2011

HEALTH TECHNOLOGY ASSESSMENT REPORT

MOH/P/PAK/232.12 (TR)

MINISTRY OF HEALTH MALAYSIA

COMPUTERISED COGNITIVE BEHAVIOURAL THERAPY FOR ADULTS WITH DEPRESSION

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MINISTRY OF HEALTH MALAYSIA

Health Technology Assessment Report

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DISCLAIMER

This Health Technology Assessment has been developed from analysis, interpretation and synthesis of scientific research and/or technology assessment conducted by other organisations. It also incorporates, where available, Malaysian data, and information provided by experts to the Ministry of Health Malaysia. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of the review.

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ACKNOWLEDGEMENT

The authors of this Health Technology Assessment Report would like to express their gratitude and appreciation to the following for their contribution and assistance:

- Health Technology Assessment and Clinical Practice Guidelines Council.
- Technical Advisory Committee for Health Technology Assessment.

DISCLOSURE

The authors of this report have no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health Malaysia.

EXECUTIVE SUMMARY

Background

Depression is common and affects 121 million people worldwide. It is a leading cause of disability globally as well as in Malaysia. Depression can become chronic or recurrent. It can lead to substantial impairments in an individual's ability to take care of his or her daily activities of living. Depression causes the largest amount of disability accounting 12% of all disability and at its worst depression can lead to suicide, a tragic fatality associated with the loss of one million lives per year. Cognitive Behavioral Therapy (CBT) has been recommended for management of certain types of depression in adults. However, access to CBT is limited due to too few therapists available. Computerised CBT is a self-help option that offers patients the potential benefits of CBT with less therapist involvement.

Technical features

Computerised cognitive behavioural therapy (CCBT) is a form of CBT, which is delivered using a computer either via a CD-ROM, DVD or the internet. It can be used as the primary treatment with minimal therapist involvement or as augmentation to a therapist-delivered programme where the introduction of CCBT supplements the work of the therapist. There are several software packages for CCBT such as Beating the Blues (BtB); Sadness Programme, Overcoming Depression: a five areas approach; MoodGym, Deprexis and Colour Your Life. CCBT can also be delivered via email or telephone.

Objective

To evaluate the clinical effectiveness, cost effectiveness and other issues related to computerised cognitive behavioural therapy for the treatment of adults with depression.

Methods

A systematic review and meta-analysis was performed to identify all studies describing CCBT for treatment of depression among adults. The cost-effectiveness assessment included a review of the literature and estimated cost of the programme.

Results and conclusion

Twelve studies were included in the clinical effectiveness review. The analysis of these results showed that there was significant reduction of psychological score in the CCBT group in all studies. When compared to controls, CCBT was as effective as CBT and superior to wait-list. It was as effective or slightly more effective when compared with Treatment As Usual (TAU) and as effective as Problem-solving Therapy (PST) and email therapy based on CBT. The pooled results of seven studies showed that CCBT was associated with significant improvement in Beck Depression Inventory (BDI) score at post-treatment. The mean difference was -7.16 (95% CI -8.61,-5.72). There was no evidence of heterogeneity ($I^2 = 1\%$; $Chi^2 = 6.04$, df = 6 (p=0.42)). CCBT was found to be acceptable to majority of patients and the study results showed that high percentages of patients were satisfied with the treatment.

There were four studies on economic evaluation identified. All these economic evaluation were carried out alongside RCTs. The studies showed that CCBT is likely to be cost effective if the society is willing to pay a modest value for a significant change in depressive symptoms. The estimated license cost to start a CCBT programme in five psychiatric clinics in Malaysia and each clinic will see about 20 patients per month is about [redacted] per treatment package).

Recommendation

Based on the review, there was evidence to suggest that CCBT is effective for the treatment of depression. The burden of depression in Malaysia is high where it is the leading cause for Years Live with Disability (YLD) in men and women. Many patients with depression have no access to treatment and considered as unmet need. CCBT may improve the accessibility of CBT to patients with depression. Using the current version of CCBT programmes in English, the cost per treatment is fairly reasonable since CCBT can be accessed either at the clinic, at home or at the office. CCBT may be recommended to selected group of patients with mild to moderate depression. It may also be used as an adjunct to antidepressants in patients with severe depression under the supervision of an experienced psychiatrist. The patients selected for this programme should be patients who have computers and internet access at home. These patients should also be proficient in computer and English. Criteria for selecting patients for this treatment should be developed before introducing CCBT program for adults with depression.

Since there is no local data on CCBT, it is recommended that research be carried out in Malaysia to assess the effectiveness, acceptability and feasibility of CCBT in our population before a nationwide program can be introduced.

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GLOSSARY AND LIST OF ABBREVIATIONS

GLOSSARY

Cognitive Behavioural Therapy (CBT)	Refers to active, collaborative, time-limited system of psychotherapy that focuses on uncovering and understanding the relationship and influence of automatic thoughts and underlying assumptions on problematic feelings and behaviours.
Computerised Cognitive Behavioural Therapy (CCBT)	CBT delivered via a computer interface with a computer-led response. The computer program is interactive, making appropriate responses to patient input

LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance	**MD**	Mean difference
BDI	Beck Depression Inventory	**n**	number
BtB	Beating the Blues	**NHS**	National Health Service UK
CA	Clinician-assisted	**OHE**	Office of Health Economics
CANMAT	Canadian Network for Mood and Anxiety Treatments	**PANAS**	Positive and Negative Affect Scales
CBT	Cognitive Behavioural Therapy	**PHQ-9**	Patient Health Questionnaire-Nine Item
CCBT	Computerised Cognitive Behavioural Therapy	**PST**	Problem solving therapy
CDSR	Cochrane Database of Systematic Review	**QALY**	Quality Adjusted Life Years
CEAC	Cost-effectiveness acceptability curve	**RCT**	Randomised Controlled Trial
CENTRAL	Cochrane Central Database of Controlled Trials	**SD**	Standard Deviation
CES-D	Center for Epidemiologic Studies Depression Scale	**SDS**	Sheehan Disability Scale
CI	Confidence interval	**SMD**	Standardised Mean Difference
CYL	Colour Your Life	**TA**	Technician-assisted
DALY	Disability Adjusted Life Years	**TAU**	Treatment as Usual
EM	Expectation-maximisation	**TCBT**	Traditional Cognitive Behavioural Therapy
HTA	Health Technology Assessment	**UK**	United Kingdom
ICER	Incremental cost-effectiveness ratio	**WL**	Wait-list
ITT	Intention to Treat	**WTP**	Willingness to pay
K-10	Kessler 10	**YLD**	Years Live with Disability

COMPUTERISED COGNITIVE BEHAVIOURAL THERAPY FOR ADULTS WITH DEPRESSION

1 BACKGROUND

Depression is common and affects 121 million people worldwide.[1] Depression can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her daily activities of living. Depression causes the largest amount of disability accounting 12% of all disability and at its worst depression can lead to suicide, a tragic fatality associated with the loss of one million lives per year.

Depression was the leading cause of disability as measured by Years Live with Disability (YLD) and the fourth leading contributor to the Global Burden of Disease assessed in Disability Adjusted Life Years (DALYs) in 2000. By the year 2020, depression is projected to reach second place of the ranking of DALYs calculated for all ages, both sexes. Today, depression is already the second cause of DALYs in the age category of 15-44 years for both sexes combined.[1]

Unipolar depression was ranked tenth and third respectively as leading causes of disease burden in males and females in the Malaysian Burden of Disease and Injury Study, 2000. In women, unipolar depression was the leading cause of YLD, contributing 13% of the YLD. In men, unipolar depression was the second leading cause of YLD contributing 7.2%.[2] The prevalence of depression among adult primary care attendees were reported as 14.4% in a semi urban clinic[3] and 5.6% in another primary care setting in Malaysia.[3] The prevalence of depression is higher in patients with other comorbidities. For example, in a study by Ahmad *et al.* the prevalence of depression among post stroke patients was 36% and in Zuraida *et al.* study the prevalence of depression among patients with headache was 46%.[4]

The Third Malaysian National Health Morbidity Survey 2006, did a cross sectional survey of psychiatric illness among adults using 28-item version of the General Health Questionnaire (GHQ-28) and found that the overall adjusted prevalence was 11.2%. Overall, there was a 6.3% current suicidal ideation.[5] There were several community studies conducted among the elderly. The prevalence among the general elderly ranged from 6.3% to 18.0%.[4] In a large community study conducted among the Malays elderly in rural Malaysia, the prevalence of depression was 27.8%.[6] The prevalence of depression in Malaysia is expected to increase with the continuing growth of elderly population in our society.

Depression is a syndromic condition that, like many disorders, is diagnosed and monitored by assessing symptoms. The most commonly used diagnostic algorithm is based on the Diagnostic and Statistical Manual, Fourth Version (DSM-IV) and includes criteria for major depression as well as criteria for other categories of depressive disorders (see Table 1).

The following definitions which are adapted from DSM–IV are used to classify depression:[7]

- subthreshold depressive symptoms: fewer than five symptoms of depression
- mild depression: few, if any, symptoms in excess of the five required to make the diagnosis, and the symptoms result in only minor functional impairment
- moderate depression: symptoms or functional impairment are between ‘mild’ and ‘severe’
- severe depression: most symptoms, and the symptoms markedly interfere with functioning. Can occur with or without psychotic symptoms.

Table 1. DSM-IV Symptoms of Major Depression

At least one of these:

- Depressed mood
- Anhedonia

And some of these to total five symptoms present for at least 2 weeks:

- Change in appetite/weight (increase or decrease)
- Altered sleep pattern (increase or decrease)
- Lack of energy
- Difficulty concentrating
- Agitation
- Reduced self-esteem
- Suicidal thoughts or plans

Depression is often under-recognised and under-treated. It is estimated that about 30-50% of cases of depression in primary care and medical settings are not detected.[8]

Depression can be effectively managed with pharmacotherapy, psychotherapy and/or exercise therapy. However, according to World Health Organisation (WHO), fewer than 25 % of those affected (in some countries fewer than 10 %) received such treatments. Barriers to effective care include the lack of resources, lack of trained providers, and the social stigma associated with mental disorders including depression.[1]

Cognitive behavioural therapy (CBT) is a discrete, time-limited, structured psychological intervention, derived from the cognitive behavioural model of affective disorders and where the patient:[7]

- Works collaboratively with the therapist to identify the types and effects of thoughts, beliefs and interpretations on current symptoms, feelings states and/or problem areas
- Develops skills to identify, monitor and then counteract problematic thoughts, beliefs and interpretations related to the target symptoms/problems
- Learns a repertoire of coping skills appropriate to the target thoughts, beliefs and/or problem areas

CBT and group CBT have been recommended for management of certain types of depression in adults.[7] Group CBT has been shown to be effective in patients with depression in Malaysia.[9] However access to CBT is limited due to too few therapists, expense, waiting lists and patients' reluctance to enter therapy.

The use of information technology to deliver psychological treatments has been explored, for example, self-help delivered by telephone, over the internet and by computer. CBT is currently the main psychological treatment approach that has been computerised. Computerised cognitive behavioural therapy (CCBT) programmes engage the patient in a structured programme of care, the content of which is similar to and based on the same principles as treatment provided by a therapist following a standard CBT programme. Direct staff input is usually limited to introducing the programme, brief monitoring and being available for consultation.[7] CCBT is a self-help option that offers patients the potential benefits of CBT with less therapist involvement.[10]

In view of improving access of treatment for patients with depression, this review was requested by a doctor working in the Psychiatry Department of Hospital Raja Permaisuri Bainun.

2 TECHNICAL FEATURES

Computerised cognitive behavioural therapy (CCBT) is defined as a form of CBT, which is delivered using a computer either via a CD-ROM, DVD or the internet. It can be used as the primary treatment intervention with minimal therapist involvement or as augmentation to a therapist-delivered programme where the introduction of CCBT supplements the work of the therapist.[7]

There are several software packages for CCBT such as Beating the Blues (BtB); Sadness Programme, Overcoming Depression: a five areas approach; MoodGym, Deprexis and Colour Your Life. CCBT can also be delivered via email or telephone.

Beating the Blues

BtB is a CBT-based package for patients with anxiety and/or depression. It consists of a 15-minute introductory video and eight 1-hour interactive computer sessions. As described in the manufacturer's submission, the CBT strategies used include: identifying thinking errors, challenging automatic negative thoughts, modifying attributional style and identifying core beliefs. The behavioural techniques used include graded exposure, sleep management, problem solving, task breakdown and activity scheduling. The sessions are usually at weekly intervals and are completed in the routine care setting (i.e. GP's practice). Homework projects are completed between sessions and weekly progress reports are delivered to the GP or other health professional at the end of each session. These progress reports include anxiety and depression ratings and reported suicidality. According to the manufacturer, the minimum reading age is 10 years.

Sadness Programme

The Sadness Programme consists of four components: six online lessons, homework assignments, participation in an online discussion forum and regular email contact with a mental health clinician. The six online lessons represent best-practice principles used in CBT programmes for depression. Part of the content of each lesson in the Sadness Programme is presented in the form of an illustrated story about a woman with depression who, with the help of a clinical psychologist, learns how to gain mastery over her symptoms. Principles and techniques of CBT described in the Sadness Programme include behavioural activation, cognitive restructuring, problem solving and assertive skills. Each lesson includes a printable summary and homework assignment. Participants were expected to complete homework tasks prior to completing the next lesson. Participants were also expected to regularly post messages and homework assignments on a secure and confidential online discussion forum using an alias. The therapist moderated the forum and responded to postings within 24 hour. After completing each lesson the participants were emailed by the therapist. The themes of the therapist's emails varied from reinforcement for continued participation and efforts, encouragement to practise the relevant treatment skills, encouragement to complete lessons and homework assignments, enquiries about progress and responses to questions.[11]

MoodGYM

MoodGYM is an interactive web program designed to prevent and decrease depressive symptoms. It was first launched in 2001 and currently is in its third version. It was designed for young people but is helpful for people of all ages.

It consists of five modules, an interactive game, anxiety and depression assessments, downloadable relaxation audio, a workbook and feedback assessment. The modules were made available sequentially weekly.

It teaches the principles of cognitive behaviour therapy. Using flashed diagrams and online exercises, MoodGYM demonstrates the relationship between thoughts and emotions. Users are taught to come to grips with their own feelings and the 'warpy' thoughts that might accompany them. MoodGYM also works through dealing with stress, handling separation and relationship break-ups, as well as relaxation and meditation techniques. MoodGYM is available free of charge to the public at www.moodgym.anu.edu.au.[12]

Deprexis

Deprexis is a web-based intervention consists of 10 content modules representing different psychotherapeutic approaches, plus one introductory and one summary module, each of which can be completed in 10 – 60 minutes, depending on the user's reading speed, interest, motivation, and individual path through the programme. Modules are organized as simulated dialogues in which the program explains and illustrates concepts and techniques, engages the user in exercises and continuously asks users to respond by selecting from response options. Subsequent content is then tailored to the users' responses, resulting in a simulated conversational flow. All modules are accompanied by illustrations (e.g. drawings, photographs, flash animations). The modules cover a variety of therapeutic content that is broadly consistent with a cognitive-behavioural perspective, although the program is not restricted to one CBT manual. The modules theoretical rationale and content draws from theories like Behavioral Activation; Cognitive Modification; Mindfulness and Acceptance, Interpersonal Skills; Relaxation, Physical Exercise and Lifestyle Modification; Problem Solving; Childhood Experiences and Early Schemas; Positive Psychology Interventions; Dreamwork and emotion-focused Interventions and Psychoeducation.[13] The programme is written in German.

Overcoming Depression: a five areas approach

Overcoming Depression is a CD-ROM-based CBT system for patients with depression. A specific part of the remit of the system development was to offer CBT in as jargon-free form as possible. It assumes a minimum reading age of 9–12 years for all but one module. The system consists of six sessions, each of which takes about 45–60 minutes to complete. The sessions are delivered in a mixture of text, cartoon illustrations, animation, interactive text, sound and video. There is an offer of a self-help support practitioner (who may be a nurse) at the beginning of each session. Sessions are completed on a weekly basis.[10]

Colour Your Life

Colour Your Life is an online multimedia, interactive computer program for depression. It consists of eight 30-min sessions with a ninth booster session. At the end of each session, homework assignments are given. Participants were advised to complete one session per week. Participants were given log-in codes by the researchers and they accessed CCBT at home. No assistance was offered. The program is written in Dutch.

3 POLICY QUESTION

Should computerised cognitive behavioural therapy be used for treatment of adults with depression?

4 OBJECTIVE

i. To evaluate the clinical effectiveness of computerised cognitive behavioural therapy for treatment of adults with depression in terms of
    a. Improvement in psychological symptoms
    b. Interpersonal and social functioning
    c. Quality of life
    d. Prevention of relapse

ii. To evaluate the economic issues of computerised cognitive behavioural therapy for treatment of depression

iii. To assess other issues such as the patients' preference, satisfaction and acceptability of treatment; safety, social, organizational, ethical and legal impact of CCBT.

5 METHODS

5.1 Literature search strategy

A search strategy protocol was developed, presented and discussed with a group of reviewers and information specialists. The search aimed to identify all the relevant articles pertaining to effectiveness and cost-effectiveness of CCBT for depression in adults. The most recent search was carried out in August 2011.

Studies were identified by searching electronic databases and scanning references lists of articles. This search was applied to MEDLINE (in-Process & other Non-Indexed citations and Ovid Medline (R) 1948 to present), Pubmed, Science Direct, Ebscohost (Psychology and Behaviour), Cochrane Central Database of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), NHS Database of Abstracts of Reviews of Effectiveness (DARE), NHS Economic Evaluation Database (NHS EED), NHS Health Technology Assessment (HTA) Database and Office of Health Economics Health Economics Evaluation Database (OHE HEED). In addition, various HTA organisations websites, guideline producing body, trials registers and other health related websites were also searched (see Appendix 3).

A combination of subject headings and free text terms was used. "Population" search terms (e.g depression, depressive symptoms) were combined with "intervention" terms (e.g computerised cognitive behavioural therapy OR CCBT OR "computerised therapy" OR "computer assisted cognitive therapy" OR "internet psychotherapy" OR MoodGym OR Depression program OR Defeating depression, Feelbetter OR Cope OR BTSTEPS OR Good Days Ahead OR Beating the Blues OR fearfighter). This was supplemented by more specific terms such as cost, cost effectiveness, cost implications, psychological symptoms, quality of life, patients preference, patients satisfaction, interpersonal and social functioning, relapse prevention, ethical, social, reduce severity, legal and organisational impact.

Copies of the search strategies used in the major databases were included in Appendix 4.

The search was limited to human study only. No date, language, study design or publication type restrictions were applied.

5.2 Inclusion and exclusion criteria

Inclusion criteria:

i. Type of studies

For systematic review on clinical effectiveness: systematic reviews, meta-analysis, randomised controlled trials and non-randomised comparative studies on CCBT were included.

For systematic review on cost effectiveness of CCBT, all cost effectiveness studies of satisfactory quality were included.

Qualitative studies on patients' preference and patients' satisfaction for CCBT treatment were also included.

ii. Types of participants

Adults with depression

iii. Types of intervention

CCBT either alone or as part of a package, and either via a computer interface or over the telephone with a computer-led response.

iv. Comparator

1. Treatment as usual as described in the study
2. Medication
3. CBT
4. Other CCBT
5. Other psychotherapy
6. Placebo

v. Types of outcome measures

One or more of the following outcome measures were assessed:

1. Improvement in psychological symptoms
2. Interpersonal and social functioning
3. Quality of life
4. Preference, satisfaction and acceptability of treatment
5. Organisational, safety, ethical, social, legal
6. Cost per Quality Adjusted Life Years (QALY) gained
7. Incremental Cost Effectiveness Ration (ICER)
8. Cost utility analysis

Exclusion criteria

1. CCBT used for other diseases and indications
2. CCBT used among children and adolescents

5.3 Quality assessment strategy and grading of evidence

The validity of the eligible studies was assessed by two reviewers independently. Jadad score (See Appendix 5) and Critical Appraisal Skills Programme (CASP) checklist were used to assess the quality of randomised controlled trials. Jadad is a validated score which lies in the range 0-5. Studies were scored according to the presence of three key methodological features of randomisation, blinding and accountability of all patients, including withdrawals.[14] The cut-off point of three scores was taken as eligibility criteria. Critical Appraisal Skills Programme (CASP) checklist for randomised controlled trials contains 11 questions to assess the validity of the trial, the results and its applicability.

Drummond's checklist (see Appendix 5) was used to assess economic studies.[15] Critical Appraisal Skills Programme (CASP) checklists were used to assess other study designs.

The quality of the evidence was later graded according to US/Canadian Preventive Services Task Force grading system (see Appendix 6).[16]

5.4 Data extraction strategy

Data from included studies were extracted by a reviewer and checked by a second reviewer using a pre-tested data extraction form. Disagreements were resolved through discussion. A third person, whose decision is final were consulted when disagreements persists after discussion.

Information was extracted from each included trial on (1) characteristics of trial participants (2) the trials inclusion and exclusion criteria (3) type of intervention (4) type of control used (5) outcome measures (including improvement in psychological symptoms, improvement in quality of life, improvement in social function or disability, acceptability, preference, patients' satisfaction, ICER and other cost measures.

5.5 Data synthesis

All the data extracted on clinical effectiveness and cost effectiveness were summarized in evidence table. Studies were assessed for suitability for pooling with regards to the type of CCBT used, study type, populations, comparators and outcome.

5.6 Meta-analysis

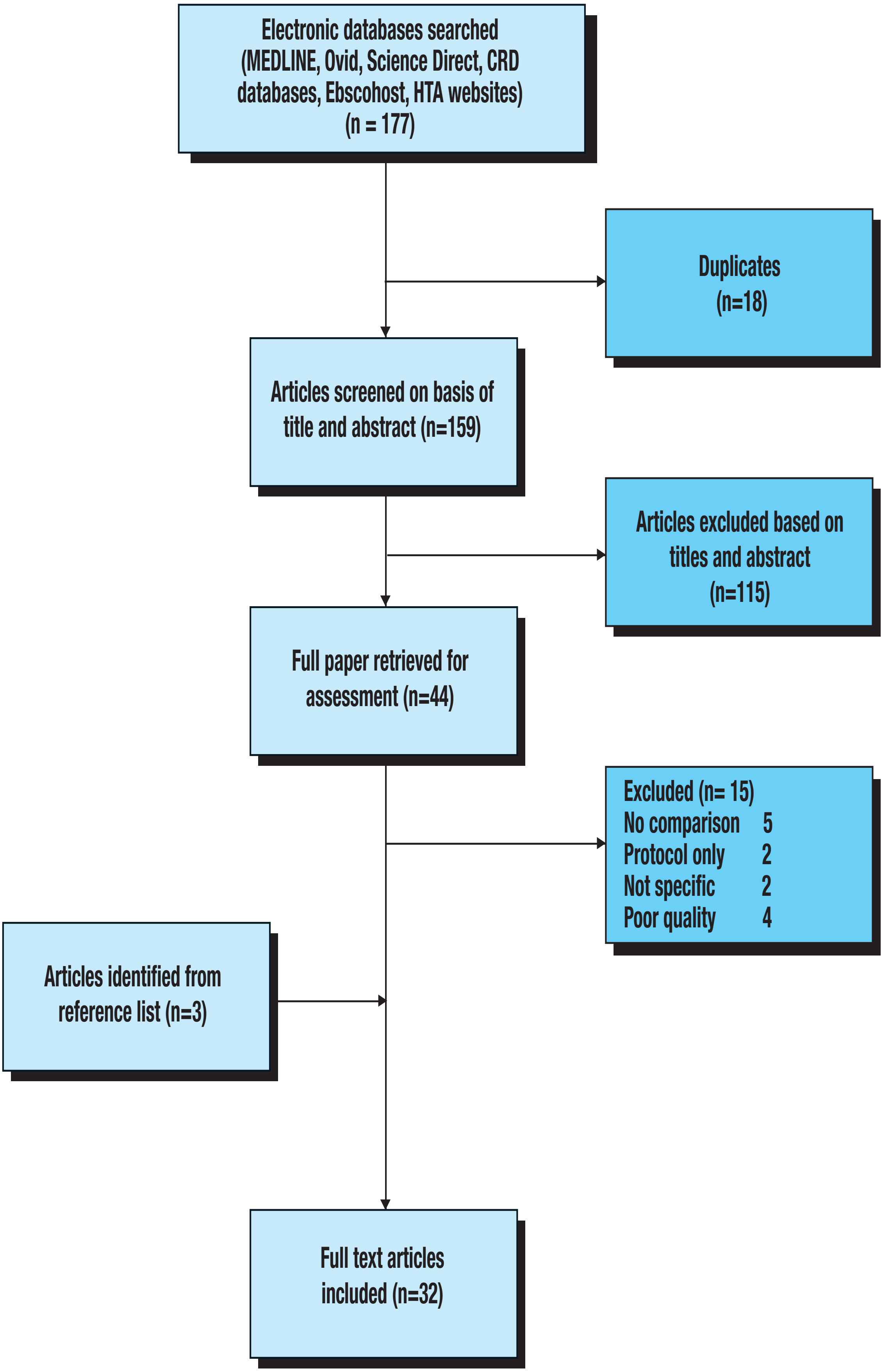
For review on effectiveness, we pooled the result of studies with similar comparison and outcome. As stated in Cochrane Handbook, since the trials were RCTs, we pooled the actual value (the mean, standard deviation (SD) and number (n) for each arm of the trial for the outcome at post treatment. In using this method we assumed that within a trial the groups were the same at baseline because of randomisation. We used Revman version 5.1 to pool the result. We attempted the inverse-variance fixed-effect method first and if there was evidence of heterogeneity, we proceeded with inverse-variance random effects method. Since all these studies reported the outcome using the same scale (BDI), we summarised the data in mean difference.

6 RESULTS

6.1 QUANTITY AND QUALITY OF RESEARCH AVAILABLE

A total of 32 full text articles were identified for inclusion in this review. The search of Medline, PubMed, Science Direct and other electronic databases provided a total of 177 citations. After adjusting for duplicates 159 articles remained. Of these, 115 studies were discarded after reviewing the abstracts since it appeared that these papers clearly did not meet the criteria. The full texts of the remaining 44 articles were examined in more detail. It appeared that 15 studies did not meet the inclusion criteria. Twenty nine studies met the inclusion criteria and were included in this review. Additional three studies were identified by checking the references of located, relevant papers. No unpublished studies were obtained. See Figure 1.

Figure 1. Flow chart of study selection


Electronic databases searched (MEDLINE, Ovid, Science Direct, CRD databases, Ebscohost, HTA websites) (n = 177)
Duplicates (n=18)
Articles screened on basis of title and abstract (n=159)
Articles excluded based on titles and abstract (n=115)
Full paper retrieved for assessment (n=44)
Excluded (n= 15)
No comparison 5
Protocol only 2
Not specific 2
Poor quality 4
Articles identified from reference list (n=3)
Full text articles included (n=32)

Characteristics of included studies

From the 32 articles included in this review, ten were systematic review and guidelines, 14 articles were on effectiveness, four articles on economic evaluation and four articles were on acceptability and satisfaction of CCBT. All these articles were in English. The evidence tables of these studies were presented in Appendix 7.

Study design

There were 14 papers on 12 studies eligible for review on effectiveness. All the studies were randomised controlled trial. The summary of the studies were as in Table 4.

There were five studies on economic evaluations of CCBT for depression in adults identified. There were four primary studies and one systematic review with modelling. The systematic review was Kaltenthaler's HTA report.[10] All the primary papers described different types of CCBT program. All the economic studies were based on RCTs. Mc Crone paper on cost effectiveness of Beating the Blues were discussed with Kaltenthaler's economic evaluation since it has been discussed in depth in their review. The summary of the economic studies included in this review were as in Table 2.

Four studies on CCBT acceptability for depression were included in the review; a randomised controlled trial, a non comparative open trial and two qualitative studies.

Participants

All the studies included participants with depression, mixed anxiety and depression or anxiety.

Intervention

All the studies used a kind of CCBT either it was a known software package or not. Only two of the studies included for effectiveness assessed the same CCBT program as shown in Table 4.

The CCBT program can either be unsupported such as Colour Your Life (CYL) and Deprexis or need minimal therapist support such Beating the Blues and MoodGYM or used as a complement to Traditional CBT in Wright *et al.* study. The CCBT program in Ruwaard *et al.* study was therapist guided but not at real-time. The CCBT used in Kessler *et al.* study was delivered by therapist at real-time.

Three studies on acceptability included the software packages, but the other study did not. The three studies with the software included were two studies of Colour Your Life (CYL) and another study on Beating the Blues.

Comparators

Five of the 12 studies included for effectiveness assessment have two comparators, Christensen 2004[17] compared CCBT (MoodGym) with Bluepages, a depression information website and another group of control who received weekly phone calls by interviewers to discuss lifestyle and environmental factors. Warmerdam 2008[18] compared CCBT (Coping with depression) with Problem Solving Therapy (PST) and wait-list. De Graaf 2009[19] & 2011[20] compared CCBT (Colour Your Life) with TAU and another group of participants who received both TAU and CCBT. Wright 2005[21] compared CCBT with CBT and wait list. Vernmark 2010[22] compared CCBT with email therapy and waitlist. Proudfoot 2003[23] & 2004[24] compared CCBT (Beating the Blues) with TAU. Other studies compared CCBT with wait-list. See Table 4.

Outcome measures

Improvement in psychological symptoms was the main outcome in all the studies included. Majority of the studies used Beck Depression Inventory to measure the severity of depression.

Beck Depression Inventory (BDI, BDI-II) is a 21-question multiple-choice self-report inventory, one of the most widely used instruments for measuring the severity of depression. In its current version, the questionnaire is designed for individuals aged 13 and over, and is composed of items relating to symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex. There are three versions of the BDI—the original BDI, first published in 1961 and later revised in 1978 as the BDI-1A, and the BDI-II, published in 1996. The BDI is widely used as an assessment tool by health care professionals and researchers in a variety of settings. There has been consistent support for its construct validity and reliability in various samples.[20, 24]

The Centre for Epidemiological Studies Depression scale (CES-D) is another common tool used for identifying people with depressive symptomatology. Scores of 16 and higher represent a clinically significant level of depressive symptoms. The validity of CES-D has been tested in different population. The CES-D consists of 20 items and the total score varies between 0 and 60 with higher scores indicating more depression.[17]

Table 2. Studies included for review of cost-effectiveness of CCBT for adults with depression

STUDY ID	ASSOCIATED RCT	COUNTRY	TYPE OF CCBT	TYPE OF ECONOMIC ANALYSIS
Kaltenthaler 2006	Mc Crone 2004	United Kingdom	• Beating the Blues • Cope • Overcoming Depression • Fear Fighter • Bt Steps	Modelling
Hollinghurst 2010	Kessler 2009	United Kingdom	Therapist delivered internet psychotherapy	Cost effectiveness
Gerhards 2010	De Graaf 2009	Netherlands	Colour Your Life	Cost effectiveness & Cost utility
Warmerdam 2010	Warmerdam 2010	Netherlands	Coping with depression	Cost utility & cost effectiveness

Risk of Bias

Two reviewers assessed the risk of bias of the included studies. The results were summarised in Table 3. All the studies were randomised, six of the studies were adequately concealed. None of the studies were double blind due to the nature of the intervention, however in three of the studies, the assessors were blinded. All the studies except one, used intention to treat analysis to analyse the results. All the studies described about drop-outs or loss to follow up. The percentages of loss to follow-up ranged from 3 to 45%.

Table 3. Summary of risk of bias in the included studies

Study	Allocation concealment	Randomisation	Blinding	Intention to treat analysis	Description of dropouts and withdrawals; Percentage of lost to follow up
Proudfoot 2004	Y	Y	N	N	Y, 35%
Christensen 2004	N	Y	N	Y	Y, 21%
Warmerdam 2008	Y	Y	N	Y	Y, 30%
Perini 2009	Y	Y	N	Y	Y, 26%
Titov 2010	Y	Y	N	Y	Y, 25%
de Graaf 2011	N	Y	N	Y	Y, 9.2%
Meyer 2009	N	Y	N	Y	Y, 45%
Wright 2005	N	Y	Y	Y	Y, 11.1%
Andersson 2005	N	Y	N	Y	Y, 27%
Vernmark 2010	Y	Y	Y	Y	Y, 3%
Kessler 2009	Y	Y	Y	Y	Y, 29%
Ruwaard 2011	N	Y	N	Y	Y, 9%

Country

As shown in Table 4, two of the studies included for effectiveness assessment were conducted in United Kingdom,[24, 25] three studies were conducted in Australia,[11, 17, 26] three studies were conducted in Netherlands[18, 20, 27] and one study each was conducted in Germany[13] and United States.[21]

Two of the studies included for cost-effectiveness were from United Kingdom[10, 28] and another two studies were conducted in Netherlands.[29, 30] See Table 2.

As for studies included under acceptability, two of the studies were from Netherlands[31, 32] and another two studies were from United Kingdom.[33, 34]

6.2 OVERVIEW OF PUBLISHED SYSTEMATIC REVIEWS, META-ANALYSIS AND GUIDELINES

There were one HTA report, three systematic reviews with meta-analysis, three systematic reviews and three guidelines retrieved.

HTA REPORT

Kaltenthaler 2006

Kaltenthaler *et al.* conducted a systematic review and economic evaluation on computerised cognitive behaviour therapy for depression and anxiety in 2006. They included nineteen studies in their review; eight of the studies were on depression. The results of the studies were not pooled. They found that the evidence supported the effectiveness of Beating the Blues for depression and Fear Fighter for phobia and panic disorders. There was limited evidence of poorer quality that Cope and Overcoming Depression were effective. There was no RCT to support the effectiveness of BT Steps. There was some evidence that CCBT was as effective as TCBT for the treatment of depression/anxiety and phobia/panic. There was some evidence that CCBT was more effective than TAU in the treatment of depression/anxiety. They also found that in studies reporting accurate estimates of therapist time, CCBT appeared to reduce therapist time compared with TCBT and is therefore of use where access to TCBT is limited.[10] Level 1

SYSTEMATIC REVIEW WITH META-ANALYSIS

Andrews 2010

In another recent systematic review and meta-analysis, Andrews *et al.* compared CCBT with treatment as usual or wait list for depression and anxiety. Six out of the 23 studies included in the review were on depression. The results for major depression revealed effect size, Hedges g of 0.78 (95% CI 0.59 – 0.96). Heterogeneity test was not significant where the $I^2 = 0\%$. This showed that CCBT was more superior over control group. The review also showed that adherence to treatment was good where a median of 80% of people who began these programs completed all lessons (range 48% - 100%). Ten studies provided data on patient satisfaction and a median of 86% (range 70% - 100%) of patients reported that they were satisfied or very satisfied with the treatment.[35] Level 1

Andersson 2009

Andersson *et al.* in a systematic review and meta-analysis on internet-based and other computerised psychological treatment for adults with depression included 12 studies. The mean effect size of 15 comparisons between internet-based and computerised psychological treatment with control group at post–test was, cohen's $d = 0.41$ (95% CI 0.29-0.54) with moderate heterogeneity $I^2=57.49\%$. Sensitivity analysis was done but there was not much difference in the effect size as well as heterogeneity. Two factors was found to be significantly related to effect sizes namely professional support and control group.[36] Level 1

Spek 2007

In a systematic review and meta-analysis comparing internet-based cognitive behaviour therapy and waiting list or treatment as usual or psychoeducation, Spek *et al.* included 12 studies involving 2334 subjects. Five studies focused on depression and seven studies aimed at anxiety disorders. The studies on depression had a mean effect size of 0.27 (95% CI 0.15 – 0.40) in fixed effect analysis (FEA) and 0.32 (95% CI 0.08 – 0.57) according to mixed effect analysis (MEA). The I^2 test showed that there might be substantial heterogeneity where the I^2 was 70.1%. The results showed that the intervention for depression had a small effect size with significant heterogeneity.[37] Level 1

SYSTEMATIC REVIEW

Griffiths 2010

In another systematic review, Griffiths *et al.* compared self help intervention or a website intervention that incorporated a self-help component which includes CCBT and psychoeducation with attention placebo control, waiting list control or treatment as usual. Twenty-six trials were included where eight of them were on depression. The results were not pooled. Six of eight trials targeting depression yielded positive effects for CCBT. The effect size differences ranged from 0.42 to 0.65 for depression involving patients with clinically significant symptoms of depression.[38] Level 1

CADTH Rapid Assessment 2010

Canadian Agency for Drugs and Technologies in Health (CADTH) conducted a rapid assessment on self-directed cognitive behavioural therapy for adults with diagnosis of depression. They included three guidelines from NICE UK, New Zealand and Malaysia; two RCTs-De Graaf (2008&2009), Bielich (2008) and one economic paper by Vos 2005. They concluded that the evidence indicated that self-directed CBT improved the clinical ratings of depressive symptoms and that it could be a cost-effective therapy option for individuals with mild to moderate depression.[39] Level 1

ANZHSN 2009

Australia and New Zealand Horizon Scanning Network (ANZHSN) in their prioritising summary included 5 studies; Perini 2009, Kessler 2009, Spek 2008, Kaltenthaler 2008 and Kaltenthaler 2006. The report concluded that good quality evidence indicates a potential for the uptake of this technology in rural and remote areas, and the possible ability to overcome barriers to increase the treatment options especially in males.[40] Level 1

GUIDELINES

NICE Guidelines 2010

NICE guidelines on treatment and management of depression in adults published in 2010 included seven RCTs on CCBT. The guidelines recommended CCBT for people with persistent subthreshold depressive symptoms or mild to moderate depression. The guidelines had explicitly stated that CCBT for people with persistent subthreshold depressive symptoms or mild to moderate depression should:[7] Level 1

- be provided via a stand-alone computer-based or web-based programme
- include an explanation of the CBT model, encourage tasks between sessions, and use thought-challenging and active monitoring of behaviour, thought patterns and outcomes
- be supported by a trained practitioner, who typically provides limited facilitation of the programme and reviews progress and outcome
- typically take place over 9 to 12 weeks, including follow-up.

CANMAT 2009

Canadian Network for Mood and Anxiety Treatments (CANMAT) recommended CCBT as second line treatment for acute MDD.[41] Level 1

MOH 2009

Another guidelines from Ministry of Health Malaysia in 2007 which included Kaltenthaler 2006 systematic reviews and two other RCTs stated that CCBT may be used for mild to moderate depression.[8] Level 1

6.3 EFFECTIVENESS

There were 12 studies that assessed the effectiveness of CCBT for adults with depression identified. All the studies except Perini 2009[11] and Titov 2010[26] assessed different CCBT program as shown in Table 4.

Perini S *et al.* conducted a randomised controlled trial among 48 participants who met diagnostic criteria for depression. These participants were recruited via a website (www.climateclinic). Twenty-nine participants were randomised to Sadness Program and nineteen participants were randomised to wait list. Seventy-four percents of the treatment group participants completed all the six lessons within the required time. The results showed that the treatment group had significantly lower post-treatment scores than the control group. The mean PHQ-9 scores was 9.59 (SD 5.82) in the treatment group and 14.11 (SD 4.21) in the control group (p<0.01). The mean BDI-II scores was 17.30 (SD 9.86) in the treatment group and 23.33 (SD 9.29) in the control group (p<0.01). As for clinical outcomes for remission and recovery (reduction of pre-treatment PHQ-9 scores of at least 50%), 41% of the treatment group were classified as recovered compared with 6% of control group participants.[11] Level 1

Titov N *et al.* in another RCT, randomised 141 participants to three groups. The first two groups received CCBT (Sadness Program) where one group was Technician-assisted (TA) (n=47) and another group was Clinician-assisted (CA) (n=49). The other group was the control group (n=45) who received clinician-assisted program but began treatment after the intervention groups completed the Sadness Program. Eighty per cent of the TA group and 70% of the CA group participants completed all the six lessons within the required time. The results showed that the treatment group had significantly lower post-treatment score. The mean PHQ-9 score was 7.59 (SD 4.04) for TA, 7.30 (SD 4.48) for CA and 12.98 (SD 4.44) for control group. As for BDI-II the score was 15.29 (SD 9.81) for TA group, 14.59 (SD 11.12) for CA group and 26.15 (SD 10.14) for control group. Post-hoc pairwise comparisons revealed no difference on both measure between treatment groups, but significant differences between treatment groups and the control group (p<0.001). [26] Level 1

Meyer *et al.* in a RCT involving 396 adults aged between 18 to 72 years old compared CCBT (Deprexis) as an add-on treatment as usual to a 9-week delayed-access plus treatment as usual. The participants were randomly assigned in an 80:20 weighted randomization sequence. The attrition rate was 45% at T1 (post-assessment). At post-assessment the mean BDI score was 19.87 (SD 9.86) for CCBT group and 27.15 (SD 10.01) in the wait-list group. The difference between the two groups was statistically significant and the effect size d was 0.64.[13] Level 1

Andersson *et al.* in another RCT compared internet-administered self-help, including minimal therapist contact, with a waiting-list condition consisting of participation in a moderated discussion group online. Post-treatment measures were completed by 36 of 57 participants in the treatment group and 49 out of 60 participants in the control group. The attrition rate was 27%. The results showed significant difference in the post treatment score between the two groups where the BDI score was 12.2 (SD 6.8) in the treatment group and 19.5 (SD 8.1) in the control group. The effect size d was 0.94.[36] Level 1

In another multicentre RCT, 297 individuals with a score of 14 or more on BDI and confirmed diagnosis of depression were recruited from 55 general practices in Bristol, London and Warwickshire, UK. The individuals were randomised to online CBT (with a therapist online in real time) in addition to usual care or to usual care from their GP while on 8-month waiting-list for online CBT. The primary outcome was measured at four months and showed significant difference in the BDI score, SF-12 mental subscore, recovery rate and EQ-5D score between the two groups. Primary outcome data at 4 months were obtained for 210 (71%) participants. The BDI score was 14.5 (SD 11.2) in the CCBT group and 22.0 (SD 13.5) in the wait-list group. The results were persistent at 8 months for BDI score and EQ-5D score.[25] Level 1

Ruwaard *et al.* randomised 54 participants with mild to moderate depression to an 11-week immediate CCBT treatment or to a wait-list control condition. The web-based CBT involved strategies from cognitive therapy (CT) and behavioural activation. The treatment comprised a balanced set of homework assignments and scheduled therapeutic sessions in which assignments were explained and adapted to the needs of the client. The trial included no face to face contact between the participants and any mental health professional. Five participants (9%) dropped out of the study; three in the treatment group (8%) and two in the control group (11%). The treatment group took longer than 11 weeks to complete treatment (median 16 weeks). The post-treatment score was 9.8 (SD 6.5) in the treatment group and 15.6 (SD 7.6) in the control group. The improvement was maintained up to the 18-month follow-up with marginal changes from post-treatment. As for recover, which was defined as reliable change from a pretest score above the published clinical cut-off to a posttest score below the cut-off , 17 (47%) reliably recovered from depression. At follow up, again 17 (47%) of the participants had recovered. Of the 17 subjects who recovered at posttest, 13 (76%) maintained this improvement up to 18 months.[27] Level 1

Proudfoot *et al.* conducted a RCT among 274 participants from general practice patients aged 18-75 years suffering from depression, mixed anxiety and depression or anxiety disorder (including phobia or panic). These patients were randomised to CCBT (Beating the Blues) or treatment as usual (TAU). Fourty-eight patients whom all four post-randomisation BDI values were missing were not included in the analysis. The results showed a decline over time in BDI scores in both groups, with lower scores in the CCBT group. The BDI scores in the treatment group was 12.1 (SD 9.3) and 18.4 (SD 10.9) in the control group at two months follow up.[24] Level 1

Warmerdam *et al.* conducted a 3-arm RCT to compare CCBT, problem solving therapy (PST) and wait-list. A total of 263 participants with depressive symptoms (≥ 16 on the CES-D scale) were randomised to the three groups (CBT: n=88; PST: n=88; WL: n=87). The CCBT was based on the "Coping with Depression" course, Dutch version. The PST-based intervention was a Dutch adaptation of SET from Bowman and consisted of three steps. First they described what really matters to them, second they wrote down their concern, worries and problems and finally they made a plan for the future on the ways to accomplish things that matter to them. Subjects in both intervention groups received support during the intervention period by email from trained master-level students of clinical psychology. Attrition rates for the full sample were 30% at 5-week assessment. There was significant overall improvement over time for all groups on the CES-D, $F_{3,543} = 124.57$, $p < 0.001$. The mean depression scores after 5 weeks were significantly lower in PST than in WL, $t_{592} = -3.01$, $p = 0.002$. After 8 weeks, both CBT and PST showed significantly lower depression scores than WL (CBT: $t_{598} = -3.64$, $p < 0.001$, PST: $t_{596} = -2.89$, $p = 0.004$). Also after 12 weeks, CBT and PST showed significantly lower depression scores than WL (CBT: $t_{635} = -4.73$, $p < 0.001$, PST: $t_{650} = -4.34$, $p < 0.001$). No differences were found in depression scores between CBT and PST at each assessment.[18] Level 1

Christensen *et al.* conducted a RCT among 525 participants aged 18-52 years with depressive symptoms (scored 22 or above on Kessler Psychological Scale). The participants were randomly assigned to three groups; Blue Pages (n=165), MoodGym (n=182) and control (n=178). Bluepages is a depression information website and Mood Gym is a CCBT with five interactive modules. The controls received weekly phone calls by interviewers to discuss lifestyle and environmental factors. Seventy-nine percent of the participants completed the intervention. The outcome was measured at 6 weeks. The results showed that both BluePages and MoodGym were effective in reducing symptoms of depression. MoodGym but not BluePages, significantly improved dysfunctional thinking compared with control. The effect size were 0.4, 0.4 and 0.1 for MoodGym, Bluepages and control respectively.[17] Level 1

CCBT had also been compared with CBT.[21] Wright *et al.* randomly assigned 45 medication-free outpatients with nonpsychotic major depression to 8 weeks of computer-assisted cognitive therapy or standard cognitive therapy or to a wait list control group. Mean percentage adherence for standard cognitive therapy sessions was 95.1% (SD=8.1), whereas mean percentage adherence for computer-assisted cognitive therapy session was 90.5% (SD=11.4). The results showed that patients treated with computer-assisted cognitive therapy and standard cognitive therapy achieved significantly more improvement in depression severity than the patients in the wait list condition as assessed by both the Hamilton Depression Scale and the Beck Depression Inventory. As the baseline severity variables indicated that random assignment failed to equate the treatment groups, the results were reported as mean change. The drop-out rate was 11.1%. The mean change of BDI score at end point were 17.5 (SD 10.8) in the computer-assisted cognitive therapy group, 14.7 (SD 8.0) in the standard cognitive group and 5.8 (SD 6.5) in the wait-list group.[21] Level 1 The results of the study showed that CCBT and CBT produced significant reductions in major depression over eight weeks of treatment when compared to wait-list. There was no evidence of differential outcome between CCBT and CBT.

Vernmark *et al.* compared a guided self-help program (a CCBT) with email therapy and waitlist among 88 participants with major depression. The guided self-help program was based on material used by Andersson *et al.* and consisted of seven text modules totalling 114 pages, including exercises. The email therapy was based on manual created based on CBT-principles for treating depression. There were no significant between-group differences at pre-treatment. Attrition rate from pre to post treatment was 3%. On the BDI repeated measures ANOVA showed a significant interaction effect for group and time, $p < 0.001$. Post-hoc testing with Tukey's HSD showed that both the email therapy and CCBT were significantly improved compared to the waiting-list condition, $p=0.002$ and $p=0.06$. The two treatments did not differ ($p=0.41$). At six months follow up, where the control group had received CCBT, there were no significant between group differences on the outcome measures.[22] Level 1 de Graaf *et al.* conducted a three arms randomised trial among 303 depressed participants. The participants were randomly allocated to CCBT (Colour Your Life) (n=100), TAU (n=103) and CCBT & TAU (n=100). The attrition rate was 9.2%. The results showed that unsupported online CCBT was not superior to TAU by a GP for depression. The effect size, d at 12 months was 1.26 for CCBT; 1.09 for TAU and 1.11 for CCBT&TAU, but the between group effect sizes were small (d=0.17 for CCBT vs TAU; d=0.02 for CCBT&TAU vs TAU. There was no significant difference in the number of participants who had remitted, 36 (40.9%) for CCBT, 34 (37.4%) for TAU and 33 (37.5%) for CCBT&TAU. There was no significant difference for relapse rate between the groups.[20] Level 1

Table 4. Summary of included studies evaluating the efficacy of CCBT for adults with depression

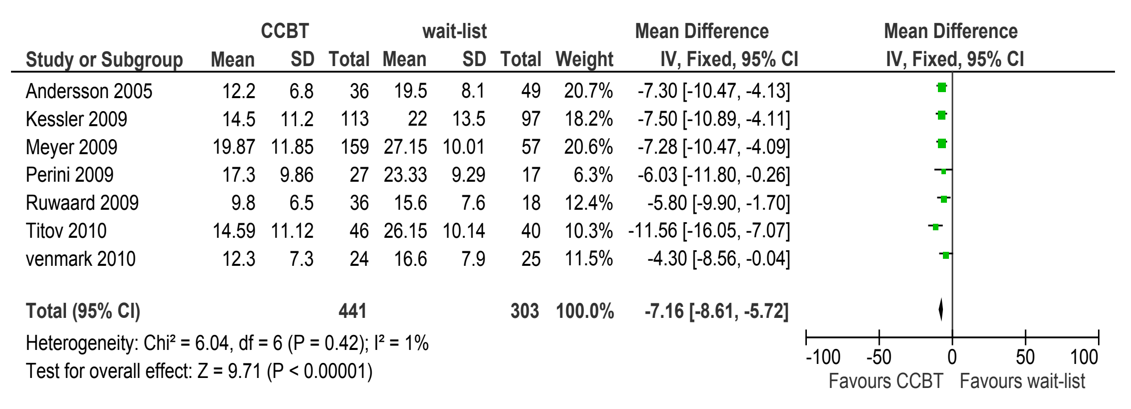
STUDY ID	COUNTRY	NO. OF PARTICIPANTS	PARTICIPANTS STATUS	TYPE OF CCBT	COMPARATOR	DURATION OF INTERVENTION	DURATION OF FOLLOW UP	OUTCOME MEASURES	RESULTS
Proudfoot 2003 & 2004	United Kingdom	274	General practice patients with depression, mixed anxiety and depression or anxiety disorder who scored 4 or more on GHQ-12 and 12 or more on CIS-R	Beating the blues	Treatment as usual	8 weeks	8 months	BDI BAI WSA	At 2 months BDI in CCBT group 12.1 (9.3), TAU 18.4 (10.9)
Christensen 2004	Australia	525	Patients with depression age between 18-52 years old. Scored 22 or above on Kessler psychological distress scale.	MoodGYM	1. Blue Pages 2.Control received weekly phone calls	6 weeks	6 weeks	Symptoms of depression CES-D; after 6 weeks	After 6 weeks: Mean difference for MoodGYM vs control 3.2 (95% CI, 0.9 to 5.4); and BluePages vs control 2.9 (0.6 to 5.2)
Warmerdam 2008	Netherlands	263	Patients with depression aged > 18 years old from Netherlands. Scored 16 or more on CES-D	Coping with Depression	1.Problem Solving Therapy 2. Wait-list	12 weeks	12 weeks	CES-D	Mean difference of CES-D for CBT;PST and WL were 0.76(0.27);0.76(0.27) and 0.66(0.27)
Perini 2009	Australia	48	> 18 years old Australian, not in CBT, not experiencing psychotic mental illness or severe symptoms of depression > 23 on PHQ-9 or > 2 to Question 9 on suicidal ideation. Mild or subthreshold depression > 5 on PHQ-9, taking the same dose for at least 1 month	Sadness Program	Wait-list	8 weeks	8 weeks	Improvement in psychological symptoms	PHQ-9 and BDI-II score for intervention were 9.59(5.82); 17.30(9.86) and for control 14.11(4.21);23.33(9.29).
Titov 2010	Australia	141	>18 years old, PHQ-9 between 10 and 23, responding < 2 to Question 9 on PHQ-9	Sadness Program	Wait-list	11 weeks	4 months	PHQ-9 and BDI-II	At 11 weeks, mean difference for TA vs control for PHQ-9 was 6.61(4.95-8.27) & 0.38(-0.91-1.66); BDI-II 11.85(7.85-15.85) & 0.18 (-2.12-2.77)
De Graaf 2009 & 2010	Netherlands	303	Age 18-65, access internet at home, mild to moderate depressive complaints (BDI-II score ≥ 16)	Colour Your Life	Treatment as usual Combined CCBT and TAU	9 weeks	12 months	Mean score BDI-II	Mean score for BDI-II for CCBT,TAU and combined CCBT & TAU at 2 months: 20.6(10.4),22.1(10.2), 21.7(10.1) and at 12 months 16.1(11.1),17.5(11.1),16.5 (11.1).

STUDY ID	COUNTRY	NO. OF PARTICIPANTS	PARTICIPANTS STATUS	TYPE OF CCBT	COMPARATOR	DURATION OF INTERVENTION	DURATION OF FOLLOW UP	OUTCOME MEASURES	RESULTS
Meyer 2009	Germany	396	Adults aged between 18 – 72 with depressive symptoms	Deprexis	Wait-list	9 weeks	6 months	Mean score of BDI-II	At 9 weeks, mean BDI-II for CCBT vs WL was 19.87(11.85) & 27.15(10.01),*p*<0.001
Wright 2005	United States	45	Mean age 38.2 years recruited through advertisements or referral	Computer-assisted cognitive therapy	Standard Cognitive therapy Wait list	9 weeks	6 months	Depression severity	At 8 weeks, mean score of BDI for CCBT, CBT and WL were 19.0(10.1),15.2(7.1) and 5.2(6.4) respectively. . At 6 months:17.5(10.8), 14.7(8.0) and 5.8(6.5); average cohen's *d*=1.14 for CCBT and 1.04 for standard cognitive therapy
Andersson 2005	Sweden	117	Mild to moderate depression	Internet self-help with minimal therapist contact	Wait list	6 weeks	6 months	Improvement in depression post treatment	Mean difference of BDI score for treatment vs control was 8.3(5.7 – 10.9) and 1.4 (-1.1-3.9). Mean score at follow up: 13.1(9.1) in treatment group and 13.1 (7.6) in control group.
Vernmark 2010	Sweden	88	At least 18 years old, MADRS-S >14 and <31, <4 on item 9 (suicidal thoughts) on MADRS-S	Self help treatment; Based on material used by Andersson	Email therapy based on CBT manual Waiting list	6 weeks	6 months	Depression outcome & Quality of life	Post-treatment mean score of BDI-II for email, self help & control group were 10.3(5.2), 12.3(7.3), 16.6(7.9). At 6 months: 9.0(5.6), 10.9(9.8) and 9.7(7.2)
Kessler 2009	United Kingdom	297	Patients aged 18-75 years old from primary care with new episode of depression. BDI> 14.	Therapist delivered internet psychotherapy	Wait list	10 weeks	8 months	BDI Score	At 4 months, BDI score for intervention vs control was 14.5(11.2) and 22.0(13.5). At 8 months:14.7(11.6) & 22.2(15.2)
Ruwaard 2011	Netherlands	54	With chronic moderate depression from general population in Netherlands. Mean age – 42 years ; BDI score between 10-29	Standardised therapist guided web-based CB	Wait list	11 weeks	18 months	BDI-IA Satisfaction	At 11 weeks, mean BDI-IA post treatment for treatment vs control was 9.8(6.5) and 15.6(7.6)

CCBT versus wait-list

Seven studies that compared CCBT with waitlist and measured the psychological status using Beck Depression Inventory were included in this analysis. A total of 441 participants who received CCBT and 303 participants who were put on wait-list were included. Depending on the types of the CCBT used, the post-treatment outcome was measured at different time-point, ranging from 5 weeks to 4 months.

Figure 2. Forest plot of seven studies that compared CCBT with wait-list at post-treatment based on fixed effect analysis



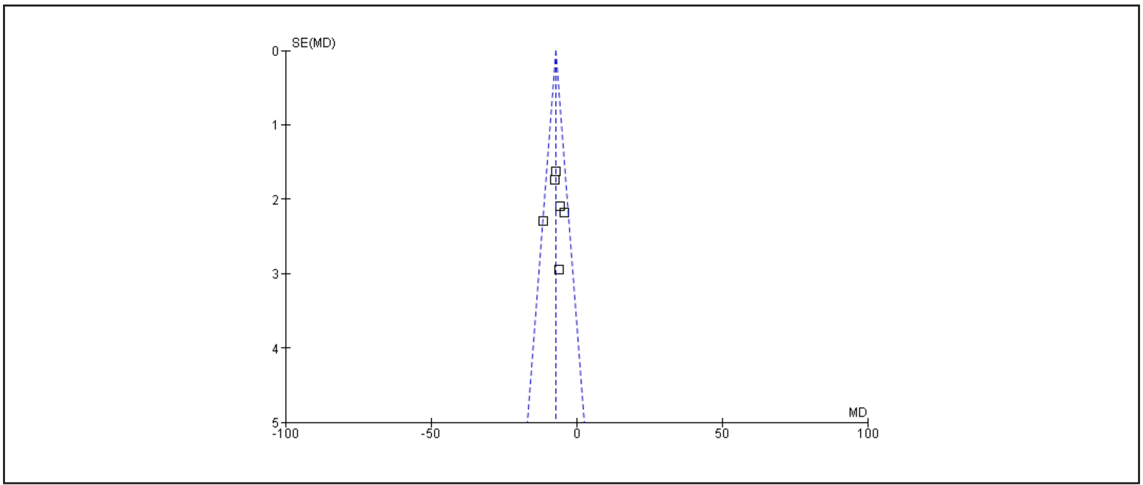
	CCBT			wait-list				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Andersson 2005	12.2	6.8	36	19.5	8.1	49	20.7%	-7.30 [-10.47, -4.13]
Kessler 2009	14.5	11.2	113	22	13.5	97	18.2%	-7.50 [-10.89, -4.11]
Meyer 2009	19.87	11.85	159	27.15	10.01	57	20.6%	-7.28 [-10.47, -4.09]
Perini 2009	17.3	9.86	27	23.33	9.29	17	6.3%	-6.03 [-11.80, -0.26]
Ruwaard 2009	9.8	6.5	36	15.6	7.6	18	12.4%	-5.80 [-9.90, -1.70]
Titov 2010	14.59	11.12	46	26.15	10.14	40	10.3%	-11.56 [-16.05, -7.07]
venmark 2010	12.3	7.3	24	16.6	7.9	25	11.5%	-4.30 [-8.56, -0.04]
Total (95% CI)			**441**			**303**	**100.0%**	**-7.16 [-8.61, -5.72]**

Heterogeneity: Chi² = 6.04, df = 6 (P = 0.42); I² = 1%
Test for overall effect: Z = 9.71 (P < 0.00001)

After performing an analysis using fixed effects model, the pooled result showed that CCBT was associated with significant improvement in BDI score at post-treatment. The mean difference was -7.16 (95% CI -8.61,-5.72). There was no evidence of heterogeneity ($I^2 = 1\%$; $Chi^2 = 6.04$, df = 6 (p=0.42)). The other two studies that were not pooled in this meta-analysis due to the difference in the outcome measure also showed improvement in the psychological score in the treatment group.[18, 21] Level 1

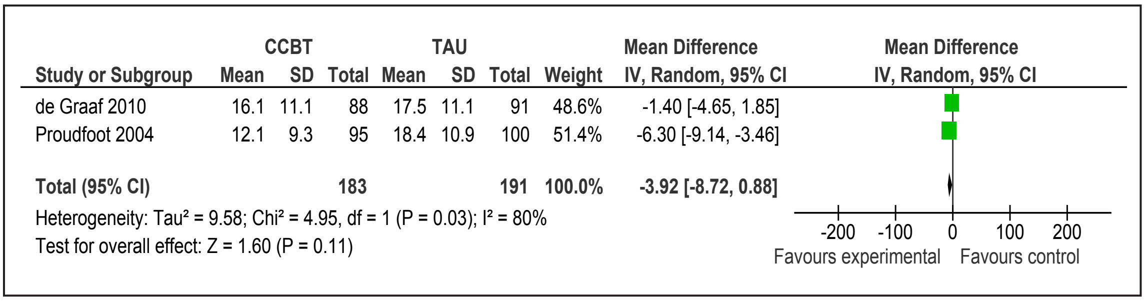
In order to assess publication bias, we drew funnel plots, which appear symmetry (see Figure 3). The x-axis is the mean difference and y-axis is the standard error of mean difference. We did not conduct further test to assess funnel plot asymmetry since the number of study pooled was less than 10.

Figure 3. Funnel plot for studies that compared CCBT with wait-list CCBT versus Treatment as Usual (TAU)



Two studies compared CCBT with TAU. A total of 183 participants who received CCBT and 191 participants who received TAU were included. We detected significant heterogeneity within this comparison (I^2 = 80%; Chi^2 =4.95, df = 1 (p=0.03)). The pooled result obtained from random effect analysis showed that there was no significant difference between CCBT and TAU (mean difference -3.92, 95% CI -8.72, 0.88).

Figure 4. Forest plot of two studies that compared CCBT with TAU



	CCBT			TAU				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
de Graaf 2010	16.1	11.1	88	17.5	11.1	91	48.6%	-1.40 [-4.65, 1.85]
Proudfoot 2004	12.1	9.3	95	18.4	10.9	100	51.4%	-6.30 [-9.14, -3.46]
Total (95% CI)			**183**			**191**	**100.0%**	**-3.92 [-8.72, 0.88]**

Heterogeneity: Tau² = 9.58; Chi² = 4.95, df = 1 (P = 0.03); I² = 80%

Test for overall effect: Z = 1.60 (P = 0.11)

6.4 ECONOMIC EVALUATION

6.4.1. Review of Literature

Kaltenthaler *et al.* in their HTA report reviewed the literature and the evidence submitted by the sponsors for each of the products being reviewed. They also conducted detail cost-effectiveness models of the five products being reviewed namely Beating the Blues, Cope, Overcoming Depression, FearFighter and BT Steps. Only one paper on cost-effectiveness analysis of BtB against treatment as usual and a costing of the intervention was available.[10 Level 1] Mc Crone paper[42] aimed to determine the cost-effectiveness of CCBT using BtB compared with TAU among primary care patients with anxiety and/or depression. The trial recruited 274 patients with anxiety and/or depression from seven general practices in the south-east of England and randomised them to receive either CCBT (146 patients) or TAU (128 patients). The chosen form of economic analysis was cost-effectiveness analysis in which data on reported clinical outcomes were combined with cost data to produce a cost per point reduction in the BDI and a cost per symptom-free day. A cost utility analysis was undertaken by applying utility to days with and without symptoms.[10 Level 1] An ITT analysis revealed that the mean service cost for CCBT was £397 compared with £357 for TAU, resulting in incremental service cost of £40 (90% CI -£28 to £148). Total costs including lost employment costs were less for the BtB group, at £533 compared with £900 for TAU. Mc Crone concluded that BtB was cost-effective against TAU in terms of cost per QALY of £1250. There were few limitations of this study such as estimation of QALYs but they have been addressed in the modelling.[10 Level 1]

The depression model was developed to assess the impact of each CCBT product on the costs and effectiveness of treating patients with depression in a primary care setting compared with TAU. In this model, patients were assumed to arrive in primary care for treatment with either mild to moderate, moderate to severe or severe depression. The main model results were based on the distribution in the Proudfoot trial[24] but a subgroup analysis was performed to examine variation in cost-effectiveness. For BtB and TAU, the transition probabilities between the four severity categories before and after treatment have been estimated by Mc Crone[42] and for Overcoming Depression from Whitfield. For Cope, these have been estimated from mean values presented in published studies. Other than transition probabilities, the parameters included were compliance, relapse rates, longevity and quality of life. [10 Level 1]

The review stated that CCBT has an impact on costs in two ways. One was from the cost of the intervention itself and the other comes from the fact that it altered the distribution of patients between depression severity categories which in turn has implications for the use of services. The provision of CCBT results in costs from the following: licence fees, computer hardware, screening of patients for suitability, clinical support, capital overheads (for facilities for computer and clinician) and the training of staff.[10 Level 1]

The costs for BtB were estimated for a single-copy licence and a 20-copy licence. The single copy licence was equivalent to a one to five GP practice purchasing the product. The 20 copy licence was equivalent to a PCT purchasing a licence. The estimated cost of these was £219.30 and £104.62 respectively per treated patient.[10 Level 1]

BtB was found to be more effective and more costly than TAU. The incremental cost per QALY of BtB over TAU was £1801. Based on CEAC, the probability of accepting BtB over TAU at 30,000 was 86.8%. For Cope were £7139 and 62.6% and for Overcoming Depression were £5391 and 54.4%. The strength of BtB lies in the fact that it has been evaluated in the context of an RCT with a control group. The subgroup analysis found no differences across severity groupings.[10 Level 1]

Hollinghurst *et al.* conducted a cost effectiveness analysis alongside Kessler's randomised controlled trial[25] on therapist delivered online cognitive-behavioural therapy compared with usual care.[28 Level 1] A total of 297 participants were recruited to the trial, 149 to the online CBT group, and 148 to the usual care group. The analysis was based on NHS perspectives. NHS resources, personal costs incurred by participants, and or lost productivity due to time off work were each measured separately. Personal costs included private sector healthcare, over the counter drugs, social and domestic help, travel costs and out of pocket loss of earnings. All healthcare resources were valued using unit costs derived from nationally available data.

All costs were valued in British pounds sterling at 2007 prices, adjusted for inflation where necessary. The results showed that online CBT was more expensive than usual care although the outcomes were better. Using complete case data, cost per QALY gain was £17173. There was 56% chance that online CBT is cost-effective at the £20000 per QALY level and 71% chance at the £30000 per QALY threshold. Using imputed data, there was 94% chance that the intervention is cost-effective at £20000 per QALY.[28 Level 1]

Gerhards *et al.* conducted an economic evaluation of online computerised cognitive behavioural therapy without support (Colour Your Life) for depression in primary care alongside de Graaf study[20]. They included 303 participants with at least mild to moderate depressive complaints based on BDI-II score from the general population. The economic evaluation consisted of cost-effectiveness analysis and cost utility analysis. They were based on societal perspectives. The costs were divided into categories: health sector costs, costs for patient and family, and productivity costs. Healthcare costs were measured by means of a monthly healthcare use questionnaire. The patient and family costs consisted of travelling costs and lost time because of the intervention, TAU and/or CCBT. Productivity costs were based on the modules of the PROductivity and DISease Questionnaire (PRODISQ), and calculated according to the friction cost method. All costs were presented in Euros for the year 2007. Depression severity was measured with the BDI-II. Quality of life was measured with the EuroQol EQ-5D and the Short Form 6D (SF-6D). Costs during the follow-up period were calculated as the cumulative costs per participant 12 months after baseline. The results showed that CCBT has the lowest societal as well as health care costs even after regression correction for baseline difference. At 6 months base-case analysis, the societal cost for CCBT was €9092, CCBT plus TAU was €10534 and €9765 for TAU alone. Corrected case-base analysis showed a mean QALY of 0.71 for CCBT, 0.71 for CCBT plus TAU, and 0.72 for TAU. CCBT was also found to be the most optimal treatment when compared with both TAU and CCBT plus TAU with a probability of about 65% of being the most efficient strategy at a threshold value of €0 per QALY.[29 Level 1]

Warmerdam *et al.* conducted an economic evaluation on internet based cognitive behavioural therapy (Coping with Depression) among 263 participants with clinically significant depressive symptoms from Netherlands.[30 Level 1] The study was conducted alongside a randomised controlled trial.[18 Level 1] Eighty-eight participants in this study received CCBT, another 88 participants received problem solving therapy and another 87 participants were put on wait-list. The economic evaluation consisted of a cost-effectiveness analysis and a cost utility analysis based on societal perspectives. Costs were determined at 5, 8 and 12 weeks follow up. Total cumulative costs over 12 weeks were determined by adding up the costs of each of the 3 time intervals with missing cost data imputed using expectation-maximization (EM) algorithm.

Cost utility analysis showed that median ICER for CCBT versus waiting list placement resulted in €22609 per QALY gained. The ICERS quadrant showed that there was a 28% probability that CCBT is a better treatment at lower costs and 67% at additional costs. The median ICER for PST versus WL resulted in extra costs of €11,523 per QALY. There was 37% probability that it is more effective at lower cost and 58% at extra costs. As for acceptability, the cost-utility analysis showed that there was 28% and 38% probability respectively that CCBT and PST were more cost-effective than WL if society places a zero value on one gained QALY. With willingness to pay of €30,000 per gained QALY the probability was 52% and 61% respectively.

The results of cost-effectiveness analysis showed that the median ICER for CCBT versus WL was €1817 for a health gain of one additional reliably improved participant. There was a 69% probability that a participant will change with CCBT therapy but at additional costs. The ICER for PST versus WL was €1248 per reliably improved participant. There was 60% probability that PST is more effective but at additional costs. As for acceptability, with no willingness to pay, there was 30% probability for CCBT compared with WL. With willingness to pay of €5000 and €10,000, CBT has a probability of 75% and 91% respectively of being more cost-effective compared with WL. As for PST, the probability was 38% at no willingness to pay. With WTP of €5000 and of €10,000 resulted in probabilities of 75% and 89% respectively.[30] Level 1

6.4.2 Cost

Based on other countries experiences, the total annual operating costs will depends on whether the prices includes: computer system, technical support, training and clinical support.

The cost per completed treatment will depends on the licence cost, the amount of facilitator input required, level of qualification, training of the facilitator and the number of individuals who could use the programmes. As all of these software are not in Malay language, there are several options that can be considered. First, is to develop Malaysia own version of CCBT. The second option is to translate the available software packages.

According to Ultrasis, the licence cost for Beating the Blues may vary depending on the needs of the country or organization. For example in UK, the average cost within the NHS is about [redacted] per treatment which includes all the eight sessions of Beating the Blues. The price also includes all hostings and updates of the programme.

As for translation to Malay language, according to Ultrasis it can be done in two ways. First is to have full translation of all video, screens, voice over and other media of Beating the Blues. The cost to create a Malay version will be in the region of [redacted] Another option is to have subtitling of video and voice over only. The estimated cost is around [redacted] (personal communication).

Assuming that we are going to introduce CCBT at five psychiatric clinics and each clinics will see about 20 patients per month, using the current US or UK version of Beating the Blues, the cost is around [redacted] per annum license fee (around [redacted] per treatment)(personal communication).

Another software package in English is MoodGYM. MoodGYM is a free software package and can be accessed from its website www.moodgym.anu.edu.au.

6.5 OTHER ISSUES

6.5.1 ACCEPTABILITY AND SATISFACTION

Acceptability

de Graaf *et al.* conducted a randomised controlled trial on the use and acceptability (i.e. expectancy, credibility, and satisfaction) of unsupported online computerised cognitive behavioural therapy Colour Your Life (CYL) for depression and the association with clinical outcome, in 200 general population (age 18–65) with at least mild to moderate depression (BDI-II score ≥16) in South Netherlands (100 CYL; 100 CYL and TAU). They found that the scores on the treatment expectancy and credibility were moderately high (18.3 vs 19.0 and 18.8 vs 19.2 in CYL vs CYL and TAU respectively, with score range of 3 to 27). Majority of the patients expected that they would be less depressed after treatment or that they would learn to cope with their depression. Most patients in both groups were satisfied with their treatment allocation. More patients in the CYL & TAU group completed all the 8 sessions than those in the CYL only group (26 vs 14, $p<0.05$). CYL was rated as an acceptable treatment in terms of expectancy, credibility, and pre- and post-treatment satisfaction. For factors related to improvement in depression, many usage indices such as number of logins, mood diaries, and total time were positively associated with short-term (3 months) depressive improvement. In the long term (9 months), expectancy was significantly associated with the outcome. The author concluded that good acceptability and high uptake were indications for the feasibility of unsupported online CCBT for individuals' depression. Although CCBT might be a feasible and acceptable treatment for depression, means to improve treatment adherence are needed for unsupported online CCBT in moderately to severely depressed patients.[31] Level 1

Gerhards SA *et al.* conducted a qualitative study to gain knowledge on patient experiences / perspectives with the online self-help CCBT program Colour Your Life (CYL) for depression, and find explanations for the low treatment adherence and effectiveness in 18 patients (age 18–65) selected from a CCBT CYL trial (both groups; CYL, CYL and TAU) with at least mild to moderate depressive symptoms (score≥16 on (BDI-II)) in South Netherlands. Data was collected through semi-structured interviews with an inductive, content analysis of the interviews was performed in line with the Grounded Theory approach. They found the main theme throughout the interviews was barriers and motivators experienced with CCBT, which were related to the course content and to contextual factors (i.e. social aspects, computer aspects and research aspects). The most important barriers said were experiences of a lack of identification with and applicability of CCBT-CYL, lack of support to adhere with the program or to gain deeper understanding, inadequate computer/ internet skills, equipment, or location, confusion between CCBT and internet questionnaires resulted in no CCBT uptake of some study participants and negative experiences with some components (e.g. homework or mood diary). Among the motivators elicited from the interview were positive experience with the CCBT course content (experiencing self-identification; useful information to create more awareness of the symptoms, and on how their thinking and doing are interrelated with the depression symptoms) and improvement (reduction of depression) through CCBT-CYL, participating in a scientific study, the freedom (opportunity to do the therapy at your own time, pace and place) and anonymity associated with online computer self-help and user possesses the right computer skills and equipment. There was suggestion on the need of support to CCBT as an improvement towards adherence and the course content as CYL in its current form does not work for a large group of people with depressive symptoms. The author concluded that more tailoring, the provision of support (professional or lay) and good computer conditions could improve CCBT.[29]

Beattie A *et al.* also conducted a qualitative study using pre- and post-therapy interview to explore expectations and experiences of online cognitive behavioural therapy (CBT) among primary-care patients with depression, focusing on how this mode of delivery impacts upon the therapeutic experience in 24 patients nested within IPCRESS trial with at least moderate depression (BDI score 20-28) who were offered 10 sessions of CBT delivered via internet by qualified psychologist in southwest England (Bristol). They found two key themes regarding expectations and experiences of online CBT which were developing a virtual relationship with a therapist and the process of communicating thoughts and emotions via an online medium (expressing oneself in written form) with each own expectation and experience. Expectation of the former include question whether trusted and committed relationship could be developed online, absence of face-to face contact leading to impersonal/mechanical relationship and opportunity to probe deeply might be diluted (with the absence of visual cues), while experiences found were diverse perspective expressed, most were able to establish good relationship, more able to disclose and openly discussed issues (due to anonymity) and for the withdrew patient it was found that they were frustrated at the quality of relationship and the absence of face-to-face (closeness) interaction. Expectations of the latter include various expectations whether truly to be able to express feeling and be understood on online medium; anticipate to be more able to express feeling through writing compared to talking, worry that they may omit important things/express wrongly in written form, uncertainty whether solely written or combination of both written and face-to-face interaction better and absence of non-verbal cues hinder further communication; while experiences found were participants were able to tell stories online, online medium was not necessarily a barrier to meaningful interaction, therapist could pick up their emotion; participants were able to experience empathy and sympathy, and concern that they may be misunderstood (withdrew) and worry of interpretation of expression written in the absence of face-to-face cues. The author concluded that online CBT seemed to be acceptable to, and experienced as helpful by certain subgroups of patients with depression; those who were familiar with computers, feel comfortable with writing their feelings down, enjoy the opportunities to review and reflect that written (or typed) communication offers were attracted to the ‘anonymity’ of an online therapeutic relationship and open to the proactive requirements of CBT itself. However, on-line CBT may feed into the vulnerability of depressed people to negative thoughts, given the absence of visual cues and the immediate response of face-to-face interaction.[34]

Cavanagh K *et al.* conducted a non comparative open trial (pragmatic study) to examine the acceptability of Beating the Blues, a CCBT which was offered on eight scheduled clinic visits with brief face-to-face support in routine primary and secondary care among 219 adults age 16 to 75 years with anxiety, depression, or both. Patient-level pre treatment data were established at intake, and post treatment data were collected immediately after the final computer session. The result demonstrated that on pre treatment expectation average ratings of CBT credibility were significantly higher than the neutral midpoint (0) on the CB-OPP scale (M = 1.8, SD = 0.8), t (186) = 29.5, p <0.001, and average item ratings of the acceptability of CCBT were also significantly higher than the midpoint (M=6.3, SD = 1.1), t(183) = 29.42, p <0.001; CCBT was rated higher than the midpoint (4) on all items of the A-CCBT (all p <0.001), finding it logical, useful, understandable, and engaging and having confidence in its benefits before treatment. On post treatment feedback and evaluation: both satisfaction and usefulness were significantly above the mid-point; average satisfaction scale ratings were above the neutral mid-point of 3 on the PFQ-CCBT Satisfaction rating scale (M = 4.1, SD = 0.67), t (81) = 15.22, p <0.001, and average ratings of its usefulness were above the midpoint of 2.5 (M = 3.2, SD = 0.7), t (80) = 9.78, p <0.001. The author concluded that Beating the Blues was an acceptable treatment for common mental health problems in routine care.[33] Level II-1

Satisfaction

Perini *et al.* in their study found that 82% of treatment group participants reported being either very satisfied or mostly satisfied with the treatment they received. Ninety four percents rated the quality of the program as excellent or good; 71% rated the quality of internet correspondence with therapist as excellent or good while 29% as satisfactory.[11] Level 1

In Titov *et al.* study, in terms of satisfaction, there was no significant difference between TA and CA. Eighty-seven percents of the participants reported the treatment as being either satisfied or mostly satisfied, 13% reported neutral or somewhat dissatisfied and 0% reported very dissatisfied.[26] Level 1

Multiple regression model fitted to satisfaction with treatment in Proudfoot *et al.* study showed that treatment, drug and age were predictive of this variable. Average satisfaction in CCBT group was 1.68 (95% CI 0.82 – 2.54) points higher than in the treatment-as-usual group; for those given drugs compared with those not given drugs the corresponding figure was 1.28 (95% CI 0.63 – 1.94). For age, the regression coefficient was 0.028 (95% CI 0.0045 – 0.052).[24] Level 1

In Ruwaard *et al.* study, on a scale ranging from 1 to 10 for satisfaction , the average score was 7.7 (SD 1.2).[27] Level 1

6.5.2 SAFETY

There was no retrievable study on the safety of CCBT. However, most of the studies included participants with mild to moderate depression only and excluded patients with suicidal ideation.[21, 24, 26, 27]

6.5.3 ETHICAL ISSUES

The spread of computer-based therapy services has created new ethical issues not encountered in face to face therapy.[43] Among the issues were concerns on how patients should be diagnosed and selected for treatment. Other issues concern who should be responsible for the treatment and how the patient's response to treatment should be monitored. International Society for Mental Health Online (ISMHO) and the Psychiatric Society for Informatics (PSI) have jointly developed detailed operating principles to guide clinicians who provide online clinical mental health and for patients who receive such services. The guidelines have been endorsed across professional disciplines and national boundaries. They involved informed consent about the process, information about the clinician, the potential risks and benefits, safeguards and alternatives; standard operating procedures (such as legal requirements, confidentiality, the structure of the service, records, evaluation) and emergency procedures and back-up.[43]

7 DISCUSSION

Twelve RCTs were identified in the clinical effectiveness review. Seven of the nine studies that compared CCBT and wait-list were pooled and the results suggested that CCBT was more effective than wait-list. The other two studies that were not pooled also showed improvement in the psychological score in the treatment group. The result was in line with other reviews conducted earlier although some of the studies were overlapped.[35, 36] Andersson *et al.* in their study found a moderate effect size of d=0.41. In their subanalysis, they found that for computerised intervention with support, the effect size was d=0.61 and for unsupported treatment the effect size had a much smaller effect of d=0.25.[36] Andrews *et al.* in their meta-analysis obtained an effect size of 0.78 (95%CI 0.59-0.96) for major depression disorder.[35] Our meta-analysis only combined studies with similar comparison and outcome measures and there was no evidence of heterogeneity.

Two studies compared CCBT with TAU. Significant heterogeneity was observed between these two studies. Both studies showed significant improvement in the psychological score after treatment but in de Graaf study the improvement was not significantly different when compared to the TAU group and the TAU&CCBT group. The types of CCBT packages used in these studies were different. The participants were also different.[20] De Graaf only included participants who were not on continuous antidepressant treatment for at least three months prior to entry whereas Proudfoot included participants who received pharmacotherapy or whatever therapy the general practitioner prescribed.[24] Gerhards *et al.* conducted qualitative study to explore the patient perspectives with the online self-help CCBT program Colour Your Life (CYL) for depression, and find explanations for the low treatment adherence and effectiveness in de Graaf study. The most important barriers identified were experiences of a lack of identification with and applicability of CCBT-CYL, lack of support to adhere with the program or to gain deeper understanding, inadequate computer/internet skills, equipment, or location and confusion between CCBT and internet questionnaires.

In one of the study, CCBT was shown to be as good as CBT.[21] Another study compared CBT with email therapy which was based on CBT, the results showed that there was significant improvement in both groups and the outcomes did not significantly differed.[22] Similar results were obtained when CCBT was compared with PST.[18]

The review of published studies found four papers on cost-effectiveness of CCBT for depression in adult patient. All these studies were of good quality and carried out alongside RCTs. Three of the studies compared CCBT and TAU.[10, 28, 29] The results of the two studies that was based on NHS perspectives showed that CCBT was likely to be cost effective if society is willing to pay at least £20,000 per QALY in one study and £30,000 per QALY in another study.[10, 28]

Another study that was based on societal perspectives found that CCBT led to lower societal as well as healthcare cost.[29] Another study compared CCBT with PST and WL. The results showed that there was 69% probability that a participant will change with CCBT therapy but at additional costs.[30] The estimated cost provided by Ultrasis for Ministry of Health Malaysia to start CCBT at five centres using the available version is [redacted]
This is quite reasonable when compared to a CBT session at private practice which may be charged around [redacted] per session. Another alternative is MoodGYM, a free software, although the effect size was only low to moderate.

The review also showed that CCBT was acceptable and most of the patients who underwent the treatment were satisfied. The factors identified that may enhance CCBT usage includes support received from lay or professional facilitators, familiarity with computer programme and good condition of computers.

Although the evidence showed that CCBT is effective and acceptable for the treatment of depression, all the studies were conducted in developed countries and mostly in English speaking countries. In other countries like Germany, Sweden and Netherlands, the software used were in German, Swedish and Dutch respectively. In Malaysia, where we have multi-racial and multi-lingual population, language will possibly be a barrier in using CCBT especially in the rural area and in the elderly.

The population in the majority of the included studies were patients with mild to moderate depression. However, in Proudfoot *et al.* study, 12.5% of the subjects had severe depressive episode[43] and patients with severe symptoms of depression were allowed in Warmerdam *et al.* study.[18]

The availability and accessibility of traditional CBT is limited in Malaysia. Currently CBT can be delivered by trained CBT practitioner who can either be a clinical psychologist, psychologist, psychiatrist or non-psychologist. According to Malaysian CBT Association currently there are 20-30 registered CBT practitioners in Malaysia. However, in Ministry of Health Malaysia facilities, the number of Clinical Psychologist is very few and there is no post for CBT practitioner. The ratio of psychiatrist to population is far from adequate. According to American Psychiatric Association (APA), an area is considered shortage of psychiatrist if the ratio of the number of person in the population group to the number of full time equivalent psychiatrist serving the population is greater than or equal to 20,000:1.

Although this review showed that CCBT is as good as CBT or TAU or PST, the advantage of CCBT especially the package which only need minimal therapist involvement is that it enhanced access to evidence-based psychotherapy and reduced the amount of therapist time needed to achieve improvement in symptoms.

Another possible advantage of CCBT is in reaching patients who may not accept traditional therapy because of stigma or negative attitudes about treatment. The use of technology may allow patients to access care in a less threatening way in which they have more control of the pace and flow of therapy.[44]

Limitations

Our study has several limitations. We tried to include all the relevant papers, however due to accessibility of the electronic databases, we might missed some studies. Although we did not limit our search to English language paper only but finally only full-text articles in English were included. Furthermore, there was no local paper on CCBT and limited papers on CBT were identified.

Another limitation was the different type of CCBT used in the studies. We would like to compare the therapist time and healthcare consumption between CCBT and usual care, however only de Graaf study reported about therapist time.

We pooled the actual value at certain time point, unlike other meta-analysis on CCBT retrieved which pooled the effect size. Despite these limitations, our study indicates that CCBT is effective.

8 CONCLUSION

8.1 EFFECTIVENESS

There was good level and sufficient evidence to support the effectiveness of CCBT for the treatment of depression among adults. There was some evidence that CCBT is as effective as traditional CCBT for the treatment of depression. There is conflicting evidence when CCBT was compared with TAU. CCBT was found to be well accepted and many of the patients were found to be satisfied with the treatment.

8.2 COST EFFECTIVENESS

There was evidence to support the cost-effectiveness of CCBT. The cost per treatment in Malaysia is about [redacted] using the available version of one of the CCBT programme. The cost will escalate if the programme is to be translated into Malay language.

8.3 SAFETY

There was no study retrieved on safety. Patients with suicidal ideation should be excluded from the treatment.

9 RECOMMENDATION

Based on the review, there was evidence to suggest that CCBT is effective for the treatment of depression. The burden of depression in Malaysia is high where it is the leading cause for YLD in men and women. Many patients with depression have no access for treatment and considered as unmet need. CCBT may improve the accessibility of CBT to patients with depression. Using the current version of CCBT programmes in English, the cost per treatment is quite reasonable since CCBT can be accessed either at the clinic, at home or at the office. CCBT may be recommended to selected group of patients with mild to moderate depression. It may also be used as an adjunct to antidepressants in patients with severe depression under the supervision of an experienced psychiatrist. The patients selected for this programme should be patients who have computers and internet access at home. These patients should also be proficient in computer and English. Criteria for selecting patients for this treatment should be developed before introducing CCBT program for adults with depression.

Since there is no local data on CCBT, it is recommended that research be carried out in Malaysia to assess the effectiveness, acceptability and feasibility of CCBT in our population before a nationwide program can be introduced.

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APPENDIX 1

HTA PROTOCOL

TITLE: COMPUTERISED COGNITIVE BEHAVIOURAL THERAPY (CCBT) FOR ADULTS WITH DEPRESSION

1. BACKGROUND INFORMATION:

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide, a tragic fatality associated with the loss of about 850 000 lives every year.

Depression is the leading cause of disability as measured by YLDs and the 4th leading contributor to the global burden of disease (DALYs) in 2000. By the year 2020, depression is projected to reach second place of the ranking of DALYs calculated for all ages, both sexes. Today, depression is already the second cause of DALYs in the age category of 15-44 years for both sexes combined.

The Third Malaysian National Health Morbidity Survey 2006, did a cross sectional survey of psychiatric illness among adults using 28-item version of the General Health Questionnaire (GHQ-28) and found that the overall adjusted prevalence was 11.2%. Overall, there was a 6.3% suicidal ideation and 25.8% rate of chronic suicidal ideation.

Unipolar depression is ranked tenth and third respectively as leading causes of disease burden in males and females in Malaysian Burden of Disease and Injury Study. In women, unipolar depression is the leading cause of YLD, contributing 13% of the YLD. In men, unipolar depression is the second leading cause of YLD contributing 7.2%.[2] The prevalence of depression among adult primary care attendees were reported as 14.4% in a semi urban clinic[3] and 5.6% in another primary care setting in Malaysia

Depression is usually managed with pharmacotherapy, psychotherapy and/or exercise therapy.

Cognitive behavioural therapy (CBT) is a discrete, time-limited, structured psychological intervention, derived from the cognitive behavioural model of affective disorders and where the patient:

- Works collaboratively with the therapist to identify the types and effects of thoughts, beliefs and interpretations on current symptoms, feelings states and/or problem areas
- Develops skills to identify, monitor and then counteract problematic thoughts, beliefs and interpretations related to the target symptoms/problems
- Learns a repertoire of coping skills appropriate to the target thoughts, beliefs and/or problem areas

CBT has been recommended for management of certain types of depression in adults[7] and group CBT has been recommended for mild depression in children and young people.[45] However access to CBT is limited due to too few therapists, expense, waiting lists and patients' reluctance to enter therapy. In Ministry of Health Malaysia, to date there are only three clinical psychologists available. Computerised cognitive behavioural therapy (CCBT) is a self-help option that offers patients the potential benefits of CBT with less therapist involvement.

Computerised cognitive behavioural therapy (CCBT) is defined as a form of CBT, which is delivered using a computer either via a CD-ROM, DVD or the internet. It can be used as the primary treatment intervention with minimal therapist involvement or as augmentation to a therapist-delivered programme where the introduction of CCBT supplements the work of the therapist.

NICE guidelines for management of depression in adults patient recommended CCBT as an alternative treatment for people with persistent subthreshold depressive symptoms or mild to moderate depression. Malaysian evidence-based Clinical Practice Guidelines on Management of Major Depressive Disorder published in 2007 stated that CCBT may be used for mild to moderate depression.

There are several software packages for CCBT such as Beating the Blues (BtB); Overcoming Depression: a five areas approach; Cope; MoodGym; Good Days Ahead; Feelbetter and Defeating Depression. CCBT can also be delivered via email or telephone.

The review was requested by a doctor working in the Psychiatry Department of Hospital Raja Permaisuri Bainun in view of providing the treatment for patients with depression.

2. POLICY QUESTION

Should computerised cognitive behavioural therapy be used for treatment on adults with depression?

3. OBJECTIVE

i. To evaluate clinical effectiveness of computerised cognitive behavioural therapy for treatment of depression in terms of
    a. Improvement in psychological symptoms
    b. Interpersonal and social functioning
    c. Quality of life
    d. Preference, satisfaction and acceptability of treatment
    e. Prevention of relapse

ii. To evaluate the economic issues of computerised cognitive behavioural therapy for treatment of depression

Other issues such as the safety, social, organizational, ethical and legal impact of CCBT will also be assessed.

4. METHODS

To evaluate the clinical effectiveness, a systematic review following the principles used by Cochrane Collaboration will be conducted.

As for, economic evaluation, first, the literature on cost-effectiveness of CCBT will be reviewed. Next, the local direct cost will be estimated.

4.1 Search strategy

Literatures on computerised cognitive behavioural therapy for treatment of depression will be searched from the following sources:

i. Electronic databases as follows; MEDLINE, PubMed, Cochrane database, Cochrane central registers for controlled trials, HTA databases, NHS Economic Evaluation Databases, Science Direct, PsycInfo,

ii. Additional information will be searched through other website such as ARIF, Clinical Practice Guidelines websites, mental health or psychiatric society websites

iii. Additional articles will be identified from reviewing the bibiliographies of retrieved articles.

iv. Expert in the area will be contacted when necessary to get further information.

v. Handsearching of evidence in finding unpublished evidence

The search will be limited to human study only. The following search terms will be used either singly or in combinations: Computerised cognitive behavioural therapy OR CCBT OR "computerised therapy" OR "computer assisted cognitive therapy" OR "internet psychotherapy" OR MoodGym OR Depression program OR Defeating depression, Feelbetter OR Cope OR BTSTEPS OR Good Days Ahead OR beating the Blues OR fearfighter, depression, cost, cost effectiveness, cost implications, psychological symptoms, quality of life, patients preference, patients satisfaction, interpersonal and social functioning, relapse prevention, ethical, social, reduce severity, legal, organisational

4.2 Inclusion And Exclusion Criteria

Inclusion criteria:

Type of studies

For systematic review on clinical effectiveness, systematic reviews, meta-analysis, randomised controlled trials and non-randomised comparative studies on CCBT will be included.

For systematic review on cost effectiveness of CCBT, all cost effectiveness study of satisfactory quality will be included.

Qualitative studies on patients' preference and patients' satisfaction for CCBT treatment will also be included.

Types of participants

Adults with depression

Types of intervention

CCBT either alone or as part of a package, and either via a computer interface or over the telephone with a computer-led response.

Comparator

1. Treatment as usual as described in the study
2. Medication
3. CBT
4. Other CCBT
5. Other psychotherapy

6. Placebo

Types of outcome measures

One or more of the following outcome measures will be assessed:

1. Improvement in psychological symptoms
2. Interpersonal and social functioning
3. Quality of life
4. Preference, satisfaction and acceptability of treatment
5. Organisational, safety, ethical, social, legal
6. Cost per Quality Adjusted Life Years (QALY) gained
7. ICER
8. Cost utility analysis
9. Cost implications
10. DALY

Exclusion criteria

1. CCBT used for other diseases and indications
2. CCBT used among children and adolescents

4.2 Data extraction strategy

Data will be extracted by a reviewer and checked by a second reviewer using a pre-tested data extraction form. Disagreements will be resolved through discussion. A third person, whose decision is final will be consulted when disagreements persists after discussion.

4.3 Quality assessment strategy

The quality of the selected studies will be assessed by two reviewers using Critical Appraisal Skills Programme (CASP) checklists depending on the type of study design. Jadad score will also be used to assess randomised clinical trial.

4.4 Methods of analysis/synthesis

Data on clinical effectiveness and cost effectiveness will be summarized in evidence table. A decision on whether to pool the data on effectiveness will be taken after assessing the heterogeneity of the articles retrieved.

5. REPORT WRITING

APPENDIX 2

ELECTRONIC BIBLIOGRAPHIC DATABASES SEARCHED

1. Medline
2. Science direct
3. Ebscohost - Psychology and Behaviour
4. Cochrane Central Database of Controlled Trials (CENTRAL)
5. Cochrane Database of Systematic Reviews (CDSR)
6. NHS Database of Abstracts of Reviews of Effectiveness (DARE)
7. NHS Economic Evaluation Database (NHS EED)
8. NHS Health Technology Assessment (HTA) Database
9. Office of Health Economics Health Economics Evaluation Database (OHE HEED)

APPENDIX 3

OTHER SOURCES CONSULTED

1. Australian Safety and Efficacy Register of New Interventional Procedures (ASERNIP-S)
2. National Institutes for Health and Clinical Excellence (NICE)
3. Clinical Practice Guidelines and Protocols in British Columbia
4. Columbia British
5. Canadian Agency for Drugs and Technologies in Health (CADTH)
6. International Network of Agencies for Health Technology Assessment (INAHTA)
7. World Health Organisation (WHO)
8. Google
9. EuroSCAN
10. Australia and New Zealand Horizon Scanning Network
11. Guidelines International Network (G-I-N)
12. ClinicalTrials.gov
13. International Society for Pharmacoeconomics and Outcomes Research (ISPOR)

APPENDIX 4

SEARCH STRATEGIES USED IN THE MAJOR ELECTRONIC BIBLIOGRAPHIC DATABASES

Pubmed

#1 computerised cognitive behavioural therapy
#2 computerised cognitive behavioral therapy
#3 internet psychotherapy
#3 computer assisted cognitive therapy
#4 moodGYM
#5 BTSTEPS
#6 beating the blues
#7 internet therapy
#8 (#1) OR (#2) OR (#3) OR (#4) OR (#5) OR (#6) OR (#7)
#9 depression
#10 depressive disorder
#11 major depressive disorder
#12 (#9) OR (#10) OR (#11)
#13 (#8) AND (#12)

Ovid Medline (R) in-Process & other Non-Indexed citations and Ovid Medline (R) 1948 to present.

1. Depression/or depressive disorder/ or anxiety disorders
2. Depression$ patient.tw.
3. (depressive adj (syndrome$ or disorder$ or symptom$)).tw.
4. Emotional depression.tw.
5. Major depressive disorder$.tw.
6. 1 or 2 or 3 or 4 or 5
7. Therapy, computer-assisted/or cognitive therapy/
8. Therapy?$cognitive.tw.
9. (cognitive behavior adj (therapy?$ or psychotherapy)).tw.
10. Computer?assisted therapy.tw.
11. ((therapy adj computer assisted$)or assissed protocol-directed).tw.
12. (therapy adj (computer or internets)).tw.
13. 7 or 8 or 9 or 10 or 11 or 12
14. 6 and 13
15. Cognitive therapy/or behavior therapy/
16. Behavior therapy$.tw.
17. Psychotherapy/or psychotherapy,group/
18. Psychotherapy$.tw.
19. Group psychotheraphy$.tw.
20. Antidepressive agents/
21. (antideprressiv? Adj(agents or drugs?)).tw.
22. 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 13 and 22

EBM Cochrane Clinical trial, CDSR

1. Depression$.tw.
2. (depressive adj (syndrome$ or disorder$ or symptom$)).tw.
3. Emotional depression.tw.
4. Major depression.tw.
5. 1 or 2 or 3 or 4
6. Therapy?$cognitive.tw.
7. (cognitive behavior adj (therapy?$or psychotherapy)).tw.
8. Computer?assisted therapy.tw.
9. (therapy adj computer assisted$ or assisted protocol-directed).tw.
10. Therapy adj(computer or internets).tw.
11. Email therapy.tw
12. Internet guided therapy.tw.
13. 6 or 7 or 8 or 9 or 10
14. 5 and 13
15. 11 or 12

APPENDIX 5

QUALITY ASSESSMENT CHECKLIST – JADAD SCORE AND DRUMMOND CHECKLIST

JADAD SCORE FOR ASSESSMENT OF RCT

QUESTION	YES	NO
1. Was the study described as random?	1	0
2. Was the randomization scheme described and appropriate?	1	0
3. Was the study described as double-blind?	1	0
4. Was the method of double blinding appropriate? (Were both the patient and the assessor appropriately blinded?)	1	0
5. Was there a description of dropouts and withdrawals?	1	0

DRUMMOND CHECKLIST FOR ECONOMIC EVALUATION

Well defined question	Yes	Can’t tell	No
Description of alternatives	Yes	Can’t tell	No
Effectiveness established?	Yes	Can’t tell	No
All relevant costs and consequences	Yes	Can’t tell	No
Appropriate measurement?	Yes	Can’t tell	No
Credible valuation?	Yes	Can’t tell	No
Differential timing?	Yes	Can’t tell	No
Incremental costs and consequences?	Yes	Can’t tell	No
Allowance made for uncertainty?	Yes	Can’t tell	No
Appropriate interpretation of results?	Yes	Can’t tell	No

APPENDIX 6

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomised controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

APPENDIX 7

EVIDENCE TABLES

This appendix contains the evidence tables with data extracted from the 29 studies included in this HTA report.

The evidence tables are arranged in four parts. Part 1 is the evidence tables for health technology assessment report, systematic reviews and meta-analysis, systematic reviews and guidelines. Part 2 is the evidence tables for primary papers on effectiveness, all were RCTs. Part 3 is the evidence obtained on acceptability and satisfaction which included qualitative and cross-sectional studies. Part 4 is the evidence table for economic studies.

PART 1

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Kaltenthaler E, Brazier J, Nigris ED, Tumur I, Ferriter M, Beverley C, Parry G, Rooney G, Sutcliffe P. Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation. Health Technology Assessment 2006;10(33).
Study type and Methods	Systematic Review
LE	1
Num. of pts and Pt characteristics	8 articles included Cavanagh 2004 - BtB (non-comparative) Proudfoot 2004 - Cope (non-comparative) Marks 2003 - Cope (non-comparative) Osgood-Hynes 1998 - Cope (non-comparative) Whitfield 2004 - Overcoming Depression (non-comparative) Christensen 2004 - MoodGym Clarke 2002 - ODIN (RCT) Yates 1996 - Balance (pseudo-RCT)
Intervention	CBT delivered alone or in a package of care either via a computer interface (personal computer or internet) or over the telephone with a computer response including these packages; BtB, Overcoming Depression, FF, Cope and BT Steps
Comparison	Current standard treatment including TCBT, non-directive counseling, primary care counseling, routine methods and alternative methods.
Follow up	Up to 12 months
Outcome measures	**Evidence support the effectiveness of BtB and FF**. There is limited evidence of poorer quality that Cope and Overcoming Depression are effective. There is no RCT to support the effectiveness of BT Steps. There is some evidence that CCBT is as effective as TCBT for the treatment of depression/ anxiety and phobia/panic. There is some evidence that CCBT is more effective than TAU in the treatment of depression/ anxiety. In studies reporting accurate estimates of therapist time, CCBT appears to reduce therapist time compared with TCBT and is therefore of use where access to TCBT is limited.
General comments	Results were not pooled

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Spek V, Cuijpers P, Nyklicek I, *et al.* Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. Psychological Medicine. 2007;37:319-28
Study type and Methods	Systematic Review of RCTs
LE	1
Num. of pts and Pt characteristics	12 studies included (2334 subjects) Clarke 2002 Clarke 2005 Christensen 2004 Andersson 2005 Patten 2003 Klein 2001 Klein 2006 Carlbring 2001 Carlbring (in press) Andersson (in press) Hirai 2005 Kenardy 2005 5 studies focused on depression (4 on treatment and one on prevention) (total no of subjects 1982)
Intervention	Internet-based CBT – standardized CBT treatment that the participants work through more or less independently on the internet.
Comparison	Waiting list or treatment as usual (TAU) or psychoeducation
Follow up	4 – 32 weeks
Outcome measures	Effect size , d, 0.27 (95% CI 0.15, 0.40) I^2-70.1% - considerable heterogeneity Subanalysis without Andersson 2005 d = 0.22 (95% CI 0.09, 0.35), moderate heterogeneity I^2 – 47.8%
General comments	All the results were pooled eventhough the outcome was different! However sub analysis was done.

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Andrews G, Cuijpers P, Craske MG, *et al.* Computer Therapy for the Anxiety and Depressive Disorders is Effective, Acceptable and Practical Health Care: A Meta-Analysis. PLoS ONE. 2010;5(10):e13196.
Study type and Methods	Systematic reviews and meta-analysis of RCT
LE	1
Num. of pts and Pt characteristics	23 studies were included (6 on Major Depression) ● Andersson 2005 ● Kessler 2009 ● Perini 2009 ● Selmi 1990 ● Titov 2010 ● Wright 2005
Intervention	Computerised CBT or computerised CBT with therapist support
Comparison	Waitlist or treatment as usual
Follow up	9 – 26 weeks
Outcome measures	For major depression, Hedges g = 0.78, 95% CI 0.59-0.96 Adherence was good and a median of 80% of people who began these programs completed all lessons (range 48% - 100%) Ten studies provided data on patient satisfaction and a median of 86% (range 70% - 100%) of patients reported that they were satisfied or very satisfied.
General comments	

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Griffiths KM, Farrer L, Christensen H. The efficacy of internet interventions for depression and anxiety disorders: areview of randomised controlled trials. MJA. 2010;192(11):S4-S11.
Study type and Methods	Systematic review of RCT
LE	1
Num. of pts and Pt characteristics	26 trials were included, of which eight trials were on depression 1. (Christensen 2004, Griffiths 2004, Mackinnon 2008) 2. Spek 2007, Spek 2008 3. Warmedam 2008 4. Perini 2009 5. Meyer 2009 6. Patten 2003 7. Clarke 2002 Clarke 2005
Intervention	Self help intervention or a website intervention that incorporated a self-help component. These includes CCBT and psychoeducation
Comparison	Attention placebo control, waiting list control or treatment as usual
Follow up	Up to 12 months
Outcome measures	Effect size difference – For short term – 6 trials showed that CBT was overall effective with medium effect size (range 0.30 – 0.65) Long term effect 3 trials showed CBT was effective
General comments	Results not pooled due to heterogeneity of studies

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

Bibliographic citation	Andersson G, Cuijpers P. Internet-Based and Other Computerised Psychological Treatments for Adult Depression: A Meta-Analysis. Cognitive Behaviour Therapy. 2009;38(4):196-205.
Study type and Methods	Systematic Review and meta-analysis of randomised controlled trials
LE	1
Num. of pts and Pt characteristics	12 studies included Andersson 2005 Christensen 2004 Clarke 2002 Clarke 2005 Clarke 2009 Proudfoot 2004 Ruwaard 2009 Selmi 1990 Spek 2007 Van Straten 2008 Warmerdam 2008 Wright 2005
Intervention	Internet based CBT and computerised psychological treatments conditions
Comparison	Wait-list, care as usual and/or other types of control group
Follow up	Not available
Outcome measures	Mean effect size of 15 comparisons between internet-based and computerised psychological treatment vs control group at post –test, cohen's d = 0.41 (95% CI 0.29-0.54) Moderate heterogeneity I^2=57.49 Sensitivity analysis was done but not much difference in the effect size as well as heterogeneity. Publication bias assessed-no indication of significant publication bias. Two factors was significantly related to effect sizes i.e. professional support and control group
General comments	

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION
QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

Bibliographic citation	Boudreau R, Moulton K, Cunningham J. Self-directed Cognitive Behavioural Therapy for Adults with Diagnosis of Depression: Systematic Review of Clinical Effectiveness, Cost-effectiveness, and Guidelines. Canadian Agency for Drugs and Technologies in Health. Ottawa, 2010.
Study type and Methods	Systematic Review
LE	1
Num. of pts and Pt characteristics	Included 3 guidelines- NICE UK, New Zealand and Malaysia; two RCTs-De Graaf (2008&2009), Bielich (2008) and one economic paper by Vos 2005
Intervention	Computerised and non-computerised self directed cognitive behavioural therapy
Comparison	Not clearly stated. The papers included compared with wait-list, TAU
Follow up	Not stated
Outcome measures	Only qualitative summary The evidence indicated that self-directed CBT improved the clinical ratings of depressive symptoms and that it could be a cost-effective therapy option for individuals with mild to moderate depression.
General comments	

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION
QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Mundy L, Hiller J. Internet delivered cognitive behavioural therapy for patients with depression. Adelaide Health Technology Assessment, Australia and New Zealand Horizon Scanning Network. Adelaide, 2009.
Study type and Methods	Systematic Review
LE	1
Num. of pts and Pt characteristics	Included 5 studies - Perini 2009 - Kessler 2009 - Spek 2008 - Kalthentaler 2008 - Kalthentaler 2006
Intervention	CCBT
Comparison	TCBT
Follow up	4-12 months
Outcome measures	The good quality evidence indicates a potential for the uptake of this technology in rural and remote areas, and the possible ability to overcome barriers to increase the treatment options especially in males.
General comments	Methods of review not clearly delineated

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	National Collaborating Centre for Mental Health. Depression: The treatment and management of depression in adults. (Updated version)National Clinical Practice Guidelines 90. The British Psychological Society and the Royal College of Psychiatrist. London, 2010
Study type and Methods	Guidelines
LE	1
Num. of pts and Pt characteristics	7 RCTS ANDERSSON2005 CHRISTENSEN2004 CHRISTENSEN2004 SPEK2007 CLARKE2002 CLARKE2005 PROUDFOOT2004A Selmi1990 SPEK2007*
Intervention	CCBT
Comparison	Control or active comparator
Follow up	6 – 12 months
Outcome measures	CCBT vs WL SMD -0.27 (CI -0.54 to 0.01), CCBT vs TAU: SMD -0.62 (CI -0.91 to -0.33); CCBT vs discussion control: SMD -0.61 (CI -1.22 to 0); CCBT vs information control: SMD -0.23 (CI -0.43 to -0.02); CCBt vs any control: SMD -0.40 (CI -0.58 to -0.22) Recommendation: Computerised cognitive behavioural therapy (CCBT) is one of the interventions recommended for people with persistent subthreshold depressive symptoms or mild to moderate depression CCBT for people with persistent subthreshold depressive symptoms or mild to moderate depression should: • be provided via a stand-alone computer-based or web-based programme • include an explanation of the CBT model, encourage tasks between sessions, and use thought-challenging and active monitoring of behaviour, thought patterns and outcomes • be supported by a trained practitioner, who typically provides limited facilitation of the programme and reviews progress and outcome • typically take place over 9 to 12 weeks, including follow-up.
General comments	

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

Bibliographic citation	Parikh SV, Segal ZV, Grigoriadis S, *et al.* Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults. II. Psychotherapy alone or in combination with antidepressant medication. Journal of Affective Disorders. 2009;117(Supplement 1):S15-S25.
Study type and Methods	Systematic Review /guidelines
LE	1
Num. of pts and Pt characteristics	Spek 2007 meta-analysis Marks 2003 Andersson 2005 Proudfoot 2004
Intervention	Computer-based/internet based psychotherapy
Comparison	TAU, wait list OR TCBT
Follow up	Not mentioned
Outcome measures	Recommended as second line treatment for acute MDD.
General comments	Results were not pooled

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

Bibliographic citation	Ministry of Health Malaysia. Clinical Practice Guidelines on Management of Major Depressive Disorder. Putrajaya: Ministry of Health, 2007
Study type and Methods	Systematic Review /guidelines
LE	1
Num. of pts and Pt characteristics	NICE Technology Appraisal 97, 2006-Kalthenthaler Wright 2005 Christensen 2004
Intervention	CCBT
Comparison	Wait-list or other therapy
Follow up	-
Outcome measures	CCBT may be used for mild to moderate depression (Grade A)
General comments	Results were not pooled

PART 2

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS BEATING THE BLUES EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Proudfoot J, Goldberg D, Mann A, <i>et al.</i> Computerized, interactive, multimedia cognitive-behavioural program for anxiety and depresion in general practice. Psychological Medicine. 2003;33:217-27

Proudfoot J, Ryden C, Everitt B, <i>et al.</i> Clinical efficacy of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. British Journal of Psychiatry. 2004;185:46-54</td></tr>
<tr><td>Study type and Methods</td><td>Randomised controlled trial</td></tr>
<tr><td>LE</td><td>I</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>274 patients from 11 general practice in United Kingdom. Aged 18-75 years suffering from depression, mixed anxiety and depression or anxiety disorder not currently receiving any form of psychological treatment or counseling, who scored 4 or more on GHQ-12 and 12 or more on CIS-R</td></tr>
<tr><td>Intervention</td><td>N= 146
CCBT – Beating the blues

Patients could also receive pharmacotherapy if the general practitioner wished to prescribe it, and/or general support and practical or social help, but not face to face counseling or psychological intervention.</td></tr>
<tr><td>Comparison</td><td>N=128
Treatment as usual

Received whatever therapy the general practitioner prescribed.</td></tr>
<tr><td>Follow up</td><td>8 months</td></tr>
<tr><td>Outcome measures</td><td>
<table>
<tr><th></th><th>Baseline</th><th>2 mths</th><th>3 mths</th><th>5 mths</th><th>8 mths</th></tr>
<tr><td colspan="6">BDI</td></tr>
<tr><td>TAU</td><td>24.7 (9.2)</td><td>18.4 (10.9)</td><td>16.4 (11.0)</td><td>13.5 (10.3)</td><td>14.9 (11.3)</td></tr>
<tr><td>CCBT</td><td>24.9 (10.8)</td><td>12.1 (9.3)</td><td>12.1 (10.3)</td><td>9.6 (8.2)</td><td>9.3 (8.5)</td></tr>
<tr><td colspan="6">Work and Social Adjustment</td></tr>
<tr><td>TAU</td><td>19.1 (8.3)</td><td>14.6 (8.5)</td><td>14.0 (9.5)</td><td>11.54 (8.5)</td><td>11.8 (10.0)</td></tr>
<tr><td>CCBT</td><td>18.4 (9.2)</td><td>11.2 (7.6)</td><td>10.5 (8.5)</td><td>9.1 (7.7)</td><td>7.9 (7.8)</td></tr>
</table>

Satisfaction with treatment
Multiple regression model fitted to satisfaction with treatment showed that treatment, drug and age were predictive of this variable. Average satisfaction in CCBT group was 1.68 (95% CI 0.82 – 2.54) points higher than in the treatment-as-usual group; for those given drugs compared with those not given drugs the corresponding figure was 1.28 (95% CI 0.63 – 1.94). For age, the regression coefficient was 0.028 (95% CI 0.0045 – 0.052)</td></tr>
<tr><td>General comments</td><td>Withdrawal
Phase I – 35%
Phase II – 22%</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS MOODGYM EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Christensen H, Griffiths KM, Jorm AF. Delivering interventions for depression by using the internet: randomised controlled trial. BMJ. 2004, 23 January 10.1136/bmj.37945.566632.EE.</td></tr>
<tr><td>Study type and Methods</td><td>Randomised controlled trial

Parallel – 3 arms</td></tr>
<tr><td>LE</td><td>1</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>525 subjects age between 18-52 years old.</td></tr>
<tr><td>Intervention</td><td>N = 182
MoodGYM – consisted of five interactive modules which were made available sequentially weekly.

N = 165
Bluepages

Lay interviewers contacted participants weekly by phone to direct their use of the websites.</td></tr>
<tr><td>Comparison</td><td>N = 178

Participants were phoned weekly by interviewers to discuss lifestyle and environmental factors that may have an influence on depression</td></tr>
<tr><td>Follow up</td><td>6 weeks</td></tr>
<tr><td>Outcome measures</td><td>Symptoms of depression after 6 weeks
CES-D
<table>
<tr><th></th><th>Mean (SD)</th></tr>
<tr><td>Blue pages</td><td>3.9 (9.1)</td></tr>
<tr><td>MoodGYM</td><td>4.2 (9.1)</td></tr>
<tr><td>Control</td><td>1.0 (8.4)</td></tr>
</table>
<table>
<tr><th></th><th>Difference (95% CI)</th></tr>
<tr><td>BluePages v MoodGYM</td><td>-0.3 (-2.6 to 2.0)</td></tr>
<tr><td>MoodGYM v control</td><td>3.2 (0.9 to 5.4)</td></tr>
<tr><td>BluePages v Control</td><td>2.9 (0.6 to 5.2)</td></tr>
</table>
</td></tr>
<tr><td>General comments</td><td>Recruited via questionnaire posted to 27000 randomly selected participants from electoral roll.

Attrition rate for MoodGYM – 25%
Bluepages – 15%</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS COPING WITH DEPRESSION EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Warmerdam L, Straten Av, Twisk J, <i>et al.</i> Internet-based treatment for adults with depressive symptoms: randomised controlled trial. Journal of Medical Internet Research. 2008, Oct-Dec;10(4):e44</td></tr>
<tr><td>Study type and Methods</td><td>Randomised Controlled Trial</td></tr>
<tr><td>LE</td><td>1</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>263 participants aged > 18 years old from Netherlands.</td></tr>
<tr><td>Intervention</td><td>88 subjects
CBT based on Coping with Depression – 8 lessons, one lesson a week with ninth lesson took place 12 weeks later. Use information, exercises and audio visual aids.</td></tr>
<tr><td>Comparison</td><td>88 subjects
Problem Solving Therapy
3 steps – first step – subjects described what really matters
Second step – subjects wrote down their concern, worries and problems
3rd steps – subjects made plan for their future.

87 subjects
Wait - list</td></tr>
<tr><td>Follow up</td><td>12 weeks</td></tr>
<tr><td>Outcome measures</td><td>Outcome measures
<table>
<tr><th></th><th>Baseline</th><th>5 W</th><th>8 W</th><th>12 W</th></tr>
<tr><td colspan="5">CES-D</td></tr>
<tr><td>CBT</td><td>31.2 (9.3)</td><td>22.9 (10.6)</td><td>19.4 (11.3)</td><td>17.9 (11.7)</td></tr>
<tr><td>PST</td><td>31.9 (9.3)</td><td>20.6 (11.2)</td><td>20.6 (11.3)</td><td>18.4 (12.1)</td></tr>
<tr><td>WL</td><td>32.1 (9.3)</td><td>25.6 (9.9)</td><td>25.2 (9.9)</td><td>25.8 (10.4)</td></tr>
<tr><td colspan="5">EQ5D</td></tr>
<tr><td>CBT</td><td>0.64 (0.18)</td><td>0.68 (0.27)</td><td>0.73 (0.27)</td><td>0.76 (0.27)</td></tr>
<tr><td>PST</td><td>0.59 (0.18)</td><td>0.73 (0.27)</td><td>0.73 (0.27)</td><td>0.76 (0.27)</td></tr>
<tr><td>WL</td><td>0.59 (0.18)</td><td>0.69 (0.27)</td><td>0.65 (0.27)</td><td>0.66 (0.27)</td></tr>
</table>
Effect Size
<table>
<tr><th></th><th></th><th>5 W</th><th>8 W</th><th>12 W</th></tr>
<tr><td>CES-D</td><td>CBT</td><td></td><td>0.54 (0.25-0.84)</td><td>0.69 (0.41-0.98)</td></tr>
<tr><td></td><td>PST</td><td>0.47 (0.17 – 0.77)</td><td></td><td>0.65 (0.36-0.95)</td></tr>
<tr><td>EQ5D</td><td>CBT</td><td></td><td>0.30 (0.02 – 0.59)</td><td>0.36 (0.07 – 0.65)</td></tr>
<tr><td></td><td>PST</td><td>0.14 (-0.14 – 0.42)</td><td></td><td>0.38 (0.09 – 0.68)</td></tr>
</table>
</td></tr>
<tr><td>General comments</td><td>Recruitment through advertisement.

Patients with CES-D >32 were also included

Attrition rate 30% at 5 weeks assessment</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS SADNESS PROGRAM EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Perini S, Titov N, Andrews G. Clinician-assisted internet-based treatment is effective for depression: randomised controlled trial. Australian and New Zealand Journal of Psychiatry. 2009;43:571-8</td></tr>
<tr><td>Study type and Methods</td><td>RCT</td></tr>
<tr><td>LE</td><td>1</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>48 participants

Volunteers recruited via website (www.climateclinic)

> 18 years old, resident of Australia, not in CBT, not experiencing psychotic mental illness or severe symptoms of depression > 23 on PHQ-9 or > 2 to Question 9 on suicidal ideation. Mild or subthreshold depression > 5 on PHQ-9, taking the same dose for at least 1 month

MINI 5.0 - DSM IV criteria for depression</td></tr>
<tr><td>Intervention</td><td>N= 29
Sadness Programme
(supported CCBT)</td></tr>
<tr><td>Comparison</td><td>N=19
Wait list</td></tr>
<tr><td>Follow up</td><td>8 weeks</td></tr>
<tr><td>Outcome measures</td><td>Primary outcome
Improvement in psychological symptoms.
<table>
<tr><th></th><th>Intervention Mean (SD)</th><th>Control Mean (SD)</th><th>Effect size (cohen's d)</th></tr>
<tr><td>PHQ-9</td><td>9.59(5.82)</td><td>14.11 (4.21)</td><td>0.89</td></tr>
<tr><td>BDI-II</td><td>17.30(9.86)</td><td>23.33 (9.29)</td><td>0.63</td></tr>
</table>
Secondary outcome
No significant difference between treatment and control group for PANAS, PANAS-negative, K-10 and SDS

Clinical outcomes: remission and recovery (reduction of pre-treatment PHQ-9 scores of at least 50%)
41% of treatment group were classified as recovered compared with 6% of control group participants.

Satisfaction: 82% of treatment group participants reported being either very satisfied or mostly satisfied. 94% rated the quality of the program as excellent or good; 71% rated the quality of internet correspondence with therapist as excellent or good while 29% as satisfactory.</td></tr>
<tr><td>General comments</td><td></td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS SADNESS PROGRAM EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Titov N, Andrews G, Davies M, <i>et al.</i> Internet Treatment for Depression: A Randomised Controlled Trial Comparing Clinician vs. Technician Assistance. PLoS ONE. 2010;5(6):e109.</td></tr>
<tr><td>Study type and Methods</td><td>Randomised Controlled Trial</td></tr>
<tr><td>LE</td><td>I</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>141 participants randomised via www.random.org

>18 years old, PHQ-9 between 10 and 23, responding < 2 to Question 9 on PHQ-9</td></tr>
<tr><td>Intervention</td><td>CCBT – Sadness Program

Technician Assisted Treatment (N=47)
Technician provide weekly email or telephone to provide encouragement and support and where possible to respond to participants' general questions by referring them to the materials in the Sadness program.

Clinician-Assisted Treatment (N=49)
Participants received weekly email or telephone contact with clinician and has access to an online discussion forum where they could post questions to the clinician about the program content. Clinicians actively engaged with each participant in treatment including goal setting, problem solving and discussion of strategies for overcoming hurdle to progress.</td></tr>
<tr><td>Comparison</td><td>Wait list
N=45

Received the clinician assisted program after the intervention group completed the Sadness Program</td></tr>
<tr><td>Follow up</td><td>4 months</td></tr>
<tr><td>Outcome measures</td><td>Post-treatment (11-week)
<table>
<tr><th></th><th>n</th><th>Pre Mean (SD)</th><th>Post Mean (SD)</th><th>Pre-post Mean diff (95%CI)</th></tr>
<tr><td colspan="5">PHQ-9</td></tr>
<tr><td>CA</td><td>46</td><td>14.15 (4.39)</td><td>7.30 (4.48)</td><td>6.85 (5.40-8.29)</td></tr>
<tr><td>TA</td><td>41</td><td>14.20 (4.20)</td><td>7.59 (4.04)</td><td>6.61
(4.95-8.27)</td></tr>
<tr><td>Control</td><td>40</td><td>13.35 (4.62)</td><td>12.98 (4.44)</td><td>0.38 (-0.91-1.66)</td></tr>
<tr><td colspan="5">BDI-II</td></tr>
<tr><td>CA</td><td>46</td><td>28.96 (11.51)</td><td>14.59 (11.12)</td><td>14.36 (10.62-18.11)</td></tr>
<tr><td>TA</td><td>41</td><td>27.15 (9.96)</td><td>15.29 (9.81)</td><td>11.85 (7.85-15.85)</td></tr>
<tr><td>Control</td><td>40</td><td>26.33 (10.46)</td><td>26.15 (10.14)</td><td>0.18 (-2.12-2.77)</td></tr>
</table>
Effect size: Within group, On BDI-II, 1.27 and 1.20 for the CA and TA respectively
On PHQ-9, 1.54 and 1.60 respectively.

Between groups, BDI-II 0.07 (95%CI, 0.35 to 0.49). For PHQ-9, 0.07 (95%CI, 0.36 to 0.49)

At follow up:
<table>
<tr><th></th><th>n</th><th>Follow-up</th><th colspan="2">Effect size</th></tr>
<tr><td colspan="3">PHQ-9</td><td>within</td><td>TA vs CA</td></tr>
<tr><td>CA</td><td>38</td><td>8.67 (5.42)</td><td>1.11</td><td>0.46</td></tr>
<tr><td>TA</td><td>30</td><td>6.49 (3.94)</td><td>1.89</td><td></td></tr>
<tr><td colspan="5">BDI-II</td></tr>
<tr><td>CA</td><td>38</td><td>16.22 (13.16)</td><td>1.03</td><td>0.40</td></tr>
<tr><td>TA</td><td>40</td><td>11.66 (9.58)</td><td>1.59</td><td></td></tr>
</table>
Recovered – Post-treatment 61% TA group, 43% CA group, and 3% control
At follow – up, 66% TA, 43% CA
Reliable clinical change – 56% TA, 61% CA and 8% Control
At follow-up, 59% of TA, and 59% of CA

Treatment satisfaction: No significant difference between TA and CA. 87% reported the treatment as being either satisfied or mostly satisfied, 13% reported neutral/somewhat dissatisfied and 0% reported very dissatisfied.</td></tr>
<tr><td>General comments</td><td>Participants recruited via website www.virtualclinic.org.au</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS COLOUR YOUR LIFE EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>de Graaf LE, Gerhards SAH, Arntz A, <i>et al.</i> Clinical effectiveness of online computerised cognitive-behavioural therapy without support for depression in primary care: randomised trial. The British Journal of Psychiatry. 2009;195(1):73-8

de Graaf LE, Gerhards SAH, Arntz A, <i>et al.</i> One-year follow-up results of unsupported online computerised cognitive behavioural therapy for depression in primary care: A randomised trial. Journal of Behavior Therapy and Experimental Psychiatry. 2011;42(1):89-95.</td></tr>
<tr><td>Study type and Methods</td><td>Randomised Controlled Trial

3 arms parallel</td></tr>
<tr><td>LE</td><td>1</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>303

Age 18-65, access internet at home, mild to moderate depressive complaints (BDI-II score ≥ 16)</td></tr>
<tr><td>Intervention</td><td>N = 100
Online CCBT without support - Colour Your Life</td></tr>
<tr><td>Comparison</td><td>N=103
Treatment as usual – delivered by participant's own GP who was advised to follow guidelines from the DutchCollege of General Practitioner

N= 100
Combined CCBT and TAU</td></tr>
<tr><td>Follow up</td><td>12 months</td></tr>
<tr><td>Outcome measures</td><td>Mean scores based on ITT
Depression –BDI-II
<table>
<tr><th></th><th>CCBT</th><th>TAU</th><th>CCBT+TAU</th></tr>
<tr><td>Baseline</td><td>28.2 (7.7)</td><td>27.9 (7.5)</td><td>27.4 (8.2)</td></tr>
<tr><td>2 mths</td><td>20.6 (10.4)</td><td>22.1 (10.2)</td><td>21.7 (10.1)</td></tr>
<tr><td>3 mths</td><td>20.4 (11.2)</td><td>21.4 (11.0)</td><td>19.1 (10.9)</td></tr>
<tr><td>6 mths</td><td>17.8 (10.6)</td><td>18.9 (11.8)</td><td>17.5 (2.2)</td></tr>
<tr><td>9 mths</td><td>15.5 (10.8)</td><td>18.0 (11.8)</td><td>17.6 (12.8)</td></tr>
<tr><td>12 mths</td><td>16.1 (11.1)</td><td>17.5 (11.1)</td><td>16.5 (11.1)</td></tr>
</table>
Unsupported online CCBT is not superior to TAU by a GP for depression

Effect size at 12 months (d=1.26 for CCBT; d=1.09 for TAU; d=1.11 for CCBT&TAU), but the between group effect sizes were small (d=0.17 for CCBT vs TAU; d=0.02 for CCBT&TAU vs TAU.
<table>
<tr><th>SF-36</th><th>CCBT</th><th>TAU</th><th>CCBT+TAU</th></tr>
<tr><td>Baseline</td><td>44.7 (13.7)</td><td>44.5 (13.9)</td><td>45.1 (14.3)</td></tr>
<tr><td>3 mths</td><td>50.4 (16.5)</td><td>51.9 (15.7)</td><td>52.8 (17.5)</td></tr>
</table>
No significant difference in the number of participants who had remitted.
36 (40.9%) for CCBT, 34 (37.4%) for TAU, 33 (37.5%) for CCBT&TAU.

No significant different for relapse rate.</td></tr>
<tr><td>General comments</td><td>Random selection of general population

Attrition rate – 9.2%</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION
QUESTION : IS DEPREXIS EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Meyer B, Berger T, Caspar F, <i>et al.</i> Effectiveness of a Novel Integrative Online Treatment for Depression (Deprexis): Randomised Controlled Trial. J Med Internet Res. 2009;11(2):e15</td></tr>
<tr><td>Study type and Methods</td><td>Randomised Controlled Trial</td></tr>
<tr><td>LE</td><td>1</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>396 adults aged between 18 – 72</td></tr>
<tr><td>Intervention</td><td>CCBT – Deprexis
(N=320)</td></tr>
<tr><td>Comparison</td><td>Wait-list (N=76)
Participants in wait list received access to the programme after 9 weeks</td></tr>
<tr><td>Follow up</td><td>Up to 6 months</td></tr>
<tr><td>Outcome measures</td><td>Outcome measures depression and social function
<table>
<tr><td colspan="4">Social Dysfunction (WSA)</td></tr>
<tr><td>T0 (baseline)</td><td>5.66 (1.66), 315</td><td>5.89 (1.50), 75</td><td>P=0.27 (d=0.15)</td></tr>
<tr><td>T1 (9 weeks)</td><td>4.80 (2.14), 154</td><td>6.06 (1.42, 57</td><td>P<0.001 (d=0.64)</td></tr>
<tr><td>T2 (18 weeks)</td><td>4.48 (2.26), 109</td><td>4.65 (1.92), 34</td><td>P=0.69 (d=0.08)</td></tr>
<tr><td>T3 (27 weeks)</td><td></td><td>4.86 (2.30), 24</td><td></td></tr>
<tr><td>T4
(6 months follow-up)</td><td>4.10 (2.41), 83</td><td>4.07 (2.74), 12</td><td>P=-0.97 (d=0.01)</td></tr>
</table>
<table>
<tr><td></td><td>CCBT
M (SD), N</td><td>Wait-list
M (SD), N</td><td>Mean comparisons and effect size</td></tr>
<tr><td colspan="4">Depression (BDI)</td></tr>
<tr><td>T0 (baseline)</td><td>26.72 (9.86), 320</td><td>27.11 (8.98), 76</td><td>P=0.76
d=0.04</td></tr>
<tr><td>T1 (9 weeks)</td><td>19.87 (11.85), 159</td><td>27.15 (10.01), 57</td><td>P<0.001
d=0.64</td></tr>
<tr><td>T2
(18 weeks)</td><td>17.23 (11.85), 111</td><td>20.39 (12.92), 35</td><td>P=0.18
d=0.25</td></tr>
<tr><td>T3
(27 weeks)</td><td></td><td>19.07 (15.32, 25</td><td></td></tr>
<tr><td>T4
(6 months follow-up)</td><td>16.50 (12.93), 85</td><td>15.25 (14.80), 14</td><td>P=0.74
d=0.09</td></tr>
</table>
</td></tr>
<tr><td>General comments</td><td>Recruitment via Internet depression forums
Attrition rate at T1 (9 weeks) – 45%</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

Bibliographic citation	Wright JH, Wright AS, Albano AM, *et al.* Computer-Assisted Cognitive Therapy for Depression: Maintaining Efficacy While Reducing Therapist Time. Am J Psychiatry. 2005;162:1158-64
Study type and Methods	Randomised controlled trial
LE	1
Num. of pts and Pt characteristics	45 patients recruited through advertisements or referral Mean age 38.2 years
Intervention	Computer-assisted cognitive therapy (N=15) Nine sessions with a therapist (first session= 50 minutes, subsequent session= 25 minutes) and eight computer sessions (20 – 30 minutes that followed immediately after session 1-9
Comparison	Cognitive therapy – received cognitive therapy (N=15) Wait list – no treatment during the 8-week waiting period (N=15)
Follow up	6 months post-treatment
Outcome measures	Depression severity, measured as mean difference. At 8 weeks
General comments	Assessors blinded

Outcome measures – At 8 weeks:

	CCBT	CBT	Waitlist
HDRS	8.2 (6.4)	8.4 (6.3)	2.1 (5.6)
BDI	19.0 (10.1)	15.2 (7.1)	5.2 (6.4)

At end-point (6 months)

	CCBT	CBT	Waitlist
HDRS	7.5 (6.3)	8.3 (6.6)	1.9 (5.5)
BDI	17.5 (10.8)	14.7 (8.0)	5.8 (6.5)

Average Cohen's d=1.14 for CCBT and 1.04 for standard cognitive therapy. No differences between computer assisted cognitive therapy and standard cognitive therapy d=0.10

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Andersson G, Bergstrom J, Hollandare F, <i>et al.</i> Internet-based self-help for depression: randomised controlled trial. Br J Psychiatry. 2005;187:456-61</td></tr>
<tr><td>Study type and Methods</td><td>Randomised Controlled Trial</td></tr>
<tr><td>LE</td><td>1</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>117 patients with mild-to-moderate depression.</td></tr>
<tr><td>Intervention</td><td>N= 57

Internet administered self help with minimal therapist contact

Based on Beck's cognitive therapy. 89 pages of text divided into 5 modules: introduction; behavioural activation; cognitive restructuring; sleep and physical health; and relapse prevention and future goals. The sleep module was based on a programme for insomnia. Each module ended with aquiz, with questions on the context of the module. Responses were automatically sent to the therapist, who in turn gave an email feedback on the answers and gave the participant access to the next treatment module within 24 hour.</td></tr>
<tr><td>Comparison</td><td>N= 60

Waiting list
-participate in a moderate discussion group online.</td></tr>
<tr><td>Follow up</td><td>6 months</td></tr>
<tr><td>Outcome measures</td><td>Improvement in depression at post-treatment
<table>
<tr><th></th><th>n</th><th>Pre Mean (SD)</th><th>Post Mean (SD)</th><th>Pre-post diff Mean(95% CI)</th></tr>
<tr><td colspan="5">BDI</td></tr>
<tr><td>Treatment</td><td>36</td><td>20.5 (6.7)</td><td>12.2 (6.8)</td><td>8.3 (5.7 to 10.9)</td></tr>
<tr><td>Control</td><td>49</td><td>20.9 (8.5)</td><td>19.5 (8.1)</td><td>1.4 (-1.1 to 3.9)</td></tr>
<tr><td colspan="5">MADRS-S</td></tr>
<tr><td>Treatment</td><td>36</td><td>20.1 (5.7)</td><td>12.7 (8.3)</td><td>5.5 (4.6 to 10.1)</td></tr>
<tr><td>Control</td><td>49</td><td>21.6 (7.2)</td><td>19.0 (7.6)</td><td>2.6 (-0.4 to 4.8)</td></tr>
<tr><td colspan="5">QoLi</td></tr>
<tr><td>Treatment</td><td>36</td><td>-0.1 (1.1)</td><td>0.5 (1.6)</td><td>0.6 (0.2 to 1.1)</td></tr>
<tr><td>Control</td><td>49</td><td>-0.2 (1.6)</td><td>0.0 (1.5)</td><td>0.2 (-0.2 to 0.6)</td></tr>
</table>
At 6 months
<table>
<tr><th></th><th>n</th><th>Follow-up score Mean (SD)</th><th>Pre-treatment to follow-up difference Mean (95% CI)</th></tr>
<tr><td colspan="4">BDI</td></tr>
<tr><td>Treatment</td><td>36</td><td>13.1 (9.1)</td><td>7.8 (4.6 to 11.3)</td></tr>
<tr><td>Control</td><td>35</td><td>13.1 (7.6)</td><td>7.4 (4.0 to 10.7)</td></tr>
<tr><td colspan="4">MADRS_S</td></tr>
<tr><td>Treatment</td><td>36</td><td>14.6 (9.2)</td><td>6.3 (3.2 to 9.3)</td></tr>
<tr><td>Control</td><td>35</td><td>14.5 (9.3)</td><td>6.8 (3.9 to 9.7)</td></tr>
<tr><td colspan="4">QoLI</td></tr>
<tr><td>Treatment</td><td>36</td><td>0.7 (1.7)</td><td>0.9 (0.4 to 1.4)</td></tr>
<tr><td>Control</td><td>35</td><td>0.9 (1.8)</td><td>1.0 (0.5 to 1.4)</td></tr>
</table>
Participation in a web-based discussion group only had no effect on depressive symptoms.</td></tr>
<tr><td>General comments</td><td>Subjects recruited through advertisement-volunteers
Self –report, no formal diagnosis
Allocation concealment
Withdrawal 27%</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Vernmark K, Lenndin J, Bjärehed J, <i>et al.</i> Internet administered guided self-help versus individualized e-mail therapy: A randomised trial of two versions of CBT for major depression. Behaviour Research and Therapy. 2010;48(5):368-76</td></tr>
<tr><td>Study type and Methods</td><td>Randomised comtrolled trial
3 arms
Therapist were randomly assigned to participants in each group.
Participants were randomi</td></tr>
<tr><td>LE</td><td>I</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>88 participants
At least 18 years old, MADRS-S >14 and <31, <4 on item 9 (suicidal thoughts) on MADRS-S</td></tr>
<tr><td>Intervention</td><td>N=29
Self-help treatment

Based on material used in an earlier study (Andersson 2005). Consisted of seven text modules totaling 114 pages; including exercises. Included an introduction to CBT, depression from a CBT-perspective with a behavioural focus, behavioural activation, cognitive restructuring, sleep management, defining goal/values and relapse prevention</td></tr>
<tr><td>Comparison</td><td>N=30
Email therapy

Manual based on CBT-principles for treating depression with a focus on case conceptualization, functional analysis and subsequent applications of components commonly used in CBT for depression including behavior activation and cognitive restructuring. Participants received one treatment mail per week and assistant mails were used to answer shorter questions of practical or technical nature.

N=29
Waiting list</td></tr>
<tr><td>Follow up</td><td>6 months</td></tr>
<tr><td>Outcome measures</td><td>Depression outcome and Quality of life
<table>
<tr><th></th><th>Pre Mean (SD)</th><th>Post Mean (SD)</th><th>6 mth Mean (SD)</th></tr>
<tr><td colspan="4">BDI</td></tr>
<tr><td>Email</td><td>22.2 (5.3)</td><td>10.3 (5.2)</td><td>9.0 (5.6)</td></tr>
<tr><td>Self-help</td><td>22.2 (6.3)</td><td>12.3 (7.3)</td><td>10.9 (9.8)</td></tr>
<tr><td>Control</td><td>21.8 (6.6)</td><td>16.6 (7.9)</td><td>9.7 (7.2)</td></tr>
<tr><td colspan="4">Quality of Life</td></tr>
<tr><td>Email</td><td>0.04 (1.67)</td><td>0.99 (1.85)</td><td>1.65 (1.94)</td></tr>
<tr><td>Self-help</td><td>0.04 (1.51)</td><td>1.10 (1.56)</td><td>1.17 (2.06)</td></tr>
<tr><td>Control</td><td>-0.22 (1.52)</td><td>0.26 (1.82)</td><td>1.45 (1.66)</td></tr>
</table>
Both email-group and self-help groups were significantly improved compared to the waiting-list condition p=0.002 and p=0.06 respectively. The two treatments did not differ.
<table>
<tr><th>Assessments</th><th>E-mail</th><th>Self-help</th></tr>
<tr><td colspan="3">BDI</td></tr>
<tr><td colspan="3">Within Group</td></tr>
<tr><td>Posttreatment</td><td>2.27</td><td>1.46</td></tr>
<tr><td>6-month</td><td>2.42</td><td>1.56</td></tr>
<tr><td colspan="3">Between Group</td></tr>
<tr><td>Posttreatment</td><td>0.96</td><td>0.56</td></tr>
<tr><td colspan="3">Quality of Life</td></tr>
<tr><td colspan="3">Within group</td></tr>
<tr><td>Posttreatment</td><td>0.53</td><td>0.69</td></tr>
<tr><td>6-month</td><td>0.89</td><td>0.63</td></tr>
<tr><td colspan="3">Between Group</td></tr>
<tr><td>Posttreatment</td><td>0.39</td><td>0.49</td></tr>
</table>
At post-treatment 83% (n=25) of participants in the email therapy condition, 74% of the participants in the self help condition and 25% in the waiting-list condition no longer fulfilled the criteria of major depression according to DSM-IV as measured by SCID-I.</td></tr>
<tr><td>General comments</td><td>Recruitment through print and electronic media.
Interviewed with SCID-I before enrollment
Attrition rate from pre to post treatment – 3%
Assessor blinded</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION

<table>
<tr><td>Bibliographic citation</td><td>Kessler D, Lewis G, Kaur S, <i>et al.</i> Therapist-delivered internet psychotherapy for depression in primary care: a randomised controlled trial. The Lancet. 2009;374:628-34.</td></tr>
<tr><td>Study type and Methods</td><td>Randomised Controlled Trial
Multicentre</td></tr>
<tr><td>LE</td><td>1</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>297 patients aged 18-75 years old from primary care with new episode of depression. BDI> 14.</td></tr>
<tr><td>Intervention</td><td>Therapist delivered internet psychotherapy
(N=149)
10 sessions, each 55 min to be completed within 16 weeks of randomization. Participants were allocated on a rota basis to the next available therapists, and made their own appointment online. Sessions were secured by individual passwords. Participants and therapist typed free-text into the computer with messages sent instantaneously, no other media or means of communication were used.</td></tr>
<tr><td>Comparison</td><td>Wait list
(N=148)</td></tr>
<tr><td>Follow up</td><td>8 months</td></tr>
<tr><td>Outcome measures</td><td>Primary – BDI score 4 months after randomization
<table>
<tr><th></th><th>Intervention</th><th>Control</th></tr>
<tr><td>Recovery (BDI < 10)</td><td>43(38%)</td><td>23(24%)</td></tr>
<tr><td>BDI score</td><td>14.5 (11.2)</td><td>22.0 (13.5)</td></tr>
<tr><td>SF-12</td><td>41.5 (12.6)</td><td>35.4 (12.5)</td></tr>
<tr><td>EQ-5D</td><td>0.82 (0.19)</td><td>0.75 (0.23)</td></tr>
</table>
8 months
<table>
<tr><th></th><th>Intervention</th><th>Control</th></tr>
<tr><td>Recovery (BDI < 10)</td><td>46 (42%)</td><td>26 (26%)</td></tr>
<tr><td>BDI score</td><td>14.7 (11.6)</td><td>22.2 (15.2)</td></tr>
<tr><td>SF-12</td><td>41.0 (13.4)</td><td>37.1 (14.2)</td></tr>
<tr><td>EQ-5D</td><td>0.83 (0.19)</td><td>0.75 (0.26)</td></tr>
</table>
</td></tr>
<tr><td>General comments</td><td>Allocation concealment
Per-protocol analysis though stated as intention to treat analysis.</td></tr>
</table>

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT EFFECTIVE FOR ADULTS WITH DEPRESSION ?

<table>
<tr><td>Bibliographic citation</td><td>Ruwaard J, Schrieken B, Schrijver M, <i>et al.</i> Standardized web-based cognitive behavioural therapy of mild to moderate depression: a randomised controlled trial with a long term follow-up. Cognitive Behaviour Therapy. 2011;38(4):206-21</td></tr>
<tr><td>Study type and Methods</td><td>Randomised Controlled Trial</td></tr>
<tr><td>LE</td><td>I</td></tr>
<tr><td>Num. of pts and Pt characteristics</td><td>54 individuals with chronic moderate depression from general population in Netherlands.
➢ 18 years old
➢ BDI score between 10-29
Mean age – 42 years</td></tr>
<tr><td>Intervention</td><td>N=36
Immediate treatment- Standardised therapist guided web based CBT

A full treatment requires approximately 11 weeks to complete, although the schedule allows clients to adjust the pace to their own situation. The manual defines 8 treatment phases with 86 assignments and 21 feedback/instruction texts. Clients need about 2 to 4 hour per week to complete the assignment and therapists need about 20 to 40 minute to formulate their feedback</td></tr>
<tr><td>Comparison</td><td>N= 18
Wait-list

16/18 participants embarked om web-based treatment after the 11-week waiting period</td></tr>
<tr><td>Follow up</td><td>18 month</td></tr>
<tr><td>Outcome measures</td><td>Primary outcome – BDI-IA
T1-posttest at 11 weeks (ITT)
<table>
<tr><th></th><th>Pre M (SD)</th><th>Post M (SD)</th><th>Effect size d (95% CI)</th></tr>
<tr><td colspan="4">BDI-IA</td></tr>
<tr><td>Treatment</td><td>19.7 (5.5)</td><td>9.8 (6.5)</td><td>0.7 (±0.6)</td></tr>
<tr><td>Control</td><td>21.3 (5.3)</td><td>15.6 (7.6)</td><td>1.1 (±1.1)</td></tr>
</table>
Analysis of the web-CBT at pretest, posttest and after 18 months (N=39) showed that participants improved significantly from pretest to posttest ($p<0.001$), $d=1.6$) and maintained their improvements up to the 18-month follow-up.

Satisfaction
On a scale ranging from 1 to 10, the average score was 7.7 (SD1.2)</td></tr>
<tr><td>General comments</td><td>Attrition rate 9%

No formal diagnosis of depression</td></tr>
</table>

PART 3

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT COST-EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Kaltenthaler E, Brazier J, Nigris ED, Tumur I, Ferriter M, Beverley C, Parry G, Rooney G, Sutcliffe P. Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation. Health Technology Assessment 2006;10(33).
Study type and Methods	Economic Analysis Part 1 – Systematic Review of economic paper Part 2 – Cost-effectiveness Models
LE	1
Num. of pts and Pt characteristics	Part 1 – Mc Crone 2004 (based on Proudfoot 2004) No formal analysis for other CCBT package Part 2 Modelling – estimated cased on Mc Crone 2004 for BtB and Whitfield (unpublished 2004) for Overcoming depression
Intervention	CCBT
Comparison	TAU
Follow up	Modeled for 18 months
Outcome measures	Part1 Well conducted study with good internal validity. Mc Crone concluded that BtB was cost-effective against TAU in terms of cost per QALY - £1250. There are few limitations but has been addressed in the model. Part 2 The incremental cost per QALY of BtB over TAU is £1801. Based on CEAC, the probability of accepting BtB over TAU at 30,000 is 86.8%. For Cope were £7139 and 62.6% and for Overcoming Depression were £5391 and 54.4%. The strength of BtB llies in the fact that it has been evaluated in the context of an RCT with a control group. The subgroup analysis found no differences across severity groupings.
General comments	

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS THERAPIST DELIVERED PSYCHOTHERAPIST COST-EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Hollinghurst S, Peters TJ, Kaur S, *et al.* Cost-effectiveness of therapist-delivered online cognitive-behavioural therapy for depression: randomised controlled trial. The British Journal of Psychiatry. 2010;197:297-304
Study type and Methods	Cost effectiveness analysis Based on Kessler 2009 (RCT) NHS Perspectives
LE	1
Num. of pts and Pt characteristics	297 patients aged 18-75 years old from primary care with new episode of depression. BDI> 14.
Intervention	Therapist delivered internet psychotherapy
Comparison	Wait list
Follow up	8 months
Outcome measures	Online CBT was more expensive than usual care although the outcomes were better. Using complete case data, cost per QALY gain was £17173, 56% chance that online CBT is cost-effective at the £20000 per QALY level and 71% chance at the £30000 per QALY threshold. Using imputed data, there is 94% chance that the intervention is cost-effective at £20000 per QALY.
General comments	Sensitivity analysis conducted -imputation of missing data -excluding secondary care -varying cost

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT(COLOUR YOUR LIFE) COST-EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Gerhards SAH, De Graaf LE, Jacobs LE, *et al.* Economic evaluation of online computerised cognitive-behavioural therapy without support for depression in primary care: randomised trial. The British Journal of Psychiatry. 2010;196:310-8
Study type and Methods	Cost effectiveness analysis and cost-utility analysis Based on De Graaf (2009) – RCT Societal perspectives
LE	1
Num. of pts and Pt characteristics	303 Age 18-65, access internet at home, mild to moderate depressive complaints (BDI-II score ≥ 16)
Intervention	N = 100 Online CCBT without support - Colour Your Life
Comparison	N=103 Treatment as usual – delivered by participant's own GP who was advised to follow guidelines from the Dutch College of General Practitioner N= 100 Combined CCBT and TAU
Follow up	12 months
Outcome measures	CCBT has the lowest societal as well as health care costs even after regression correction for baseline diference. At 6 months base-case analysis, the societal cost for CCBT was €9092, CCBT plus TAU was €10534 and TAU €9765. Corrected case-base analysis showed a mean QALY of 0.71 for CCBT, 0.71 for CCBT plus TAU, and 0.72 for TAU. CCBT was also found to be the most optimal treatment when compared with both TAU and CCBT plus TAU with a probability of about 65% of being the most efficient strategy at a threshold value of €0 per QALY.
General comments	

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT (COPING WITH DEPRESSION) COST-EFFECTIVE FOR ADULTS WITH DEPRESSION

Bibliographic citation	Warmerdam L, Smit F, Straten Av, *et al.* Cost-utility and Cost-effectiveness of Internet-based Treatment for Adults with Depressive Symptoms: Randomised Trial. Journal of Medical Internet Research. 2010;12(5):e53
Study type and Methods	Cost utility and Cost effectiveness analysis Based on Warmerdam 2008 -Randomised controlled trial Societal perspective
LE	1
Num. of pts and Pt characteristics	263 participants aged > 18 years old from Netherlands.
Intervention	88 subjects CBT based on Coping with Depression – 8 lessons, one lesson a week with ninth lesson took place 12 weeks later. Use information, exercises and audio visual aids.
Comparison	88 subjects Problem Solving Therapy 3 steps – first step – subjects described what really matters Second step – subjects wrote down their concern, worries and problems 3rd steps – subjects made plan for their future. 87 subjects Wait – list (WL)
Follow up	12 weeks
Outcome measures	Cost- utility – ICERS Median ICER for CCBT vs WL - €22609 per QALY gained. 28% probability that CBT is a better treatment at lower costs and 67% at additional costs . Median ICER for PST vs WL resulted in extra costs of €11,523 per QALY . 37% probability that it is more effective at lower cost and 58% at extra costs. Cost-utility – Acceptability 28% and 38% probability respectively that CCBT and PST are more cost-effective tah waiting if society places a zero value on one gained QALY. With willingness to pay of €30,000 per gained QALY the probability was 52% and 61% respectively. Cost-effectiveness – ICERS Median ICER CCBT vs WL - €1817 for a health gain of one additional reliably improved participant. 69% probability that a participant will change with CCBT therapy but at additional costs Median ICER PST vs WL - €1248 per reliably improved participant. 60% probability that PST is more effective but at additional costs. Cost-effectiveness – acceptability With no willingness to pay 30% probability for CCBT vs WL. With willingness to pay of €5000 and €10,000, CBT has a probability of 75% and 91% respectively of being more cost-effective compared with WL. For PST, 38% at no willingness to pay. With WTP of €5000 and of €10,000 result in probabilities of 75% and 89%.
General comments	

PART 4

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT ACCEPTABLE FOR ADULTS WITH DEPRESSION?

Bibliographic citation	de Graaf LE, Huibers MJ, Riper H, Gerhards SA, Arntz A. Use and acceptability of unsupported online computerised cognitive behavioral therapy for depression and associations with clinical outcome. J Affect Disord. 2009 Aug;116(3):227-31.
Study type and Methods	Randomised controlled trial Objective: To have a closer look at usage and acceptability (i.e. expectancy, credibility, and satisfaction) of the intervention and how these factors were related to treatment outcome.
LE	I
Num. of pts and Pt characteristics	N=200 (general population in the South Netherlands, between 18– 65 years, only participants allocated to CCBT alone or the combination treatment were included in the analyses) Main inclusion criterion: at least mild to moderate depression (BDI-II score≥16). Mean age was 44.3 (SD 11.8) years for CYL and 45.2 (SD 10.9) years for CYL&TAU. Baseline BDI-II scores are high: 28.2 (SD 7.7) for CYL and 27.4 (SD 8.2) for CYL&TAU.
Intervention	CCBT program Colour Your Life (CYL) : an online, multimedia, interactive, self-help computer program for subthreshold depression based on the principles of CBT. The combination of text, audio, and video makes it potentially suitable for a broad public. CYL consists of eight weekly sessions, a ninth booster session, thirteen homework assignments, and a 'mood diary'. No professional assistance was offered. Use and acceptability factors were associated with depressive improvement for the short-term (3-months) and long-term (9-months) separately. Improvement was defined as a decrease of at least 9 points on the BDIII
Comparison	Treatment as usual
Follow up	nine months of follow-up
Outcome measures	Acceptability (expectancy, credibility, and satisfaction) - Treatment expectancy and rationale credibility (CEQ) - Satisfaction with treatment allocation - Evaluation questionnaire - Track-and-trace : tracks which aspects of CYL were used and for how long (total time spent, time spent per login, number of visits to various aspects of the program (sessions, homework assignments, and mood diary), number of finished sessions and number of completed homework assignments). Scores on the CEQ were moderately high. Most patients were satisfied with their treatment allocation. More patients in the CYL & TAU group completed the eighth session than those in the CYL only group (p<0.05) Factors related to improvement in depression: Most CYL usage indices, were associated with short-term reduction in depression (all p <0.05). In the long-term, expectancy and all usage variables showed significant associations with depressive improvement (all p<0.05) Uptake was sufficient, but dropout was high. Many usage indices were positively associated with short-term depressive improvement, whereas only homework was related to long-term improvement. Acceptability was good and expectancy could predict long-term, but not short-term outcome. CYL was rated as an acceptable treatment in terms of expectancy, credibility, and pre- and post-treatment satisfaction. Furthermore, expectancy, but not credibility, was positively related to long-term depressive improvement. Conclusion good acceptability and high uptake are indications for the feasibility of unsupported online CCBT for depression. Although CCBT might be a feasible and acceptable treatment for depression, means to improve treatment adherence are needed for unsupported online CCBT in moderately to severely depressed individuals.
General comments	At follow up, data were available for 178 participants (attrition rate 11%)

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT ACCEPTABLE FOR ADULTS WITH DEPRESSION?

Bibliographic citation	Gerhards SA, Abma TA, Arntz A, de Graaf LE, Evers SM, Huibers MJ, Widdershoven GA. Improving adherence and effectiveness of computerised cognitive behavioural therapy without support for depression: a qualitative study on patient experiences. J Affect Disord. 2011 Mar;129(1-3):117-25.
Study type and Methods	Qualitative study (data collected through semi-structured interviews with an inductive, content analysis of the interviews was performed in line with the Grounded Theory approach (Charmaz, 2000). Open questions guided by a topic list, between April 2007 and June 2008, after three pilot interviews the initial topic list adjusted according to relevant emergent topics. All interviews were audio-recorded and transcribed. A 'member check' performed to check the validity. Objective: To gain knowledge on patient experiences / perspectives with the online self-help CCBT program Colour Your Life (CYL) for depression, and find explanations for the low treatment adherence and effectiveness
LE	III
Num. of pts and Pt characteristics	N=18 patients. Interviewees were selected from a CCBT trial (200 participants). Trial inclusion criteria: - age 18–65; - at least mild to moderate depressive symptoms (score≥16 on(BDI-II)); - duration of depressive symptoms 3 months or more; - no current psychological treatment for depression; - no continuous antidepressant treatment for at least 3 months prior to entry; - fluent in Dutch; - no alcohol or drug dependence; - no severe psychiatric co-morbidity. Trial participants randomly allocated to 1) CCBT, or 2) treatment as usual by a GP (TAU), or 3) a combination of both CCBT & TAU. Further trial details described in de Graaf *et al.*, 2009b, 2008 Interview participants recruited from the CCBT and COMBI groups. Partcipant selection: based on maximal variation on age, sex, treatment group (CCBT & TAU), time period between the inclusion in the research project and the moment of the interview, and adherence to CCBT.
Intervention	Self-help CCBT program **"Colour Your Life" (CYL)** is an online, multimedia, interactive computer programme for depression. The programmes consist of 8 weekly session and a ninth booster session. Each session contains video fragments to illustrate the theory. In total, 13 homework assignments are given. The program offers option to keep a 'mood diary'. CCBT: offered as a self-help intervention, no professional assistance offered. Patients could reach the program wherever they had a computer with Internet access. The usage and acceptability of the CCBT program presented elsewhere (de Graaf *et al.*, 2009a).

Comparison	-
Follow up	-
Outcome measures	Main theme throughout the interviews: **barriers and motivators** experienced with CCBT. They were related to the course content and to contextual factors (i.e. social aspects, computer aspects and research aspects). The most important barriers : - experiences of a lack of identification with and applicability of CCBT-CYL, - lack of support to adhere with the program or to gain deeper understanding, and - Inadequate computer/Internet skills, equipment, or location. - Confusion between CCBT and Internet questionnaires resulted in no CCBT uptake of some study participants. - negative experiences with some components (e.g. homework or mood diary), Motivators : - positive experience with the CCBT course content (experiencing self-identification; useful information to create more awareness of the symptoms, and on how their thinking and doing are interrelated with the depression symptoms) and improvement (reduction of depression) through CCBT-CYL, - participating in a scientific study - the freedom (opportunity to do the therapy at your own time, pace and place) and anonymity associated with online computer self-help. - user possesses the right computer skills and equipment The addition need of support to CCBT was suggested as an improvement towards adherence and the course content ; reasons to create self-discipline, to have personal contact Author's conclusion: The CCBT program CYL in its current form does not work for a large group of people with depressive symptoms. More tailoring, the provision of support (professional or lay) and good computer conditions could improve CCBT.
General comments	Out of 18 interviewees, 8 completed all CCBT sessions Among the 10 noncompleters, 3 had never started CCBT nor changed to another form of help while 7 interviewees had started. Among these 7, 3 experienced CCBT as inconvenient and therefore changed to another form of help for depression symptoms while 4 interviewees did not

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION : IS CCBT ACCEPTABLE FOR ADULTS WITH DEPRESSION?

Bibliographic citation	Beattie A, Shaw A, Kaur S, Kessler D. Primary-care patients' expectations and experiences of online cognitive behavioural therapy for depression: a qualitative study. Health Expect. 2009 Mar;12(1):45-59.
Study type and Methods	Qualitative study (using repeat semi-structured interviews with pt before & after therapy), nested within IPCRESS trial Pre-therapy interview : expectation Post therapy : experience (Interviews conducted between Feb 2006 & Apr 2007) Objective: To explore expectations and experiences of online cognitive behavioural therapy (CBT) among primary-care patients with depression, focusing on how this mode of delivery impacts upon the therapeutic experience.
LE	III
Num. of pts and Pt characteristics	24 individuals with depression from 5 GP in southwest England (Bristol). - Who were offered 10 sessions of CBT delivered via internet by qualified psychologist. - No age range - New episode depression (ICD-10) diagnosis - At least moderate depression (BDI score 20-28) Age range – 24-66 years Majority- female
Intervention	N=24 - Online CBT provided by PsychologyOnline.co.uk delivering live therapy from a qualified psychologist for anyone with computer & internet access -After consent, patient was given manual with information : how to access therapy session, booking & attend appt. Interacted by typing in Q & A (instant messaging)
Comparison	-
Follow up	-

Outcome measures	Two key themes regarding **expectations and experiences** of online CBT were: i. developing a virtual relationship with a therapist, expectation : - question whether trusted & committed relationship could be developed online - absence of face-to face contact lead to impersonal/mechanical relationship - opportunity to probe deeply might be diluted (absence of visual cues) experiences: - diverse perspective expressed - most able to establish good relationship - more able to disclose & openly discuss issues (due to anonymity) - most withdrew : frustrated at quality of relationship, absence of face-to-face (closeness) ii. the process of communicating thoughts and emotions via an online medium (expressing oneself in written form) Expectation: - various expectation whether truly be able to express feeling & be understood on online medium - anticipate more able to express feeling through writing compared to talking - worried may omit important things/express wrongly in written form - uncertainty whether solely written or combination of both written & face-to-face interaction better - absence of non-verbal cues hinder further communication Experiences: - able to tell stories online - online medium was not necessarily barrier to meaningful interaction - therapist can pick up their emotion; able to experience empathy & sympathy - concern that they may be misunderstood (withdrew) & worried of interpretation of expression written in the absence of face-to-face cues esp in earlier session - aspects impacted upon pt therapeutic experience: i. visual dimension of seeing own thoughts and therapist response ii. time within online exchange Advantage : convenience and fitting therapy into their daily routine, with any technical problems quickly resolved Helpfulness/benefit: happier, less agitated, improved sleep & better relationship, gain insight to possible cause of depression. Online CBT seems to be acceptable to, and experienced as helpful by certain subgroups of patients with depression; iii. those who are familiar with computers, iv. feel comfortable with writing their feelings down, v. enjoy the opportunities to review and reflect that written (or typed) communication offers are attracted to the 'anonymity' of an online therapeutic relationship vi. open to the proactive requirements of CBT itself. However, on-line CBT may feed into the vulnerability of depressed people to negative thoughts, given the absence of visual cues and the immediate response of face-to-face interaction.
General comments	14 completed therapy; 9 of 24 withdrew; all pretherapy interviewed; post therapy : 20 only.

EVIDENCE TABLE: COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION

QUESTION: IS CCBT ACCEPTABLE FOR ADULTS WITH DEPRESSION?

Bibliographic citation	Elsegood K & Powell D. Computerised cognitive-behaviour therapy (cCBT) and older people: A pilot study to determine factors that influence willingness to engage with CCBT. Counselling and Psychotherapy Research, September 2008; 8(3): 189-192
Study type and Methods	Cross sectional study (Using a short questionnaire: designed to ascertain whether participants would be interested in using computerised therapy, and if so whether they would be willing to learn the necessary computer skills). Objective: The aim of this study was to explore whether older people with depression and/or anxiety were potentially willing to engage with computerised cognitive-behaviour therapy (cCBT).
LE	III
Num. of pts and Pt characteristics	60 service users of older people's mental health service. (41 outpatients, 16 attended a day hospital, 3 inpatients for functional disorders). Age range: 65 to >85 yrs Inclusion criterion : mild to moderate depression and/or anxiety (based on clinical judgment). Exclusion criteria : severe depression or anxiety (based on clinical judgment) or a diagnosis of dementia.
Intervention	Computerised cognitive-behaviour therapy (cCBT)
Comparison	
Follow up	
Outcome measures	Result: 44.7% of the respondents were interested in using cCBT, and would be willing to learn the necessary computer skills. Qualitative analysis found some common themes : - lack of motivation to try computerised therapy due to depression: - fear/rejection of technology: - concern that cognitive abilities are inadequate for using a computer - concern that sensory and/or motor abilities are inadequate for using a computer - feeling too old to learn new skills: - preference for human contact: - enthusiasm to learn computer skills, having never had the opportunity before: Six negative themes and only one positive, the occurrence of the positive theme was of similar frequency to the negative. Conclusion: This pilot study suggests that older people with anxiety and/or depression may be willing to engage with cCBT. However, a number of important factors are highlighted that would need to be considered in deciding whether to develop access to cCBT for older people.
General comments	38 out of 60 responded (63.3% response rate)

EVIDENCE TABLE : COMPUTERISED COGNITIVE BEHAVIOUR THERAPY FOR ADULTS WITH DEPRESSION
QUESTION : IS CCBT ACCEPTABLE FOR ADULTS WITH DEPRESSION?

Bibliographic citation	Cavanagh K, David Alan Shapiro DA, Van Den Berg S, *et al.*The Acceptability of Computer-Aided Cognitive Behavioural Therapy: A Pragmatic Study. Cognitive Behaviour Therapy Vol 38, No 4, pp. 235–246, 2009
Study type and Methods	Non comparative open trial (Pragmatic study) Objective: To examine the acceptability of CCBT when accessed in routine primary and secondary care. It measures treatment principle credibility and pretreatment expectations of CCBT and, for those completing treatment post therapy evaluation of the experience.
LE	II-I
Num. of pts and Pt characteristics	Study population: N= 219 adults with anxiety, depression, or both; identified by health professional in 11 participating primary and secondary health care practices (eight general practices, two community mental health teams, one primary care clinical psychology service) Inclusion criteria: (1) age range of 16 to 75 years; (2) suffer from depression, mixed anxiety/depression, or anxiety disorder (including panic or phobias); (3) score 4 or higher on the 12-item General Health Questionnaire (GHQ). Exclusion criteria: currently receiving face-to-face psychological treatment or counselling for the target condition; experiencing suicidal ideation; or having a current diagnosis of psychosis, organic mental disorder, or primary alcohol/substance use disorder. Participants age range: 19 to 70 years
Intervention	CCBT programme **Beating the Blues** (for more details, see www.ultrasis.com), comprises eight treatment sessions with brief face-to-face support, in addition to a 15-min introductory video, viewed on the computer and included a 2-hr staff training course on how to use the programme. The eight interactive therapy sessions are normally taken at weekly intervals. Each session lasts about 50 min and is completed in the routine care setting (GP office, community mental health team centre, mental health resource centre, clinical psychology service), with homework projects to complete between sessions (e.g. problem diaries, thought records, behavioural experiments).
Comparison	
Follow up	

Outcome measures	Outcomes: Pretreatment measures: Demographic information, treatment history and previous computer experience. Pre and posttreatment measures explored: the relationship among programme acceptability, treatment continuation, and outcomes for people accessing the programme in routine care. Result: 191 (87%) completed the pretreatment measures. Analysis of treatment acceptability for CCBT indicated a positive patient experience with the programme. **Pretreatment expectation:** - Average ratings of CBT credibility were significantly higher than the neutral midpoint (0) on the CB-OPP scale (M ¼ 1.8, SD ¼ 0.8), t (186) ¼ 29.5, p <0.001. - Average item ratings of the acceptability of CCBT were significantly higher than the midpoint (M ¼ 6.3, SD ¼ 1.1), t(183) ¼ 29.42, p <0.001; CCBT was rated higher than the midpoint (4) on all items of the A-CCBT (all p <0.001), finding it logical, useful, understandable, and engaging and having confidence in its benefits before treatment. Pretreatment expectancies predicted CCBT treatment completion but not outcomes. No differences were found between men and women on pretreatment measures **Post treatment feedback and evaluation:** Satisfaction: Average satisfaction scale ratings were above the neutral mid-point of 3 on the PFQ-CCBT Satisfaction rating scale (M = 4.1, SD = 0.67), t(81) = 15.22, p <0.001. Usefulness: Averaged ratings of its usefulness were above the midpoint of 2.5 (M = 3.2, SD = 0.7), t(80) = 9.78, p <0.001. Comparison with other treatments: No significant differences were found between groups receiving different prior treatment types (medication, M = 3.6, SD = 1.0; talking therapies, M = 3.9, SD = 0.9; both, M = 3.1, SD = 1.1) on comparative ratings of Beating the Blues, F(2, 65) = 1.1, p =0.3). Post treatment, women reported more favourable responses to the therapy, finding the programme more helpful and more satisfactory, than did men. No relationship between treatment acceptability and age was found. Conclusion: Beating the Blues CCBT programme is an acceptable treatment for common mental health problems in routine care.
General comments	84 (38%) completed a treatment feedback questionnaire. (high attrition rate)

APPENDIX 8

LIST OF EXCLUDED STUDIES

1. Topolovec-Vranic J, Cullen J, Michalak A, *et al.* Evaluation of an online cognitive behavioural therapy program by patients with traumatic brain injury and depression. Brain Injury. 2010;24(5):762-772. – No comparison
2. Ormrod JA, Kennedy L, Scott J, *et al.* Computerised Cognitive Behavioural Therapy in an Adult Mental Health Service: A pilot Study of Outcomes and Alliance. Cognitive Behaviour Therapy. 2010;39(3):188-192. – No comparison
3. Cavanagh K, Shapiro DA, Van Den Berg S, *et al.* The effectiveness of computerised cognitive behavioural therapy in routine care. British Journal of Psychology. 2006;45:499-514 - No comparison
4. Learmonth D, Trosh Jo, Rai S, *et al.* The role of computer-aided psychotherapy within an NHS CBT specialist service. Counselling and Psychotherapy Research. 2008;8(2):117-123. – No comparison
5. Christensen H, Griffiths K, Groves C, *et al.* Free range users and one hit wonders: community users of an internet-based cognitive behaviour program. Australian and New Zealand Journal of Psychiatry. 2006; 40: 59-62. – No comparison
6. Learmonth D, Rai B. Taking computerised CBT beyond primary care. British Journal of clinical Psychology. 2008;47:111-118. – No comparison
7. Bockting CLH, Kok GD, van der Kamp L, *et al.* Disrupting the rhythm of depression using Mobile Cognitive Therapy for recurrent depression: randomised controlled trial design and protocol. BMC Psychiatry. 2011; 11: 12pgs – Protocol only
8. Cockayne NL, Glozier N, Naismith SL, *et al.* Internet-based treatment for older adults with depression and co-morbid cardiovascular disease: protocol for a randomised, double-blind, placebo controlled trial. BMC Psychiatry. 2011;11:10pgs – Protocol only
9. Bee PE, Bower P, Lovell K, *et al.* Psychotherapy mediated by remote communication technologies: a meta-analytic review. BMC Psychiatry. 2008;8(1):60. – not CCBT and not specific to depression patients
10. Spek V, Cuijpers P, Nyklicek I, *et al.* One-year follow-up results of a randomised controlled clinical trial on internet-base cognitive behavioural therapy for subthreshold depression in people over 50 years. 2008;38:635-639. – Jadad score 2

11. Pittaway S, Cupitt C, Palmer D, *et al.* Comparative, clinical feasibility study of three tools for delivery of cognitive behavioural therapy for mild to moderate depression and anxiety provided on a self-help basis. Mental Health in Family Medicine. 2009;6:145-54. – Jadad score 1

12. Selmi PM, Klein MH, Greist JH, *et al.* Computer-administered cognitive-behavioral therapy for depression. Am J Psychiatry. 1990;147:51-56.- Jadad score 2

13. Clarke G, Reid E, Eubanks D, *et al.* Overcoming Depression on the Internet (ODIN): A Randomised Controlled Trial of an Internet Depression Skills Intervention Program. J Med Internet Res. 2002;4(3):e14. – Not all subjects were depressed (selection bias)

14. Clarke G, Eubanks D, Reid E, *et al.* Overcoming Depression on the Internet (ODIN) (2): A Randomised Trial of a Self-Help Depression Skills Program With Reminders. J Med Internet Res. 2005;7(2):e16 - Not all subjects were depressed (selection bias)

15. Thompson NJ, Walker ER, Obolensky N, *et al.* Distance delivery of mindfulness-based cognitive therapy for depression: Project UPLIFT. Epilepsy & Behavior. 2010;19(3):247-54. – specifically for epilepsy