
Wright, 2005[11] cCBT-AT vs. WL	Advertisement or referral	Yes, medical home at university-affiliated psychiatric hospital	No name	Clinical	Yes, in person	8–9	8	9
Depressive symptoms: 15 trials, 19 arms								
Clarke, 2002[12] cCBT-NS vs. WL	Mailing to HMO members	Yes, had medical home	ODIN	Nonclinical	NR	NR	7	NA

Study Comparison and Arm (if applicable)	Recruitment	Clinical Context	Program Name	Setting	Technical Support	Duration (Weeks)	Module Number	Planned Contacts
de Graaf, 2009[13] Arm 1: cCBT-NS + TAU vs. cCBT-NS or WL Arm 2: cCBT-NS vs. TAU	Mailed invitation to the general population	No established clinical relationship	a) CYL + TAU b) CYL only	Nonclinical	No	8 plus 9th booster session	9	4-5 consults with GP NA for cCBT arm
Farrer, 2011[14] Arm 1: cCBT-LS vs. cCBT-NS Arm 2: cCBT-NS vs. TAU	Callers to 24-hr telephone counseling service were invited to participate	No established clinical relationship	Blue Pages and MoodGYM	Nonclinical	a) Yes, via phone b) No	6	6	a) 6 b) none
Glozier, 2013[15] cCBT-NS vs. AC	Recruited through cohort study (age:≥45 yrs)	No established clinical relationship	E-couch	Nonclinical	Yes	12	12	NR
Griffiths, 2012 [16] Arm 1: cCBT-NS + ISG vs. cCBT-NS Arm 2: cCBT-NS vs. AC	Mailing to general populations	No established clinical relationship	a) E-couch (with ISG) b) E-couch	Nonclinical	No	12	12	NA
Hickie, 2010[17] cCBT-NS vs. TAU	Primary care	Yes, medical home	MoodGYM	Nonclinical	No	8 (for taking five 20-40 min modules)	5	NA
Levin, 2011[18] cCBT-S vs. TAU	Primary care	Yes, medical home	Wellness Workshop CD	Nonclinical	Yes, once via phone	6	5	1
Lintvedt, 2013[19] cCBT-NS vs. WL	Mailing to all registered students	No established clinical relationship	MoodGYM + Blue Pages	Nonclinical	NR	8	5	NA
McKinnon, 2008[20] cCBT-S vs. AC/IC (lifestyle)	Mailed questionnaire via voter rolls	No established clinical relationship	MoodGYM	Nonclinical	Yes, via phone	6	5	6
Moritz, 2012[21] cCBT-NS vs. WL	Online advertising	No established clinical relationship	Deprexis	Nonclinical	NR	8	10	NR
Spek, 2007 [22] cCBT-NS vs. traditional CBT or WL	Mailed invitation letter to all older adults	No established clinical relationship	Based on CWD	Nonclinical	Yes, could call or email	10	8	NA
van Bastelaar, 2008[23] cCBT-S vs. WL	Website/mail: Open-access study website	No established clinical relationship	CYL-DM	Nonclinical	No	8	8	8
Van der Zanden, 2012[24] cCBT-LS vs. WL	Mixed ads: GP offices, educational institutions, websites	Population was mixed: some had GP and others may not have had GP relationship	Master Your Mood	Nonclinical	NR	6	6	6
Wagner, 2013[25] cCBT-S vs. Face-to-face	Newspaper advertisements, websites, local facilities	No established clinical relationship	No name	Nonclinical	Yes, via therapist	8	8	16
Warmerdam, 2008[26] Arm 1: cCBT-S vs. WL Arm 2: cPST-S vs. WL	Website and newspaper advertisement	No established clinical relationship	a) CWD b) PST	Nonclinical	No	a) 8 9th (review) 12 wk later b) 5	a) 8 b) 5	a) 8 b) At least 5

Study Comparison and Arm (if applicable)	Recruitment	Clinical Context	Program Name	Setting	Technical Support	Duration (Weeks)	Module Number	Planned Contacts
Mixed depression and anxiety: 3 trials, 3 arms								
Newby, 2013[27] cCBT-LS vs. WL	Waitlist from previous studies and online advertising	No established clinical relationship	Worry and Sadness Program	Nonclinical	NR	10	6 (with additional supple-mental modules)	NR; received regular contact via email and telephone
Proudfoot, 2003[28] cCBT-NS vs. TAU	Primary care	Yes, medical home	Beating the Blues®	Clinical, GP clinics	Yes, limited from RN	8	1, 15-min intro video, then 8 modules	NR
Proudfoot, 2004[29] cCBT-NS vs. TAU	Primary care	Yes, medical home	Beating the Blues®	Clinical, GP clinics	Yes, limited from RN	8	1, 15-min intro video, then 8 modules	NR
Generalized anxiety disorder: 4 trials, 5 arms								
Anderson, 2012[30] cCBT-S vs. WL	Advertisement (Website and newspaper)	No established clinical relationship	No name	Nonclinical	NR	8	8	8
Paxling, 2011[31] cCBT-S vs. WL	Advertisement (newspaper and website) to general population	No established clinical relationship	No name	Nonclinical	NR	8	8	8
Robinson, 2010[32] Arm 1: cCBT-LS (clinician) vs. WL Arm 2: cCBT-LS (technician) vs. WL	Website www.virtualclinic.org.au	No established clinical relationship	Worry Program	Nonclinical	yes	10	6	At least 6
Titov, 2009[33] cCBT-LS vs. WL	Website www.virtualclinic.org.au	No established clinical relationship	Worry Program	Nonclinical	NR	9	6	Variable depending on patient's questions
Panic disorder: 10 trials, 11 arms								
Bergstrom, 2010[34] cCBT-S vs. traditional CBT	Primary care or self-referral	May or may not have medical home	No name	Nonclinical	NR	10	10	10 or more
Carlbring, 2001[35] cCBT-S vs. WL	Website for panic disorder and mass media advertisements	May or may not have had clinical relationship	No name	Nonclinical	NR	6–12	6	At least 6
Carlbring, 2005[36] cCBT-S vs. F2F	Recruited from WL from another study (initially, website or media ad)	May or may not have had clinical relationship	No name	Nonclinical	NR	10	10	At least 1 per wk
Carlbring, 2006[37] cCBT-LS vs. WL	Recruited from WL from another study (initially, website or media ad)	May or may not have had clinical relationship	No name	Nonclinical	NR	10	10	At least 1 per wk

Study Comparison and Arm (if applicable)	Recruitment	Clinical Context	Program Name	Setting	Technical Support	Duration (Weeks)	Module Number	Planned Contacts
Kenardy, 2003[38] cCBT-AT vs. WL	Primary care and mental health specialty	Yes, medical home	No name	Nonclinical (palmtop)	NR	6	6	6
Kiroupolos, 2008[39] cCBT-S vs. F2F	Website advertisement	No established clinical relationship	Panic Online	Nonclinical	NR	12	6	6
Klein, 2006[40] cCBT-S vs. IC	Website and mail advertisement	No established clinical relationship	Panic Online	Nonclinical	NR	6	6	6
Richards, 2006[41] Arm 1: cCBT-S vs. IC Arm 2: cCBT-S + SM vs. IC	From panic website, links to other mental health websites and mass media	No established clinical relationship	a) Panic Online b) Panic Online + stress management	Nonclinical	Yes, via therapist	8	a) 6 Panic Online b) 6 Panic Online, 6 stress management	Variable
Silfvernagel, 2012[42] cCBT-S vs. WL	Information on website; recruited via email	No established clinical relationship	No name	Nonclinical	NR	8	6-8 (2 fixed, 4-6 chosen from menu)	Variable, but minimum of 8
Wims, 2010[43] cCBT-S vs. WL	Website gave information about study, link to apply to study	No established clinical relationship	Panic Program	Nonclinical	NR	8	6	Variable
PTSD: 2 trials, 2 arms								
Litz, 2007[44] cCBT-LS vs. AC (self-monitor ADL)	Ad on Department of Defense website (PTSD from 9/11 Pentagon attack)	May or may not have had clinical relationship with VA or other medical facility	DE-STRESS	Nonclinical	yes	8	8	8 or more, variable
Spence, 2011[45] cCBT-LS vs. WL	Email news and mail, newspaper ads referring to website www.virtualclinic.org.au	No established clinical relationship	No name	Nonclinical	Yes	8	7	8 or more, variable
Anxiety symptoms: 2 trials, 2 arms								
Kenardy, 2006[46] cCBT-NS vs. WL	Psychology classes	No established clinical relationship	No name	Nonclinical	NO	6	6	NA
Ruwaard, 2010[47] cCBT-S vs. WL	Mail and media advertisements referred to a website	No established clinical relationship	Interapy	Nonclinical	NR	11	7	14 "feedback moments"

Table D-4. Type and intensity of support in cCBT interventions

Study	cCBT level Program Name[a]	Therapist Training	Therapist Time per Patient	Email or Text	Phone	Online Group Component	Instant Messaging	Face to Face
Major depressive disorder: 11 trials, 15 arms								
Andersson, 2005[1]	cCBT-S No name	NR	NR	Feedback on end of module quizzes	NR	Moderated discussion group	NR	No
Berger, 2011[2]	Arm 1: cCBT-S Deprexis Arm 2: cCBT-NS	Arm 1: licensed professionals & supervised students Arm 2: NA	Arm 1: 10 min per session Arm 2: NA	Arm 1: Supportive feedback via email from therapist weekly Arm 2: Program is interactive	NR	NR	NR	No
Carlbring, 2013[3]	cCBT-S *Depressionshjalpen*	Supervised PhD students	12 min (average)/wk	Feedback support	NR	No	NR	No
Choi, 2012[4]	cCBT-LS Sadness (adapted to Chinese)	Supervised PhD graduate student	NR, variable because over phone	Autoreminders	Yes, weekly	No, but access to prior transcriptions	No	No
Johansson, 2012[5]	Arm 1: CCBT-S (Standard) No name Arm 2: cCBT-S (tailored)	Supervised MS graduate students	Arm1 standard 74.1 min total, 9.3 min/ module Arm 2 tailored 95.2 min total, 9.7 min/ module	Feedback on homework support	NR	Control was online discussion group	No	No
Kessler, 2009[6]	cCBT-LS No name	Licensed MS or PhD	55 min/ session	Autoreminders	No	No	Yes, entire session	No
Perini, 2009[7]	cCBT-S Sadness	PhD	Variable; emailed response to forum post within 24 hr	Autoreminders, reinforcement and feedback	NR	Discussion forum	No	No
Titov, 2010[8]	Arm 1: cCBT-LS SADNESS Arm2: cCBT-LS	Arm 1: clinician Arm 2: technician	Average 10 min per session by forum, email or phone	Arm 1: feedback, goal-setting, problem-solving, therapeutic strategies Arm 2: scripted feedback on module and support	Yes, weekly	Arm 1: Moderated discussion forum Arm 2: No	No	No
Vernmark, 2010[9]	Arm 1: cCBT-S (self-help) No name Arm 2: cCBT-S (tailored)	Supervised master's students	Arm 1: 53 ± 28 min For all sessions Arm 2: 509 ±176 min	Arm 1: Supportive feedback on progress Arm 2: All materials and discussion over individualized, tailored email	Only if no response to email	No	No	No
Williams, 2013[10]	CCBT-LS Sadness	Licensed MS or PhD	NR, but no difference between groups	Email support but no feedback on homework	Yes	No	No	No
Wright, 2005[11]	cCBT-AT No name	PhD, master, MD, LCSW	25 min/ 50 min session	NR	NR	No	No	Yes

Study	cCBT level Program Name[a]	Therapist Training	Therapist Time per Patient	Email or Text	Phone	Online Group Component	Instant Messaging	Face to Face
Depressive symptoms: 15 trials, 19 arms								
Clarke, 2002[12]	cCBT-NS ODIN	NA	NA	NR	NA	NA	NA	No
de Graaf, 2009[13]	Arm 1: cCBT-NS CYL + TAU Arm 2: cCBT-NS CYL	Arm 1: GP for TAU Arm 2: NA	NA	Arm 1: If part of TAU Arm 2: NA	Arm 1: If part of TAU Arm 2: NA	NA	NA	No
Farrer, 2011[14]	cCBT-LS MoodGYM cCBT-NS	Arm 1: Lay crisis counselor Arm 2: NA	Arm 1: NR Arm 2: NA	Feedback on homework is automated within program	Arm 1: Yes, for weekly support Arm 2: NA	NA	NA	No
Glazier, 2013[15]	cCBT-NS E-couch	Arm 1: NA Arm 2: NA	NA	Reminders to complete next module	Reminders to complete next module	NR	NR	No
Griffiths, 2012[16]	Arm 1: cCBT-NS eCOUCH + ISG Arm 2: cCBT-NS eCOUCH	Arm 1: No therapist Arm 2: No therapist	NA - staff only moderated forum to enforce rules	Autoreminders via email	Automated phone reminder if needed	Arm 1: Support forum moderated only for rules Arm 2: NA	NA	No
Hickie, 2010[17]	cCBT-NS MoodGYM	NA	NA	NR	No	NR	NR	No
Levin, 2011[18]	cCBT-S Wellness Workshop	Licensed therapist does initial interview	After initial assessment, only once, <5 min via phone	NR	Yes, brief prompt to begin	NR	NR	No
Lintvedt, 2013[19]	cCBT-NS MoodGYM/ Blue Pages	NA	NA	NA	NA	NA	NA	No
McKinnon, 2008[20]	cCBT-S MoodGYM	Technician discussed lifestyle	NR	NR	Yes, weekly	No	No	No
Moritz, 2012[21]	cCBT-NS Deprexis	Arm 1: NA	Arm 1: NA	Reminders to complete modules	NR	NR	NR	No
Spek, 2007[22]	cCBT-NS No name	No therapist after intake	Initial assessment only for all patients	NR	NR	NR	NR	No
van Bastelaar, 2008[23]	cCBT-S CYL-DM	Supervised graduate students & psychiatry residents	NR	Autoreminders, feedback on homework	NR	Moderated discussion group forum	No	No
van der Zanden, 2012[24]	cCBT-LS Master Your Mood	Trained MH promotion workers	90 min/ chat room session	Autoreminders	NR	Web chat between therapist and up to 5 patients	NR	No

Study	cCBT level Program Name[a]	Therapist Training	Therapist Time per Patient	Email or Text	Phone	Online Group Component	Instant Messaging	Face to Face
Wagner, 2013[25]	cCBT-S No name	Psychologists or psychotherapists	20-50 min/text	Feedback on homework and answers to questions	NR	NR	NR	No
Warmerdam, 2008[26]	Arm 1: cCBT-S No name Arm 2: cPST-S	Supervised master's students	20 min per wk	Autoreminders, feedback on homework, support, suggestions	NR	NR	NR	No
Mixed depression and anxiety: 3 trials, 3 arms								
Newby, 2013[27]	cCBT-S Worry and Sadness Program	Supervised practice manager	23.37 min on average	Email as required based on elevated distress scores	Yes; not described in detail	NR	NR	No
Proudfoot, 2003[28]	cCBT-NS BTB	NA	NA	NA	NA	NA	NA	No
Proudfoot, 2004[29]	cCBT-NS BTB	NA	NA	NA	NA	NA	NA	No
Generalized anxiety disorder: 4 trials, 5 arms								
Andersson, 2012[30]	cCBT-S no name	Supervised graduate students	92 +/- 61 min for all sessions	Feedback, responses to questions	NR	NR	NR	No
Paxling, 2011[31]	cCBT-S No name	Supervised graduate students	97 +/- 52 min for all sessions	Feedback, responses to questions	NR	NR	NR	No
Robinson, 2010[32]	Arm 1: cCBT-LS (clinician) Worry program Arm 2: cCBT-LS (technician)	Arm 1: PhD-level clinician Arm 2: technician	Arm 1: 10 min per wk + discussion forum Arm 2: 10 min per wk + discussion forum	Arm 1: Encouragement, problem-solving, goal setting Arm 2: Support from script	Yes, if not responsive over email	Arm 1: Moderated discussion forum Arm 2: No	NR	No
Titov, 2009[33]	cCBT-LS Worry program	PhD	Weekly, no more detail given	Reminders & feedback	Yes	Moderated discussion forum	Yes	No
Panic disorder: 10 trials, 11 arms								
Bergstrom, 2010[34]	cCBT-S No name	Staff psychologist	35 min average for program	Responses to questions	NR	Moderated discussion forum	NR	No
Carlbring, 2001[35]	cCBT-S No name	NR	90 min total for all sessions; average 7-8 email exchanges	Feedback on homework, answers to questions	NR	NR	NR	No
Carlbring, 2005[36]	cCBT-S No name	Supervised graduate students	150 min for all sessions	Feedback on homework, answers to questions	NR	Moderated discussion board; mandatory to post weekly	NR	No

Study	cCBT level Program Name[a]	Therapist Training	Therapist Time per Patient	Email or Text	Phone	Online Group Component	Instant Messaging	Face to Face
Carlbring, 2006[37]	cCBT-LS No name	Supervised graduate students	10-12 min per session or wk	Reminders, feedback on progress	Yes	Moderated discussion board; mandatory to post weekly	NR	No
Kenardy, 2003[38]	cCBT-AT No name	Licensed psychologist	6, 1-hr sessions	5 daily palmtop reminders for patients to practice exposure	NR	NR	NR	Yes
Kiropoulos, 2008[39]	cCBT-S Panic Online	Licensed psychologist	Average of 352 min for all sessions	Feedback weekly	NR	NR	NR	No
Klein, 2006[40]	cCBT-S Panic Online	Both professionals and supervised graduate students	Average of 87 min for all sessions	Support and feedback	NR	NR	NR	No
Richards, 2006[41]	Arm 1: cCBT-S Panic Online alone Arm 2: cCBT-S Panic Online with stress modules	Both professionals and supervised graduate students	Arm 1: NR Arm 2: NA	Support and feedback on Panic Online modules; Stress management was just reading material	NR	NR	NR	No
Silfvernagel, 2012[42]	cCBT-S No name	Supervised graduate students	Averaged 19 emails for program	Reminders, feedback on homework	NR	NR	NR	No
Wims, 2010[43]	cCBT-S Panic Program	"Psychiatry registrar"	NR	Reminders, feedback, responses to questions	Called if patient did not log-in for 2 wk	Moderated discussion forum; mandatory to post weekly	NR	No
PTSD: 2 trials, 2 arms								
Litz, 2007[44]	cCBT-LS DE-STRESS	NR	Highly variable	Yes, as needed	Yes, as needed and at wk 6 prior to trauma narrative exercise	NR	NR	Yes, one initial session
Spence, 2011[45]	cCBT-LS No name	PhD	10 min per session	Reminders and feedback	Yes, as needed	Moderated discussion forum	Yes, if needed	No
Anxiety symptoms: 2 trials, 2 arms								
Kenardy, 2006[46]	cCBT-NS No name	No therapist	NA	Progress through modules monitored	NA	NA	NA	No
Ruwaard, 2010[47]	cCBT-S Interapy	Both professionals and supervised graduate students	20-40 min per session	Feedback including help structuring planned exposure assignments	NR	NR	NR	No

[a] All programs included some type of homework.

ABBREVIATIONS USED IN APPENDIX D TABLES

Abbreviation	Term
AC	attention control
ACQ	Agoraphobic Cognitions Questionnaire
ADIS	Anxiety Disorder Interview Schedule
ASI	Anxiety Sensitivity index;
ATQ	Adult Temperament Questionnaire
BA	behavior activation
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BSQ	Body Shape Questionnaire
BVS	Body Vigilance Scale
CBT	cognitive behavioral therapy
CBM	cognitive bias modification
cCBT	computerized cognitive behavioral therapy
cCBT-AT	cCBT adjunct to therapy
cCBT-LS	cCBT live support
cCBT-NS	cCBT no support
cCBT-S	cCBT supported
CES-D	Center for Epidemiologic Studies Depression scale
CIDI-SF	Composite International Diagnostic Interview-Short Form
CIS-R	Clinical Interview Schedule-Revised
CYL	Color Your Life
CWD	Coping With Depression
DASS	Depression Anxiety Stress Scale
DM	diabetes mellitus
DSM	Diagnostic and Statistical Manual for Mental Disorders
EOT	end of treatment
EQ5D	European Quality of Life scale, 5 dimensions
GAD	generalized anxiety disorder
GAD-7	Generalized Anxiety Disorder scale, 7 items
GHQ-12	General Health Questionnaire, 12 items
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
HMO	Health Maintenance Organization
HRQOL	health-related quality of life
IC	information control
ISG	internet support group
K10	Kessler Psychological Distress Scale
MADRS	Montgomery-Asberg Depression Scale
MADRS-S	Montgomery-Asberg Depression Rating Scale (self-rating version)
MDD	major depressive disorder
MINI	Mini-International Neuropsychiatric Interview
NA	not applicable

Abbreviation	Term
NR	not reported
PAID	Problem Areas in Diabetes scale
PCL	Posttraumatic Stress Disorder Checklist
PD	panic disorder
PDSS	Panic Disorder Severity Scale
PHQ-9	Patient Health Questionnaire, 9 items
PROQSY	Programmable Questionnaire System
PST	problem-solving therapy
PSWQ	Penn State Worry Questionnaire
PTSD-SS	Posttraumatic Stress Disorder Symptom Scale
QOLI	Quality of Life Inventory
RCT	randomized controlled trial
SCID	Structured Clinical Interview for DSM Disorders
SCL	Symptom Checklist
SD	standard deviation
SDS	Sheehan Disability Scale
SF-12	Short Form Health Survey , 12 items
S-STAI	Short State-Trait Anxiety Inventory
TAU	treatment as usual
WHODAS	World Health Organization Disability Assessment Schedule
WHOQOL-BREF	World Health Organization Quality of Life, shorter version
WL	waitlist
WSAS	Work and Social Adjustment Scale

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APPENDIX E. GLOSSARY

Abstract screening

The stage in a systematic review during which titles and abstracts of articles identified in the literature search are screened for inclusion or exclusion based on established criteria. Articles that pass the abstract screening stage are promoted to the full-text review stage.

Attention control

A type of control group used in nonpharmaceutical intervention studies designed to mimic a placebo control. The nonintervention (control) group is subjected to a condition that does not include procedures or information pertinent to the study intervention but does have the same data collection procedures, number of clinic visits, amount of materials provided, level of contact with study staff or other professionals, etc. Keeping these aspects consistent across study arms controls for the effect of "attention" or therapeutic relationship.

ClinicalTrials.gov

A registry and results database of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov provides information about a trial's purpose, location, and participant characteristics among other details.

Cochrane Database of Systematic Reviews

A bibliographic database of peer-reviewed systematic reviews and protocols prepared by the Cochrane Review Groups in The Cochrane Collaboration.

Cognitive behavioral therapy (CBT)

A short-term psychotherapy that focuses on how a person's thoughts and actions may be contributing to his or her depression.

Companion article

A publication from a trial that is not the article containing the main results of that trial. It may be a methods paper, a report of subgroup analyses, a report of combined analyses, or other auxiliary topic that adds information to the interpretation of the main publication.

Confidence interval (CI)

The range in which a particular result (such as a laboratory test) is likely to occur for everyone who has a disease. "Likely" usually means 95 percent of the time. Clinical research studies are conducted on only a certain number of people with a disease rather than all the people who have the disease. The study's results are true for the people who were in the study but not necessarily for everyone who has the disease. The CI is a statistical estimate of how much the study findings would vary if other different people participated in the study. A CI is defined by two numbers, one lower than the result found in the study and the other higher than the study's result. The size of the CI is the difference between these two numbers.

Data abstraction

The stage of a systematic review that involves a pair of trained researchers extracting reported findings specific to the research questions from the full-text articles that met the established inclusion criteria. These data form the basis of the evidence synthesis.

DistillerSR

An online application designed specifically for the screening and data extraction phases of a systematic review.

Embase

The Excerpta Medica database (EMBASE) produced by Elsevier, a major biomedical and pharmaceutical database indexing over 3500 international journals in the following fields: drug research, pharmacology, pharmaceutics, toxicology, clinical and experimental human medicine, health policy and management, public health, occupational health, environmental health, drug dependence and abuse, psychiatry, forensic medicine, and biomedical engineering or instrumentation. There is selective coverage for nursing, dentistry, veterinary medicine, psychology, and alternative medicine.

Exclusion criteria

The criteria, or standards, set out before a study or review. Exclusion criteria are used to determine whether a person should participate in a research study or whether an individual study should be excluded in a systematic review. Exclusion criteria may include age, previous treatments, and other medical conditions.

Full-text review

The stage of a systematic review in which a pair of trained researches evaluates the full-text of study articles for potential inclusion in the review.

GRADE

Grading of Recommendations Assessment, Development, and Evaluation (GRADE), a system of assessing the quality of medical evidence and evaluating the strength of recommendations based on the evidence.

Health-related quality of life (HRQOL)

A multidimensional concept that includes domains related to physical, mental, emotional, and social functioning. HRQOL goes beyond direct measures of population health, life expectancy, and causes of death, and focuses on the impact health status has on quality of life.

Inclusion criteria

The criteria, or standards, set out before the systematic review. Inclusion criteria are used to determine whether an individual study can be included in a systematic review. Inclusion criteria may include population, study design, sex, age, type of disease being treated, previous treatments, and other medical conditions.

Information control

A type of control group used in nonpharmaceutical intervention studies in which members of the control group are given access to equivalent quality information on a subject not directly related to the topic of the actual intervention. Similar to attention control, information control attempts to negate or nullify any positive effect from simply obtaining helpful information.

Optimal information size

The number of patients that need to be included in a pooled analysis (meta-analysis) to provide sufficient power to detect the smallest clinically important difference in treatment effect.

PRISMA

Preferred Reporting Items for Systematic Reviews and Meta-Analyses, an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses.

Publication bias

The tendency of researchers to publish experimental findings that have a positive result, while not publishing the findings when the results are negative or inconclusive. The effect of publication bias is that published studies may be misleading. When information that differs from that of the published study is not known, people are able to draw conclusions using only information from the published studies.

PubMed®

A database of citations for biomedical literature from MEDLINE®, life science journals, and online books in the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and preclinical sciences.

Randomized controlled trial (RCT)

A prospective, analytical, experimental study using primary data generated in the clinical environment. Individuals similar at the beginning of the trial are randomly allocated to two or more treatment groups and the outcomes the groups are compared after sufficient followup time. Properly executed, the RCT is the strongest evidence of the clinical efficacy of preventive and therapeutic procedures in the clinical setting.

Risk

A way of expressing the chance that something will happen. It is a measure of the association between exposure to something and what happens (the outcome). Risk is the same as probability, but it usually is used to describe the probability of an adverse event. It is the rate of events (such as breast cancer) in the total population of people who could have the event (such as women of a certain age).

Statistical significance

A mathematical technique to measure whether the results of a study are likely to be true. Statistical significance is calculated as the probability that an effect observed in a research study is occurring because of chance. Statistical significance is usually expressed as a P-value. The smaller the P-value, the less likely it is that the results are due to chance (and more likely that

the results are true). Researchers generally believe the results are probably true if the statistical significance is a P-value less than 0.05 ($p<.05$).

Strength of evidence (SOE)

A measure of how confident reviewers are about decisions that may be made based on a body of evidence. SOE is evaluated using one of four grades: (1) *High* confidence that the evidence reflects the true effect; further research is very unlikely to change reviewer confidence in the estimate of effect; (2) *moderate* confidence that the evidence reflects the true effect; further research may change the confidence in the estimate of effect and may change the estimate; (3) *low* confidence that the evidence reflects the true effect; further research is likely to change the confidence in the estimate of effect and is likely to change the estimate; and (4) *insufficient*; the evidence either is unavailable or does not permit a conclusion.

Systematic review

A summary of the clinical literature. A systematic review is a critical assessment and evaluation of all research studies that address a particular clinical issue. The researchers use an organized method of locating, assembling, and evaluating a body of literature on a particular topic using a set of specific criteria. A systematic review typically includes a description of the findings of the collection of research studies. The systematic review may also include a quantitative pooling of data, called a meta-analysis.

Waitlist control

A type of control group used in nonpharmaceutical intervention trials in which a group of participants included in an outcome study is assigned to a waiting list and receives the exact intervention at a later date, after the active treatment group has completed the study. This control group serves as a completely untreated comparison group during the study.