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Behavioural activation therapy for depression in adults with non-communicable diseases (Review)

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[Intervention Review]

Behavioural activation therapy for depression in adults with non-communicable diseases

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ABSTRACT

Background

Depression is common in people with non-communicable diseases (NCDs) such as cardiovascular disease, diabetes, cancer, and chronic respiratory conditions. The co-existence of depression and NCDs may affect health behaviours, compliance with treatment, physiological factors, and quality of life. This in turn is associated with worse outcomes for both conditions. Behavioural activation is not currently indicated for the treatment of depression in this population in the UK, but is increasingly being used to treat depression in adults.

Objectives

To examine the effects of behavioural activation compared with any control group for the treatment of depression in adults with NCDs.

To examine the effects of behavioural activation compared with each control group separately (no treatment, waiting list, other psychological therapy, pharmacological treatment, or any other type of treatment as usual) for the treatment of depression in adults with NCDs.

Search methods

We searched CCMD-CTR, CENTRAL, Ovid MEDLINE, Embase, four other databases, and two trial registers on 4 October 2019 to identify randomised controlled trials (RCTs) of behavioural activation for depression in participants with NCDs, together with grey literature and reference checking. We applied no restrictions on date, language, or publication status to the searches.

Selection criteria

We included RCTs of behavioural activation for the treatment of depression in adults with one of four NCDs: cardiovascular disease, diabetes, cancer, and chronic respiratory conditions. Only participants with a formal diagnosis of both depression and an NCD were eligible. Studies were included if behavioural activation was the main component of the intervention. We included studies with any comparator that was not behavioural activation, and regardless of reported outcomes.

Data collection and analysis

We used standard methodological procedures expected by Cochrane, including independent screening of titles/abstracts and full-text manuscripts, data extraction, and risk of bias assessments in duplicate. Where necessary, we contacted study authors for more information.

Main results

We included two studies, contributing data from 181 participants to the analyses.

Both studies recruited participants from US hospital clinics; one included people who were recovering from a stroke and the other women with breast cancer. For both studies, the intervention consisted of eight weeks of face-to-face behavioural therapy, with one study comparing to poststroke treatment as usual and the other comparing to problem-solving therapy.

Both studies were at risk of performance bias and potential conflict of interest arising from author involvement in the development of the intervention. For one study, risks of selection bias and reporting bias were unclear and the study was judged at high risk of attrition bias.

Treatment efficacy (remission) was greater for behavioural activation than for comparators in the short term (risk ratio (RR) 1.53, 95% confidence interval (CI) 0.98 to 2.38; low-certainty evidence) and medium term (RR 1.76, 95% CI 1.01 to 3.08; moderate-certainty evidence), but these estimates lacked precision and effects were reduced in the long term (RR 1.42, 95% CI 0.91 to 2.23; moderate-certainty evidence). We found no evidence of a difference in treatment acceptability in the short term (RR 1.81, 95% CI 0.68 to 4.82) and medium term (RR 0.88, 95% CI 0.25 to 3.10) (low-certainty evidence).

There was no evidence of a difference in depression symptoms between behavioural activation and comparators (short term: MD –1.15, 95% CI –2.71 to 0.41; low-certainty evidence). One study found no difference for quality of life (short term: MD 0.40, 95% CI –0.16 to 0.96; low-certainty evidence), functioning (short term: MD 2.70, 95% CI –6.99 to 12.39; low-certainty evidence), and anxiety symptoms (short term: MD –1.70, 95% CI –4.50 to 1.10; low-certainty evidence).

Neither study reported data on adverse effects.

Authors' conclusions

Evidence from this review was not sufficient to draw conclusions on the efficacy and acceptability of behavioural activation for the treatment of depression in adults with NCDs. A future review may wish to include, or focus on, studies of people with subthreshold depression or depression symptoms without a formal diagnosis, as this may inform whether behavioural activation could be used to treat mild or undiagnosed (or both) depressive symptoms in people with NCDs. Evidence from low-resource settings including low- and middle-income countries, for which behavioural activation may offer a feasible alternative to other treatments for depression, would be of interest.

PLAIN LANGUAGE SUMMARY

Behavioural activation therapy for depression in adults with long-term physical conditions

Depression is common in adults with long-term physical conditions. Long-term physical illnesses, such as cardiovascular disease, diabetes, cancer, or chronic respiratory conditions, can impact on mental health. Mental health problems can also affect how people cope with a physical condition. Behavioural activation is a type of talking therapy used to treat depression in adults and it could be an alternative to other psychological therapies or medication. This review assesses the effects of behavioural activation on depression for people with long-term physical conditions.

We included randomised controlled trials (RCTs) of behavioural activation with adults who were diagnosed with depression and cardiovascular disease, diabetes, cancer, or a chronic respiratory condition. An RCT is a study with a control group, in which participants are allocated to the treatment and control groups at random. We searched a variety of online databases, including regional databases and trial registries. The search, conducted on 4 October 2019, identified 6066 records. After screening records, we included two studies in this review and 181 participants contributed data to the analyses.

Both studies recruited participants from US hospitals. One study included participants recovering from a stroke and the other included women with breast cancer. In both studies, participants received behavioural activation delivered in eight weekly, face-to-face sessions. One study compared behavioural activation with poststroke treatment as usual, while the other compared behavioural activation with problem-solving therapy, a talking therapy.

Low to moderate-certainty evidence suggested that behavioural activation may be more effective in the treatment of depression than included comparators, but these estimates were imprecise and effects were reduced in the longer term. There was no evidence of any differences between groups in the number of people who dropped out of the studies, depression symptoms, quality of life, physical functioning, or anxiety symptoms. The studies did not report on side effects during the study period.

There were several limitations to the included studies. In both studies, participants were aware of the treatment they received. Also, researchers were involved in the design of the intervention in both studies, and may, therefore, have had an interest in a favourable

outcome for behavioural activation. In one study, missing data caused by participants dropping out of the study may have influenced results.

We did not find enough evidence in this review to know whether behavioural activation should be used to treat depression in adults with long-term physical conditions.

SUMMARY OF FINDINGS

Summary of findings 1. Behavioural activation compared with any comparator for depression in adults with non-communicable diseases

Behavioural activation compared with any comparator for depression in adults with non-communicable diseases

Patient or population: depression in adults with non-communicable diseases
Setting: recruitment in US hospitals
Intervention: behavioural activation
Comparison: any comparator

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)			№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
		Without behavioural activation	With behavioural activation	Difference			
Treatment efficacy for depression (short term: 8–9 weeks)	**RR 1.53** (0.98 to 2.38)	**Study population**			176 (2 RCTs)	⊕⊕⊖⊖ **Low** [a,b]	Remission; measured with HRSD. NNTB = 5.
		36 per 100	56 per 100 (36 more to 87 more)	19 more (1 fewer to 50 more)			
Treatment efficacy for depression (medium term: 12 months)	**RR 1.76** (1.01 to 3.08)	**Study population**			92 (1 RCT)	⊕⊕⊕⊖ **Moderate** [c]	Remission; measured with HRSD. NNTB = 4.8.
		27 per 100	48 per 100 (27 more to 83 more)	21 more (0 more to 56 more)			
Treatment efficacy for depression (long term: 24 months)	**RR 1.42** (0.91 to 2.23)	**Study population**			67 (1 RCT)	⊕⊕⊕⊖ **Moderate** [c]	Remission; measured with HRSD. NNTB = 5.3.
		45 per 100	64 per 100 (41 more to 100 more)	19 more (4 fewer to 56 more)			
Treatment acceptability (short term: 2 months)	**RR 1.81** (0.68 to 4.82)	**Study population**			80 (1 RCT)	⊕⊕⊖⊖ **Low** [d,e]	Dropouts from study.
		13 per 100	24 per 100 (9 more to 63 more)	11 more (4 fewer to 50 more)			
Treatment acceptability (medium term: 12 months)	**RR 0.88** (0.25 to 3.10)	**Study population**			101 (1 RCT)	⊕⊕⊖⊖ **Low** [d,e]	Dropouts from study.
		9 per 100	8 per 100	1 fewer			

			(2 more to 29 more)	(7 fewer to 20 more)			NNTB = 100.
Improvement in depression symptoms (short term: 5–6 months)	—	See comment	—	**MD 1.15 lower** (2.71 lower to 0.41 higher)	176 (2 RCTs)	⊕⊕⊖⊖ **Low** [a,e]	Measured with HRSD.
Improvement in depression symptoms (medium term: 12 months)	—	See comment	—	**MD 1.51 lower** (4.14 lower to 1.12 higher)	172 (2 RCTs)	⊕⊕⊖⊖ **Low** [a,e]	Measured with HRSD.
Improvement in depression symptoms (long term: 5 months)	—	See comment	—	**MD 2.00 lower** (4.71 lower to 0.71 higher)	67 (1 RCT)	⊕⊕⊕⊖ **Moderate** [c]	Measured with HRSD.
Quality of life (short term: 6 months)	—	The mean quality of life without behavioural activation was 2.2	—	**MD 0.4 higher** (0.16 lower to 0.96 higher)	80 (1 RCT)	⊕⊕⊖⊖ **Low** [c,f]	Measured with Quality of Life Inventory.
Quality of life (medium term: 12 months)	—	The mean quality of life without behavioural activation was 2.2	—	**MD 0.1 lower** (0.74 lower to 0.54 higher)	80 (1 RCT)	⊕⊕⊖⊖ **Low** [c,f]	Measured with Quality of Life Inventory.
Social adjustment and functioning (short term: 6 months)	—	The mean social adjustment and functioning score without behavioural activation was 59.5	—	**MD 2.7 higher** (6.99 lower to 12.39 higher)	80 (1 RCT)	⊕⊕⊖⊖ **Low** [c,f]	Measured with SF-36 – physical domain.
Social adjustment and functioning (medium term: 12 months)	—	The mean social adjustment and functioning score without behavioural activation was 61.7	—	**MD 2.2 higher** (6.37 lower to 10.77 higher)	80 (1 RCT)	⊕⊕⊖⊖ **Low** [c,f]	Measured with SF-36 – physical domain.
Improvement in anxiety symptoms (short term: 6 months)	—	The mean anxiety symptoms score without behavioural activation was 10.7	—	**MD 1.7 lower** (4.5 lower to 1.1 higher)	80 (1 RCT)	⊕⊕⊖⊖ **Low** [c,f]	Measured with Becks Anxiety Inventory.
Improvement in anxiety symptoms (medium term: 12 months)	—	The mean anxiety symptoms score without behavioural activation was 9.2	—	**MD 1.7 lower** (4.48 lower to 1.08 higher)	80 (1 RCT)	⊕⊕⊖⊖ **Low** [c,f]	Measured with Becks Anxiety Inventory.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **HRSD:** Hamilton Rating Scale for Depression; **MD:** mean difference; **NNTB:** number needed to treat for an additional beneficial outcome; **RCT:** randomised controlled trial; **RR:** risk ratio; **SF-36:** 36-item Short Form.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]High risk of attrition bias in one study, potential conflict of interest in both studies, unclear allocation concealment and reporting bias in one study. Downgraded one level.
[b]Wide confidence interval for one of the studies. For this binary outcome, there is insufficient information to give a precise estimate. Downgraded one level for imprecision.
[c]One study. Did not fulfil optimal information size criterion; downgraded one level for imprecision. It is impossible to assess consistency between study results with only one study, which means it was not possible to downgrade for inconsistency.
[d]Dropout rates may be affected by non-random attrition because participants were not blinded to the intervention, potential conflict of interest, and unclear allocation concealment. Downgraded one level for high risk of bias.
[e]Confidence interval was imprecise and covered both benefit and harm. Downgraded one level for imprecision.
[f]Outcome may be affected by risk of attrition bias, unclear allocation concealment, and risk of reporting bias. Downgraded one level for high risk of bias.

BACKGROUND

Description of the condition

Depression

The term 'depression' is often used to describe major depressive disorder when diagnosed in a clinical setting. It is characterised by a period of at least two weeks of depressed mood, or a persistent loss of interest or pleasure in activities that were previously considered enjoyable, or both (APA 2013). A range of symptoms may accompany these key features of depression and reduce quality of life. These include weight loss or weight gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, loss of energy, feelings of excessive guilt and worthlessness, diminished concentration, and recurrent thoughts of death (APA 2013).

Depression is the fifth global cause of disease burden in terms of years lived with a disability (YLD), and was ranked in the top 10 of YLD in 191/195 countries worldwide (Vos 2017). In 2014, 7.1% of the population living in the 28 countries of the EU was estimated to report depression, with higher rates reported by women, older people, and people living in cities (Eurostat 2014). In one national survey conducted in the US, the 12-month prevalence of depression was 10.4% and the lifetime prevalence was 20.6% (Hasin 2018). Similarly, the lifetime prevalence for depression in England was 19% in 2014 (HSE 2014). Global estimates of the burden of disease show that 4.4% of people worldwide experience depressive disorder. These figures vary considerably depending on geographical regions; for depression, rates vary from 3.6% in the Western Pacific to 5.4% on the African continent. More than 80% of people who have mental disorders live in low- and middle-income countries (Rathod 2017).

Depressive disorders can have a long-lasting impact on patients, their families, and wider society. They often occur with anxiety disorders (WHO 2017a), and are associated with marked personal and societal economic losses due to healthcare costs for mental and comorbid physical healthcare, reduced productivity in the workplace, and years of life lost (Alonso 2011; Greenberg 2015). One meta-analysis of data from 35 countries found a 52% increased risk of mortality in people with depression (Cuijpers 2014).

Non-communicable diseases

Non-communicable diseases (NCDs) are chronic diseases caused by a combination of genetic physiological, environmental, and behavioural factors. The four most common physical NCDs are cardiovascular disease (CVD), cancer, chronic respiratory diseases, and type 2 diabetes (WHO 2017a). According to the World Health Organization (WHO), 41 million people die annually due to NCDs, corresponding to 71% of all deaths worldwide. NCDs affect people of all age groups, with 15 million occurring between the ages of 30 and 69 years (WHO 2017a). Despite the resurgence of certain infectious diseases, such as tuberculosis and dengue, and outbreaks of new infectious diseases such as COVID-19, the global burden of infectious disease overall is decreasing (or becoming more stagnant in some countries), and being replaced by an increased burden of disease for NCDs, as well as common mental disorders (Vos 2017). NCDs decrease patients' health-related quality of life substantially (Dyer 2010; Solli 2010).

Comorbidity of depressive disorders in people with non-communicable diseases

NCDs commonly occur with depressive disorders (Patel 2015). There is a complex association between depression and NCDs (Ngo 2013). Co-existence of depression with an NCD worsens outcomes for both conditions and is associated with poorer self-management and treatment adherence, reduced treatment response, and higher morbidity and mortality for both the mental and the physical disorder (NICE 2009). NCDs and mental disorders are associated with similar behavioural factors, such as tobacco use, a less nutritious diet, physical inactivity, and harmful alcohol use (Stein 2019). Pathophysiological factors, such as increased cytokine levels or other inflammatory markers associated with NCDs, may increase the risk of developing depression and worsen symptoms (Katon 2003).

CVD is the leading cause of death globally (Roth 2017). Comorbid depression is common in people with CVD (approximately 15%) and the prevalence of depression in people with CVD is higher than in the general population (Hare 2014). Increased levels of depression in postmyocardial infarction (heart attack) patients are associated with a two- to three-fold increased risk of impaired outcomes within 24 months of the event (Meijer 2011). The association between depression and CVD risk factors is bidirectional (Pan 2012). Depression is thought to be a risk factor for CVD through a combination of behavioural (smoking, alcohol intake, physical inactivity, and obesity) and biological components (affecting the nervous system, hormone secretion, immune system, and cardiovascular functions) (Dhar 2016).

Prevalence estimates of major depression (15%), minor depression (20%), and anxiety disorders (10%) in people treated for cancer are more than double that observed in the general population (Pitman 2018). Two-thirds of people with cancer and depression also have clinically significant anxiety symptoms. Figures vary by cancer type and it is suggested that this is due to the differing prognoses, pain levels, and degrees of body image disruption associated with each tumour type, as well as specific tumour-related neuropsychiatric effects and treatment-related neuropsychiatric adverse effects (Pitman 2018).

Mental health problems are approximately three times more prevalent among people with chronic obstructive pulmonary disease (COPD) than in the general population. Up to 55% of people with COPD also have anxiety and depression (Laurin 2012). People with COPD show increased levels of psychological distress, which in turn leads to higher exacerbation rates. For asthma, mortality rates in the UK have been found to be twice as high for those also experiencing depression (Walters 2011).

It is estimated that depression occurs in 13% to 18% of people with diabetes, which worsens glycaemic control and is associated with increased complications. Mild depression is thought to often go undiagnosed in people with diabetes because many of the somatic symptoms are similar (Hermanns 2013).

Description of the intervention

Pharmacological and psychological interventions, alone or in combination, are recommended in clinical guidelines for the treatment of mild-to-moderate depression. Behavioural activation is one of the recommended therapies for treatment of depression in adults, but is not currently recommended for the treatment

of moderate-to-severe symptoms of depression in people with chronic physical health problems (NICE 2009).

Antidepressants are a standard treatment for moderate-to-severe depression in healthcare settings, whereas for subthreshold depressive symptoms or mild depression, low-intensity psychosocial therapy and psychological therapies are recommended (NICE 2009). While antidepressants are proven to be effective for the acute treatment of depression for some people, non-adherence to antidepressant medication is very common (Hunot 2007; Ten Doesschate 2009; Van Geffen 2009), and is associated with relapse and recurrence of depression, hospital visits and hospitalisation, worsening of depression symptoms, and a lower likelihood of recovery (Gardarsdottir 2009; Ho 2016). Non-adherence is related to many factors, including concerns about possible adverse effects of antidepressants, dependence, and experience of withdrawal symptoms (Davies 2018; Fawzi 2012; Hunot 2007; Sansone 2012). Studies of treatment for psychiatric disorders, including depression, consistently report that people prefer psychological treatment to medication (Churchill 2000; McHugh 2013; Riedel-Heller 2005).

There is a wide range of psychological therapies available for the treatment of depressive disorders. Psychological therapies may be categorised into four philosophical and theoretical schools of thought, comprising psychoanalytic/dynamic (Freud 1949; Jung 1963; Klein 1960), behavioural (Skinner 1953; Watson 1924; Wolpe 1958), humanistic (Maslow 1943; May 1961; Rogers 1951), and cognitive approaches (Beck 1979; Lazarus 1971). Each school of thought incorporates different and overlapping psychotherapeutic approaches.

Behavioural activation stems from a behavioural psychotherapy approach first developed in the 1970s by Lewisohn and colleagues (Dimidjian 2011). It is based on the concept that depression results from deprivation of positive reinforcement, and the treatment focuses on identifying and scheduling pleasurable activities, thus increasing contact with sources of positive reinforcement (Kanter 2012).

When cognitive behavioural therapy (CBT) was developed and disseminated, behavioural therapy approaches based purely on operant (learning from the consequences of behaviours) and respondent (responsive behaviour as a result of a stimulus) principles were thought insufficient. However, the interest in the feasibility of behavioural treatments for depression has since been renewed (Dimidjian 2011; Ekers 2014; Hopko 2003). Jacobson showed that the behavioural component of CBT was as effective as the full package of CBT, and investigators developed a new and more comprehensive model of behavioural activation that would be amenable to dissemination (Jacobson 1996; Jacobson 2001).

How the intervention might work

Skinner proposed that depression was associated with an interruption in established sequences of healthy behaviour that were previously positively reinforced by the social environment and were based on operant conditioning principles (in which behaviour patterns are learnt, rather than instinctive) (Skinner 1953). In subsequent expansions of this model, reduction of positively reinforced healthy behaviours has also been attributed to a decrease in the number and range of reinforcing stimuli available to the individual, lack of skill in obtaining positive reinforcement (Lewinsohn 1974), increased frequency of punishment, or a combination of these (Lewinsohn 1984).

Behavioural activation can be defined as a brief psychotherapeutic approach that seeks to change the way a person interacts with their environment, aiming to:

1. increase access to positive reinforcers of healthy behaviours;
2. reduce avoidance behaviours that limit access to positive reinforcement;
3. understand and address barriers to activation.

Treatments are collaborative and focused on the present. Many differing techniques are incorporated into treatment; however, all use self-monitoring of a mood-environment link and scheduling of new or adaptive behaviours to meet targets (Kanter 2012). In doing so, the therapy helps people to make contact with potentially reinforcing experiences (Jacobson 2001).

The original model of behavioural activation, developed by Jacobson, was defined primarily by the elimination of cognitive intervention elements (Dimidjian 2006). On the basis of its original design, behavioural activation model components commonly include developing a shared treatment rationale; increasing access to meaningful events, activities, and consequences; activity scheduling; developing social skills; and self-monitoring links between behaviour and mood. In some cases, the use of some form of problem solving or functional analysis is added to understand, consider, and overcome any potential barriers to the scheduling of activities. In contrast to CBT, no attempt is made to directly change cognitions. However, behavioural activation commonly involves an exploration of how cognitive processes, such as rumination, can limit access to behaviours and events which give positive reinforcement, for example in stopping people with depression from meeting up with friends or participating in physical exercise (Kanter 2012; Veale 2008).

It is thought that behavioural activation could be effective in the treatment of people with depression and comorbid NCDs by supporting people to identify activities they would like to engage in and reintroducing valued activities that they have stopped doing. Positive reinforcement from valued activities through self-monitoring, activity scheduling, and functional analysis helps to break the cycle of limiting activities and depressive symptoms.

Why it is important to do this review

According to the clinical guidelines produced by the National Institute for Health and Care Excellence (NICE), behavioural activation is one of the recommended treatment options for subthreshold depressive symptoms, mild-to-moderate depression, and severe depression, along with CBT and interpersonal therapy. However, the guidelines acknowledge that evidence for behavioural activation is less robust than for the other recommended therapies (NICE 2009). Behavioural activation is currently not recommended for the treatment of depression in people with NCDs.

Behavioural activation is increasingly receiving attention as a potentially cost-effective intervention for common mental disorders, including for populations with comorbid NCDs, and it may be delivered and implemented in settings with low resources or where the demand is greater than the availability of mental

health practitioners to deliver more complex treatments (Richards 2016). A recent Cochrane Review of behavioural activation for adults with depression showed low- to moderate-certainty evidence that behavioural activation is as effective as most other psychological therapies and more effective than most non-active comparators (Uphoff 2020). To allow for meaningful meta-analyses in a relatively homogeneous patient population, people with comorbidities were excluded from the review. The current review will fill this gap in the literature by specifically addressing the population of people with depression and comorbid NCDs.

OBJECTIVES

1. To examine the effects of behavioural activation compared with any control group for the treatment of depression in adults with non-communicable diseases (NCDs).

2. To examine the effects of behavioural activation compared with each control group separately (no treatment, waiting list, other psychological therapy, pharmacological treatment, or any other type of treatment as usual) for the treatment of depression in adults with NCDs.

METHODS

Criteria for considering studies for this review

Types of studies

For consistency and to facilitate interpretation of the results of this review in the wider context of evidence on behavioural activation for depression, we followed methods described in the published protocol 'Behavioural activation therapies for depression in adults' where possible (Uphoff 2020).

Randomised controlled trials (RCTs) were eligible for inclusion in this review. We included trials employing a cross-over design (while we acknowledge that this design is rarely used in psychological therapy trials), but we only used data from the first active treatment phase. Cluster-RCTs and pilot RCTs were also eligible for inclusion.

Quasi-RCTs, in which treatment assignment is decided through methods such as alternate days of the week, were not eligible for inclusion.

Types of participants

Participant characteristics

Trials with adults (aged 18 years and over) of any sex or gender were eligible for inclusion. We excluded trials with participants under 18 years of age. If a trial included both adults and children, we planned to contact authors to request data for adults only. If these data were not available, we planned to exclude the trial. Participants had to have depression (mild, moderate, or severe) with a comorbid NCD. We included studies on the four NCDs most prevalent worldwide: CVD, cancer, chronic respiratory disease, and type 2 diabetes.

Postnatal depression is considered a separate condition with contributing factors distinct from major depressive disorder, and we, therefore, excluded participants with this condition.

Setting

Trials could be conducted in a primary, secondary, specialist, or community setting.

We excluded trials involving inpatients, as these represent settings that differ with regards to the complexity of patients' healthcare needs, the way patients access care, and the way in which interventions are delivered and embedded in clinical practice. The same intervention may lead to different results in inpatient settings compared to other settings, and we would not be able to ascertain whether this would be a result of the type of participants, the delivery of the intervention, or features of the setting itself. If a trial included both inpatients and outpatient settings, we planned to contact authors to request data for participants eligible for inclusion in our review only. If these data were not available, we planned to exclude the trial.

Nursing homes in this review were considered outpatient settings, as they are places of residence. Hospice care is considered specialised medical care and we, therefore, excluded studies conducted with participants in a hospice.

We included trials that focus on specific populations – nurses, carers, participants at a specific workplace with depression – if all participants met the criteria for depression.

Studies from all countries were eligible for inclusion.

Diagnosis

We included trials that focussed on acute phase treatment of clinically diagnosed depression in people with comorbid NCDs (CVD, cancer, chronic respiratory disease, and type 2 diabetes).

Trials adopting any standardised diagnostic criteria to define participants experiencing an acute phase unipolar depressive disorder were included. Accepted diagnostic criteria include Feighner criteria, Research Diagnostic Criteria, and criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition* (DSM-III; APA 1980), *DSM-III-Revised* (APA 1987), *DSM-Fourth Edition* (DSM-IV; APA 1994), *DSM-IV-Text Revision* (APA 2000), *DSM-Fifth Edition* (DSM-5; APA 2013), and *International Classification of Diseases, Tenth Edition* (ICD-10; WHO 1992).

Earlier trials may have used *ICD-Ninth Edition* (ICD-9; WHO 1978), but ICD-9 is not based on operationalised criteria, so we excluded trials using ICD-9 to diagnose depression. We also excluded studies of participants with subthreshold depression, symptoms of depression without a formal diagnosis, or a diagnosis based on symptom scales such as Becks Depression Inventory or Hamilton Rating Scale for Depression (HRSD).

We included studies of participants diagnosed with anxiety, or with symptoms of anxiety, if they were also diagnosed with depression.

Types of interventions

Experimental interventions

Previously published Cochrane Reviews for treatment of depression provided a framework for psychological therapies including behavioural therapy (Churchill 2013; Hunot 2013; Shinohara 2013). Given recent developments in literature and practice regarding behavioural activation approaches, we considered behavioural activation to be part of behavioural therapies, rather than being classified as a 'third wave' therapy. In line with the behavioural therapy for depression review (Uphoff 2020), we created the comparator categories of psychological therapies on the basis of both treatment approach (e.g. their

theoretical background and the manuals used) and content (e.g. therapeutic techniques employed) (Appendix 1).

Behavioural activation

We included trials evaluating treatment approaches for depression and anxiety that were either explicitly called 'behavioural activation', or treatments that were described using the main elements of behavioural activation for depression, such as pleasant or rewarding events and activities, activity scheduling, positive reinforcement from the environment, and positive interaction or re-engagement with the environment. Interventions that contained some elements of behavioural therapy and elements of other approaches, such as CBT or problem-solving therapy, were not eligible for inclusion.

Format of psychological therapies

Therapies delivered by therapists of all levels were eligible for inclusion. This included psychologists or psychotherapists accredited by a professional body for psychology or psychotherapy, who completed formal training to deliver psychological therapies, as well as lay counsellors and non-specialist therapists who had been specifically trained to deliver treatment according to a behavioural activation protocol.

We included computerised and self-help interventions if they were facilitated by a therapist. This means at least some element of interaction with a therapist was required.

Psychological therapies conducted on an individual or group basis were eligible for inclusion.

The number of sessions was not limited, and we accepted psychological therapies delivered in only one session.

Comparators

All comparators were accepted if they were not a type of behavioural activation. We categorised psychological therapies as behavioural therapy, social skills training/assertiveness training, relaxation therapy, CBT, third-wave CBT, psychodynamic, and humanistic and integrative approaches.

Behavioural therapy

We planned to include any behavioural therapies that did not contain the main elements of behavioural activation as comparators.

Social skills training/assertiveness training

The social skills training model proposes that depressed people may have difficulty initiating, maintaining, and ending conversations (Jackson 1985). Because of these deficits, the individual is unable to elicit mutually reinforcing behaviour from other people in his or her environment. Social skills training subsumes assertion and conversational skills, together with more specialised subskills, such as dating and job interview skills. Different social contexts may be targeted, for example interaction with friends, family members, people at school, or at work, and interventions such as instruction, modelling, rehearsal, feedback, and reinforcement are used to enable the development of new responses (Jackson 1985). As assertiveness training represents a key component of social skills training, we included it in this category.

Relaxation therapy

Relaxation training is a behavioural stress management technique that induces a relaxation response, helping to switch off the fight/flight response and causing levels of stress hormones in the bloodstream to fall. A variety of techniques may be used to induce relaxation, the most common of which is Jacobson's progressive muscle relaxation training (Bernstein 1973).

Cognitive behavioural therapies

In CBT, therapists aim to work together with people receiving treatment to understand the link between thoughts, feelings, and behaviours, and to identify and modify unhelpful thinking patterns and underlying assumptions about the self, others, and the world (Beck 1979). Cognitive change methods for depression are targeted at the automatic thought level in the first instance and include thought catching, reality testing, and task assigning as well as generating alternative strategies (Williams 1997). Behavioural experiments are then used to re-evaluate underlying beliefs and assumptions (Bennett-Levy 2004). We categorised these therapies into six subcategories: cognitive therapy, rational emotive behaviour therapy, problem-solving therapy, self-control therapy, a coping with depression course, and other CBTs.

Third-wave cognitive and behavioural therapies

Third-wave CBT approaches have been developed more recently and now exist alongside established therapies such as CBT. Rather than focusing on the contents of thoughts, these therapies tend to focus on the process and functions of thoughts and an individual's relationship with thoughts and emotions. This may include suppressing or avoidance of emotions, thoughts, and bodily sensations (Hofmann 2008). Third-wave approaches use strategies relating to mindfulness, emotions, acceptance, relationships, values, goals, and understanding the thinking process, to bring about changes in thinking (Hayes 2006). Drawing from psychodynamic and humanistic principles, third-wave CBT approaches place great emphasis on use of the therapeutic relationship. We categorised these therapies into subcategories: acceptance and commitment therapy, compassionate mind training, functional analytic psychotherapy, metacognitive therapy, mindfulness-based cognitive therapy, dialectical behaviour therapy, and other third-wave CBTs.

Cognitive behavioural therapy bibliotherapy

When someone with depression does not have access to a qualified therapist or CBT practitioner they may seek therapy through the use of self-help materials incorporating a CBT approach (Anderson 2005).

Psychodynamic therapies

Grounded in psychoanalytic theory (Freud 1949), psychodynamic therapy uses the therapeutic relationship to explore and resolve unconscious conflict through transference (projection of feelings on to the therapist) and interpretation, with development of insight and character change (within certain boundaries) as therapeutic goals, and relief of symptoms as an indirect outcome. Brief therapy models have been devised by Malan 1963, Mann 1973, and Strupp 1984. We categorised these therapies into four subcategories: drive/structural model (Freud 1949), relational model (Luborsky 1998; Strupp 1984), integrative analytic model (Mann 1973), and other psychodynamic therapies.

Humanistic therapies

Contemporary models of humanistic therapies differ from one another somewhat in clinical approach, but all focus attention on the therapeutic relationship (Cain 2002), within which therapist 'core conditions' of empathy, genuineness, and unconditional acceptance and support (positive regard) (Rogers 1951), are regarded as cornerstones for facilitating client insight and change. We categorised these therapies into seven subcategories: person-centred therapy (Rogerian), gestalt therapy, experiential therapies, transactional analysis, existential therapy, non-directive/supportive therapies, and other humanistic therapies.

Interpersonal, cognitive analytic, and other integrative therapies

Integrative therapies are approaches that combine components of different psychological therapy models. Integrative therapy models include interpersonal therapy (Klerman 1984), cognitive analytic therapy (Ryle 1990), and Hobson's conversational model (Hobson 1985), manualised as psychodynamic interpersonal therapy (Shapiro 1990). With its focus on the interpersonal context, interpersonal therapy was developed to specify what was thought to be a set of helpful procedures commonly used in psychotherapy for depressed outpatients (Weissman 2007), drawing in part from attachment theory (Bowlby 1980), and CBT within a set timeframe (time-limited). Cognitive analytic therapy, also devised as a time-limited psychotherapy, integrates components from cognitive and psychodynamic approaches. The conversational model integrates psychodynamic, interpersonal, and person-centred model components.

Counselling interventions traditionally draw from a wide range of psychological therapy models, including person-centred, psychodynamic and cognitive behavioural approaches, applied in combination, according to the theoretical orientation of practitioners (Stiles 2008). Therefore, we will usually include trials of counselling with integrative therapies. However, if the counselling intervention consisted of a single discrete psychological therapy approach, we categorised it as such, even if the intervention was referred to as 'counselling'. If the intervention is manualised, this would inform our classification.

Motivational interviewing and other forms of integrative therapy approaches are also included in this category.

Waiting list

Participants are randomly assigned to the active intervention group or control group, and they will either receive the intervention first or be assigned to a waiting list until all participants in the intervention group have received the intervention. During the trial, people on the waiting list can receive any appropriate medical care.

Attention placebo

We defined this as a control condition that is regarded as inactive by both researchers and participants in a trial.

Psychological placebo

We define this as a control condition in a trial that is regarded by researchers as inactive but is regarded by participants as active (also called placebo therapy or sham treatment).

Medication

All medication prescribed with the goal to treat depression, most commonly antidepressants; any dose, route of administration, duration, and frequency.

Medical placebo

All types of medical placebos or 'sugar pills'.

No treatment

Trial participants not receiving any treatment for depression during the trial.

Treatment as usual

Treatment as usual, standard care, or usual care would be any appropriate medical care during the study. This may, for example, involve monitoring of the person receiving treatment, regular check-ups, no treatment, or any type of treatment. What constitutes treatment as usual will depend on the setting and healthcare system in which the study was conducted. If a study arm fitted clearly in any of the above categories, for example, 'no treatment' or a type of psychological therapy, we categorised it as such.

Excluded interventions

We excluded trials of long-term continuation or maintenance therapy interventions designed to prevent relapse of depression or to treat chronic depressive disorders from this review. Similarly, we excluded trials of interventions designed to prevent a future episode of depression.

We excluded psychological therapy models based on social constructionist principles (that focus on the ways in which individuals and groups participate in the construction of their perceived social reality), including couples therapy (Jacobson 1993), family therapy (Crane 2002), solution-focused therapy (de Shazer 1988), narrative therapy (White 1990), personal construct therapy (Kelly 1955), neurolinguistic programming (Bandler 1982), and brief problem solving (Watzlavick 1974). These therapies work with patterns and dynamics of relating within and between family, social, and cultural systems to create a socially constructed framework of ideas (O'Connell 2007), rather than focusing on individuals' reality. A previously published Cochrane Review on couples therapy for depression has been updated (Barbato 2018), and a review of family therapy for depression is to be updated (Henken 2007).

Types of outcome measures

Primary outcomes

1. Treatment efficacy for depression: the number of participants who responded to treatment, as determined by changes in scores for Beck Depression Inventory (BDI; Beck 1961), Hamilton Rating Scale for Depression (HAM-D/HRSD; Hamilton 1960), or Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery 1979), or in scores from any other validated depression scale. We used HAM-D, and, if this was not available, we used MADRS, and if MADRS was not available, then we used BDI. If BDI was not available, we used the measure most frequently used across trials. Many trials define response as 50% or greater reduction on BDI, HAM-D, etc., with some trials defining response using Jacobson's Reliable Change

Index (Jacobson 1992); we accepted the trial authors' original definition and preferred Jacobson's Reliable Change Index if this was used in addition to other response outcomes.

2. Treatment acceptability: the number of participants who dropped out of the study after being randomised and allocated to a study arm.

Secondary outcomes

1. Improvement in depression symptoms, based on a continuous outcome of group mean scores at the end of treatment. If multiple measures had been used for this outcome within one trial, we adopted the same hierarchy used for the primary outcome 'treatment efficacy for depression'.
2. Quality of life, assessed with validated measures such as the 36-item Short Form (SF-36) (Ware 1993), EQ-5D (EuroQol; Brooks 1995), and World Health Organization Quality of Life (WHOQOL; WHOQOL 1998).
3. Social adjustment and functioning, including Global Assessment of Function scores (Luborsky 1962).
4. Improvement in anxiety symptoms, measured using a validated continuous scale, either assessor-rated, such as the Hamilton Anxiety Scale (HAM-A; Hamilton 1959), or self-report, including the Trait subscale of the Spielberger State-Trait Anxiety Inventory (STAI-T; Spielberger 1983), and the Beck Anxiety Inventory (BAI; Beck 1988). We used HAM-A, and if this was not available, we used STAI-T, and if this was not available, we used BAI. If BAI was not available, we used the measure most frequently used across trials.
5. Adverse effects, such as counts of completed suicides, attempted suicides, or worsening of symptoms were summarised in narrative form.

Search methods for identification of studies

Electronic searches

Searches were developed for the concepts: Behavioural Activation, Depression, Chronic Respiratory Diseases, Type 2 Diabetes, Cardiovascular Diseases (including Stroke) and Cancer. Subject headings and free-text words were identified for use from previous systematic reviews (Hooper 2018; Uphoff 2020; Usmani 2017), the Information Specialist, and the project team members. The Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); Ovid format was used in the MEDLINE strategy. The search was peer-reviewed by an Information Specialist. See Appendix 2 for full search strategies.

The results of the database searches were stored and deduplicated in an EndNote library.

We searched the following databases during September and October 2019.

1. Cochrane Common Mental Disorders Trials Register (CCMD-CTR), all available years.
2. Cochrane Central Register of Controlled Trials (Wiley): 2019, Issue 9.
3. (Ovid) MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to 23 September 2019.
4. Embase Classic + Embase (Ovid) 1947 to 24 September 2019.
5. Global Health (Ovid) 1910 to week 36, 2019.
6. African Index Medicus (via WHO Global Health Index Medicus), all available years.
7. ClinicalTrials.gov (US NIH), all available years.
8. ISMEAR Index Medicus for the South East Asia Region (via WHO Global Health Index Medicus).
9. LILACS Latin American and Caribbean Health Sciences Literature (via WHO Global Health Index Medicus), all available years.
10. PsycINFO (Ovid) 1806 to September week 2, 2019.
11. International Clinical Trials Registry Platform (WHO), all available years.

We applied no restrictions on date, language, or publication status to the searches.

Searching other resources

Grey literature

We searched the following sources of grey literature (primarily for dissertations and theses) in September 2019.

1. Open Grey (www.opengrey.eu).
2. ProQuest Dissertations & Theses Global (www.proquest.com/products-services/pqdtglobal.html).
3. DART-Europe E-theses Portal (www.dart-europe.eu).
4. EThOS – the British Libraries e-theses online service (ethos.bl.uk).
5. Open Access Theses and Dissertations (oatd.org).

Reference lists

We checked the reference lists of included trials and relevant systematic reviews to identify additional trials missed from the original electronic searches (e.g. unpublished or in-press citations).

Personal communication

We contacted trial authors and subject experts for information on unpublished or ongoing trials, or to request additional trial data.

Data collection and analysis

Selection of studies

Two review authors (of EU, RR, DC, MPi, MPu) independently examined the abstracts of all publications obtained through the search strategy. We obtained full articles of all trials and two review authors (of EU, DC, MPi, DB) independently assessed full-texts according to the criteria relating to characteristics of the studies, participants, and interventions. We discussed reasons for disagreement with a third review author (of EU, RC, NS, DE) and contacted external experts or trial authors if necessary in order to reach agreement. We recorded reasons for excluding records at this stage in the Characteristics of excluded studies table. For all included studies, we linked multiple reports from the same study. We constructed a PRISMA flow diagram to show the process of study selection (Moher 2009).

Data extraction and management

Two review authors (of EU, PM, DB) independently extracted data from each trial. These review authors discussed any disagreements with an additional review author (of EU, MPi, NS),

and, when necessary, contacted the authors of the trials for further information.

We extracted and entered data regarding study characteristics, methods, intervention and comparator, and results into Covidence data extraction forms.These data extraction forms were piloted by two authors and amended as a result of piloting.

Management of time points

We summarised and categorised post-treatment outcomes and outcomes at each reported follow-up point as follows: short term (up to six months post-treatment), medium term (seven to 12 months post-treatment) and long term (longer than 12 months).

Assessment of risk of bias in included studies

Two review authors (of EU, PM, DB) independently assessed the risk of bias in selected trials and discussed any disagreements with a third review author (of EU, MPi, NS). Where necessary, we contacted trial authors for further information. We presented all 'Risk of bias' data graphically, and narratively in the text. We planned to use allocation concealment as a marker of trial quality for the purpose of undertaking sensitivity analyses, but these sensitivity analyses were not conducted due to a lack of available data (Differences between protocol and review).

We assessed risk of bias for each included trial using the Cochrane 'Risk of bias' tool (version 1) (Higgins 2016), which considers the following domains.

1. Risk of bias arising from the randomisation process, including allocation and randomisation.
2. Risk of bias due to deviations from the intended interventions, including blinding of participants and people delivering the interventions.
3. Missing outcome data.
4. Risk of bias in measurement of the outcome, including blinding of outcome assessors.
5. Selective outcome reporting.
6. Other sources of bias.

For cluster-RCTs and cross-over trials, we planned to use the templates specifically designed to assess these types of trials, with the same domains. However, no such trials were included.

In the 'Other sources of bias' domain, we considered any additional problems with bias, including the following issues relevant to psychological therapy trials.

1. Treatment fidelity: was the therapy monitored against a manual or a scale through audiotapes or videotapes?
2. Researcher allegiance/conflict of interest: did the researcher have a vested interest for or against the therapies under examination?
3. Therapist allegiance/conflict of interest: did the therapist have a vested interest for or against the therapies provided?

Measures of treatment effect

Continuous outcomes

Where trials used the same outcome measure for comparison, we pooled data by calculating the mean difference (MD). If trials used different measures to assess the same outcome, we planned to pool data with standardised mean difference (SMD) and calculate 95% confidence intervals (CIs). However, studies reported the same outcome measure for all meta-analyses therefore we did not use SMDs.

An SMD or MD of zero means that the intervention and control groups have equivalent treatment effects. We anticipated that, for most measures, a lower score would indicate greater improvement. For example, a lower score on depression symptom instruments indicates an improvement in symptoms. In these cases, an SMD or MD less than zero indicates that the intervention has a greater effect than the control. An SMD or MD greater than zero indicates that the intervention has a smaller effect than the control. Interpretation of the SMD or MD is reversed in cases where a greater continuous score indicates greater improvement.

Dichotomous outcomes

We analysed dichotomous outcomes by calculating a pooled risk ratio (RR) and 95% CIs for each comparison.

In addition, we calculated the number needed to treat for an additional beneficial outcome (NNTB) with 95% CIs for all dichotomous outcomes to facilitate interpretation; this is the expected number of people who need to receive the intervention rather than the comparator for one additional person to achieve a beneficial outcome (Schünemann 2017).

If one trial uses both continuous and dichotomous variables for the same outcome, we gave preference to the continuous outcome.

Unit of analysis issues

Cluster-randomised trials

We included cluster-randomised trials if proper adjustment for the intracluster correlation could be conducted in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a).

Cross-over trials

If included trials employed a cross-over design in the review, we only used data from the first active treatment phase.

Trials with multiple treatment groups

Multiple-arm trials (those with more than two intervention arms) can pose analytical problems in pair-wise meta-analysis. For trials with more than two relevant active treatment arms, we managed data in this review as follows.

Dichotomous data

We collapsed data from relevant active intervention arms into a single arm for comparison, or we split data from relevant active intervention arms equally between comparator arms (Higgins 2011b).

Dealing with missing data

We managed missing dichotomous data through intention-to-treat (ITT) analysis, in which we assumed that participants who dropped out after randomisation had a negative outcome. We also conducted best/worse-case scenarios for the clinical response outcome, in which we assumed that dropouts in the active

treatment group had positive outcomes and those in the control group had negative outcomes (best-case scenario), and that dropouts in the active treatment group had negative outcomes and those in the control group had positive outcomes (worst-case scenario), thus providing boundaries for the observed treatment effect.

We analysed missing continuous data on an endpoint basis, including only participants with a final assessment, or by using the last observation carried forward (LOCF) to the final assessment, if trial authors reported LOCF data. If standard deviations (SDs) were missing, we attempted to obtain these data by contacting trial authors. When SDs were not available from trial authors, we planned to calculate them from P values, t values, CIs, or standard errors, if these were reported in the articles (Deeks 1997).

If a vast majority of SDs were available and only a minority of SDs were unavailable or unobtainable, we planned to use the method devised by Furukawa and colleagues to impute SDs and calculate percentage responders (da Costa 2012; Furukawa 2005; Furukawa 2006).

No SDs were missing in the included studies and these methods were, therefore, not used.

Assessment of heterogeneity

We assessed statistical heterogeneity using the Chi^2 test, which provides evidence of variation in effect estimates beyond that of chance. Because the Chi^2 test has low power to assess heterogeneity when a small number of participants or trials are included, we conservatively set the P value at 0.1 (Deeks 2017). We also quantified heterogeneity using the I^2 statistic, which calculates the percentage of variability due to heterogeneity rather than to chance (Higgins 2003). We considered I^2 statistic values in the range of 50% to 90% to represent substantial statistical heterogeneity and explored them further. The importance of the observed I^2 statistic depends on the magnitude and direction of treatment effects and the strength of evidence for heterogeneity. Forest plots generated in Review Manager 5 (Review Manager 2014) provided an estimate of Tau^2, the between-trial variance in a random-effects meta-analysis (Deeks 2017).

Assessment of reporting biases

As far as possible, we minimised the impact of reporting biases by undertaking comprehensive searches of multiple sources (including trials registries), to identify unpublished material and including non-English language publications.

We tried to identify outcome reporting bias in trials by recording all trial outcomes, planned and reported, and noting where outcomes were missing. If we found evidence of missing outcomes, we attempted to obtain any available data directly from the trial authors.

We planned to construct funnel plots to establish the potential influence of reporting biases and small-trial effects (Sterne 2017). However, no funnel plots were constructed due to the small number of included studies.

Data synthesis

We conducted meta-analyses of included trials. Given the potential heterogeneity of behavioural activation approaches for inclusion, together with the likelihood of differing secondary comorbid mental disorders and different NCDs in the population of interest, we decided a-priori to use a random-effects model in all analyses.

Subgroup analysis and investigation of heterogeneity

Clinical heterogeneity

We planned to conduct the following subgroup analyses for primary outcomes treatment efficacy and treatment acceptability, for the main comparison 'behavioural activation versus any control group'.

1. Country: subgroup analyses with studies conducted in high-income countries and studies conducted in low- and middle-income countries, to account for heterogeneity due to study setting. Countries were grouped according to the World Bank income classification (World Bank 2019).
2. Level of therapist: analyses for specialist (qualified or accredited mental health specialist with substantial training), non-specialist (short training, lay workers, or primary care workers) therapists, or specialist in training (e.g. several years of training in psychotherapy or mental health nursing). Although psychotherapy has traditionally been delivered by mental health specialists, the effectiveness of behavioural activation delivered by non-specialists is of great interest in settings where the demand for mental health treatments outweighs the availability of treatments, such as low- and middle-income countries.
3. Type of NCD: CVD, cancer, chronic respiratory disease, and type 2 diabetes. We expected that these different NCDs might affect mental health differently, and factors associated with these diseases might influence success of behavioural activation therapy.

However, it was not possible to conduct these subgroup analyses due to the limited availability of data.

Sensitivity analysis

The following sensitivity analyses were planned for primary outcomes treatment efficacy and treatment acceptability, for the main comparison 'behavioural activation versus any control group'.

1. Trial quality: we would exclude low-quality trials in a sensitivity analysis, if we identified several higher-quality trials. As a marker of quality, we would have used the 'allocation concealment' criteria from the 'Risk of bias' assessment.
2. Mode of delivery: we would have excluded therapies delivered through computer-based or electronic guidance without a substantial face-to-face component.
3. Group therapy: we would have excluded trials of group therapy for behavioural activation as the mode of delivery of psychotherapy could influence effectiveness of the therapy.

However, it was not possible to conduct these sensitivity analyses due to the limited availability of data.

Summary of findings and assessment of the certainty of the evidence

We constructed a 'Summary of findings' table to present the main findings of the review. We reported the outcomes listed below and presented standardised effect size estimates and 95% CIs. We used GRADEpro GDT to create our 'Summary of findings' table (GRADEpro GDT), and followed standard methods as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011).

In line with our first objective, the comparison included in the 'Summary of findings' table was behavioural activation versus any control group.

We included the following outcomes (measured up to 24 months) in the 'Summary of findings' table.

1. Treatment efficacy for depression (number of participants responding to treatment).
2. Treatment acceptability (number of participants who dropped out).
3. Improvement in depression symptoms as a continuous score.
4. Quality of life.
5. Social adjustment and functioning score.
6. Improvement in anxiety symptoms as a continuous score.

We created the 'Summary of findings' table before writing our discussion, abstract, and conclusions, so that the review authors could jointly consider the potential impact of the certainty of the evidence for each outcome on the mean treatment effect and our confidence in these findings. Our confidence in the mean treatment effects based on the GRADE assessments was then reflected in the interpretation of the results, which informed the abstract, lay summary, and discussion sections of the review.

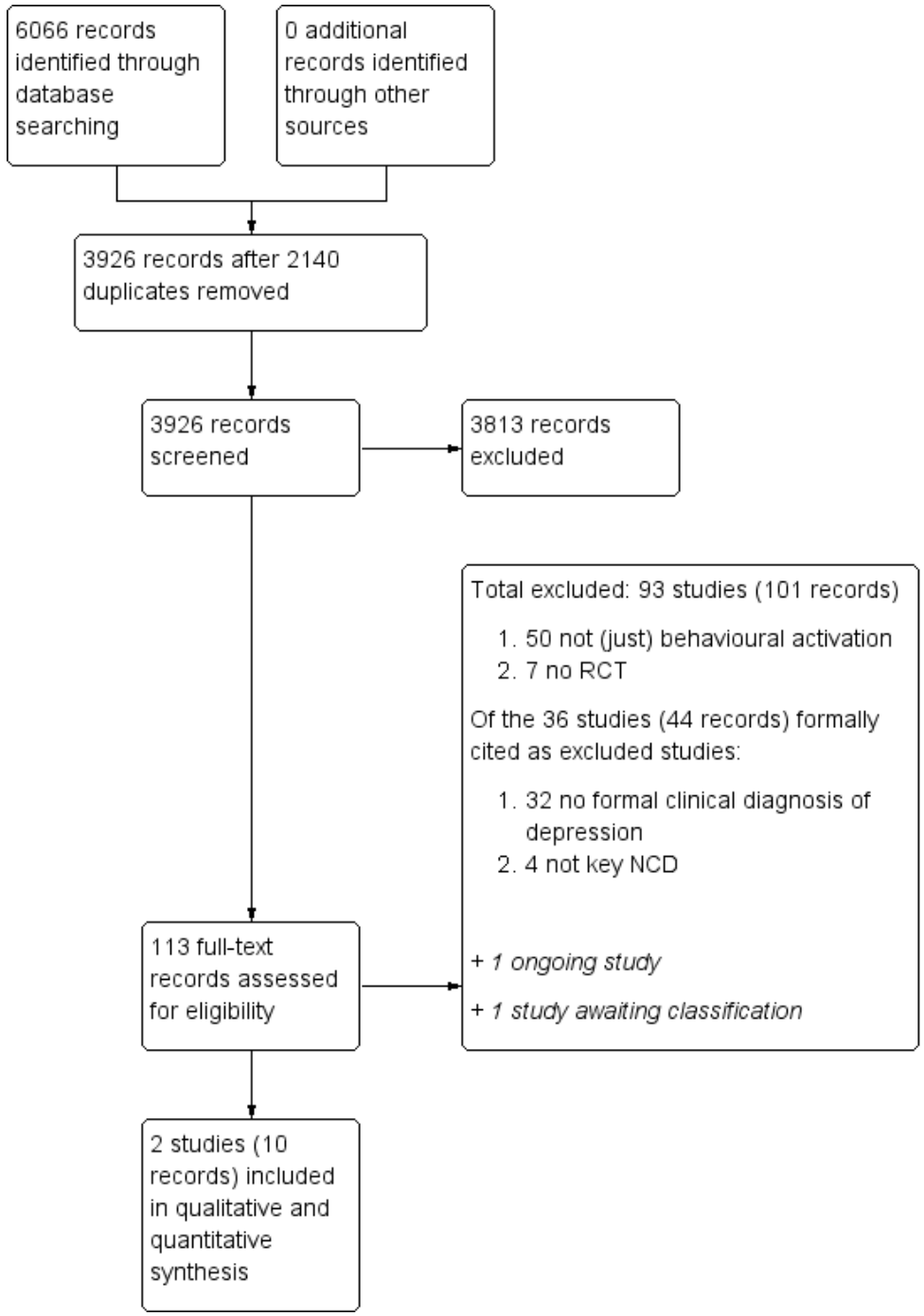
RESULTS

Description of studies

Results of the search

The database searches identified 6066 records. Once 2140 duplicates were removed there were 3926 records (Figure 1). After excluding 3813 irrelevant records, we assessed 113 records for eligibility and included two studies (10 records) in this review.

Figure 1. Study flow diagram. NCD: non-communicable disease; RCT: randomised controlled trial.



Included studies

The two included studies were both RCTs and evaluated the Living Well with Stroke intervention (Mitchell 2009) and brief behavioural activation for women with breast cancer (Hopko 2011). Together these studies included 181 participants. We contacted authors for information needed to complete data extraction and risk of bias assessments. The author of one study responded to our request (Mitchell 2009).

Setting

Both studies were conducted in the US, and participants were recruited in the hospital. In one study, participants were within four months poststroke (Mitchell 2009), while in the other study participants were receiving treatment for breast cancer (Hopko 2011).

Participants

Participants in the study by Mitchell and colleagues had a mix of gender, age, and ethnicity (Mitchell 2009), while participants in the

study by Hopko and colleagues were all women, with a mean age of 55 years, and mostly White American (Hopko 2011). Employment status varied.

One study did not report comorbidities in mental health (Mitchell 2009), while in the other study, 55/80 participants (69%) had depression and an anxiety disorder (Hopko 2011).

Depression severity was very similar, with a mean score of around 20 on the HRSD in both studies. In the study by Hopko and colleagues all participants had a moderate level of depression (Hopko 2011), while in the study by Mitchell and colleagues, some participants had moderate and others severe depression symptoms (Mitchell 2009).

Intervention

In both studies, behavioural activation was the main component of the intervention, and weekly sessions were delivered in an individual face-to-face format for eight weeks. One study used a mental health specialist to deliver the intervention (Mitchell 2009), while the other used clinical psychology doctoral students (specialists in training) (Hopko 2011).

Comparator

Comparators in both studies were similar in duration to the behavioural activation intervention. One study compared behavioural activation with an antidepressant (sertraline in the first instance) versus treatment as usual with an antidepressant (Mitchell 2009). Treatment as usual in this case primarily involved the provision of medical care after stroke. The other study used problem-solving therapy as a comparator, which was delivered with the same intensity and format as the behavioural activation intervention (Hopko 2011).

Outcomes

Both studies reported our prespecified primary outcomes, treatment efficacy and treatment acceptability (dropouts). Both studies used the HRSD to measure treatment efficacy, as indicated by remission of depression, and to measure and report depression symptoms. Criteria for remission were a score of seven or less on the HRSD in Hopko 2011 and a score of less than 10 in Mitchell 2009.

Other outcomes, reported by Hopko 2011 only, were physical functioning measured with the SF-36, quality of life measured using the Quality Of Life Inventory (QOLI), and anxiety using the BAI.

Neither study reported adverse effects. In one study, adverse effects were said to be monitored (see Mitchell 2008 under Mitchell 2009).

Both studies reported outcomes directly after the end of the treatment (nine weeks), in the short term (up to six months), and medium term (at 12 months). Mitchell 2009 also reported long-term outcomes (24 months).

Excluded studies

After obtaining full-text reports, we excluded 93 studies (101 full-text records) (Figure 1). Of the studies excluded at this stage, for 50 studies behavioural activation was not the intervention or the main component of the intervention. Seven studies were not RCTs. We were unable to exclude these studies at the stage of title and abstract screening because abstracts did not clearly specify the study design or intervention, or both. These records are not listed in the review.

Among the 36 studies (44 records) which are listed as Excluded studies in this review, reasons for exclusion were the lack of a formal clinical diagnosis of depression (32 studies) and a study population without one of the NCDs of interest to this review (four studies) (Characteristics of excluded studies table).

Studies awaiting classification

The full-text manuscript of one study could not be obtained (NCT02185482; Characteristics of studies awaiting classification table).

Ongoing studies

One study was ongoing with data collection estimated to finish in 2021 (NCT03688100; Characteristics of ongoing studies table).

Risk of bias in included studies

Allocation

Both studies used a computer programme to randomise participants, and were therefore at low risk of bias from random sequence allocation. Allocation concealment was achieved in one study (Mitchell 2009), while this was unclear for the other study (Hopko 2011).

Blinding

Both studies were at high risk of performance bias and at low risk for detection bias. Given the nature of psychological therapy, blinding of participants and personnel is very uncommon in clinical trials of this intervention. Outcome assessors were blinded to the participants' study arm allocation in both studies.

Incomplete outcome data

One study was at high risk of attrition bias, because missing outcome data for 10/42 participants in the behavioural activation study arm and 5/38 participants in the problem-solving therapy arm were imputed (Hopko 2011). Imputing outcome data may result in bias if data were not missing at random. There is a risk that attrition may be related to participant satisfaction with the intervention or allocation. The risk of attrition bias was low for the other study (Mitchell 2009). Although not all reasons for dropout were reported, dropout rates were similar in both study arms.

Selective reporting

One paper did not contain a reference to a study protocol or online trial registration and risk of reporting bias was, therefore, unclear (Hopko 2011). The authors of the other study referred to an online registration of the trial protocol, for which reported outcomes matched those presented in the results paper (Mitchell 2009).

Other potential sources of bias

For both studies, authors of the publication also developed the behavioural activation intervention and supervised therapists who delivered the intervention in the trial. These authors are likely to prefer a study result favouring behavioural activation, and we, therefore, judged them to be at high risk of 'other bias' due to a potential conflict of interest.

Effects of interventions

See: **Summary of findings 1** Behavioural activation compared with any comparator for depression in adults with non-communicable diseases

We planned to conduct meta-analyses for our prespecified primary and secondary outcomes (treatment efficacy, treatment acceptability, depression symptoms, quality of life, social adjustment and functioning, and anxiety symptoms) for behavioural activation compared with any control group, and behavioural activation compared with each control group separately. However, the inclusion of only two studies meant that a meta-analysis could only be conducted for short-term treatment efficacy of behavioural activation compared with any control group (treatment as usual and problem-solving therapy).

1. Behavioural activation versus any comparator

1.1 Treatment efficacy for depression (remission)

Short-term treatment efficacy appeared to be greater for behavioural activation than comparators (RR 1.53, 95% CI 0.98 to 2.38). Results from one study showed that this difference between study arms became less clear in the medium term (RR 1.76, 95% CI 1.01 to 3.08) and long term (RR 1.42, 95% CI 0.91 to 2.23) (Analysis 1.1).

Sensitivity analyses

We conducted sensitivity analyses to investigate the influence of missing data on the results. These analyses could only be performed for medium-term results (Analysis 1.7). The different scenarios included treatment data with an ITT approach, a best-case scenario, and a worst-case scenario. Treatment efficacy was greater for behavioural activation than for the comparator (usual care) in the ITT sensitivity analysis (RR 1.78, 95% CI 1.01 to 3.16; 1 study) and the best-case scenario (RR 2.32, 95% CI 1.34 to 4.03; 1 study), but not in a worst-case scenario (RR 1.29, 95% CI 0.79 to 2.11; 1 study).

1.2 Treatment acceptability (dropouts)

There was no evidence of a difference in the two studies in treatment acceptability in the short term (RR 1.81, 95% CI 0.68 to 4.82; 1 study) and medium term (RR 0.88, 95% CI 0.25 to 3.10; 1 study) (Analysis 1.2).

1.3 Improvement in depression symptoms

Endpoint and change from baseline data on depression symptoms have been combined for each time point. There was no evidence of a difference in depression symptoms between behavioural activation and comparators in the short term (MD –1.15, 95% CI –2.71 to 0.41), medium term (MD –1.51, 95% CI –4.14 to 1.12), or long term (MD –2.00, 95% CI –4.71 to 0.71) (Analysis 1.3).

1.4 Quality of life

One study reported on quality of life and found no evidence of a difference between study arms in the short term (MD 0.40, 95% CI –0.16 to 0.96) or in the medium term (MD –0.10, 95% CI –0.74 to 0.54) (Analysis 1.4; Hopko 2011).

1.5 Social adjustment and functioning

One study reported on the physical component of functioning and found no evidence of a difference between behavioural activation and the comparator in the short term (MD 2.70, 95% CI –6.99 to 12.39) and in the medium term (MD 2.20, 95% CI –6.37, 10.77) (Analysis 1.5; Hopko 2011).

1.6 Improvement in anxiety symptoms

One study reported no evidence of a difference between study arms in anxiety symptoms in the short term (MD –1.70, 95% CI –4.50 to 1.10) and medium term (–1.70, 95% CI –4.48 to 1.08) (Analysis 1.6; Hopko 2011).

1.7 Adverse effects

Neither study reported data on adverse effects.

DISCUSSION

Summary of main results

We included results from two RCTs with 181 participants. This means the conclusions we could draw from this review on the effectiveness of behavioural activation for the treatment of depression in adults with NCDs were limited.

Primary outcomes

Low- to moderate-certainty evidence suggested behavioural activation was more effective than comparator groups (treatment as usual and problem-solving therapy) in the short term, with differences between behavioural activation and comparators becoming less pronounced in the medium term and long term. Low-certainty evidence suggested there was no difference in treatment acceptability, measured by participants dropping out of the study, between behavioural activation and comparators.

The benefit of behavioural activation in terms of medium-term treatment efficacy was sustained in sensitivity analyses using an ITT approach to missing data and a best-case scenario, but not in the more conservative worst-case scenario.

Secondary outcomes

Evidence which was mostly of low certainty showed no differences between behavioural activation and comparators in depression symptoms, quality of life, functioning, and anxiety symptoms. Most outcomes were measured between five and 12 months after baseline measurements.

The two included studies did not report data on adverse effects.

Overall completeness and applicability of evidence

This review presents very limited evidence on behavioural activation for depression in adults with NCDs.

Our focus on diagnosed depression in people with comorbid CVD, diabetes, cancer, or respiratory illness means that studies of participants with other NCDs or depression symptoms without a formal diagnosis were not represented in this review. The evidence from these studies does, therefore, not apply to people with mild or subthreshold symptoms of depression. As commentary papers of one of the included studies highlighted, the exclusion of people with milder symptoms of depression will exclude a substantial

proportion of people who show symptoms after being diagnosed with an NCD or having experienced an event such as stroke (Barer 2010; Watkins 2009).

Although both studies reported several medium-term and long-term outcomes, we could not draw conclusions on the longer-term effectiveness of behavioural activation from the limited data available. It is possible that the efficacy of behavioural activation is affected by symptoms and the treatment process of the NCD at the time of the intervention. For example, receiving treatment for depression during or after treatment for cancer, or four months rather than eight months after a stroke, may affect the efficacy of behavioural activation.

Both studies were conducted in the US, with participants who were predominantly White Americans and middle aged. This evidence may, therefore, not apply to people in a different healthcare setting, or to people with different individual characteristics and determinants of health. In low- and middle-income countries, variation in healthcare systems and the acceptability and cultural appropriateness of mental health interventions such as behavioural activation may affect the efficacy of the treatment.

Neither study reported on adverse effects resulting from receiving the intervention or the comparator, although in one study it was stated that there was monitoring of adverse effects throughout the study (Mitchell 2008 under Mitchell 2009). As there were no data, we cannot judge to what extent behavioural activation therapy in this population may lead to adverse effects.

Quality of the evidence

Evidence was of low to moderate certainty. Evidence was downgraded for risk of bias, mostly relating to risk of attrition bias, performance bias, reporting bias, and potential conflict of interest, and for lack of precision. There was insufficient evidence for any of the outcomes to be certain that the reported estimates reflect the true estimates for these outcomes. As it is not possible to assess inconsistency in study results for outcomes with evidence based on only one study, we were unable to downgrade for inconsistency for these outcomes.

Potential biases in the review process

Our search strategy included regional and global databases and grey literature to identify studies published worldwide. However, the two studies eligible for inclusion were both conducted in the US. It is possible that relevant literature from other countries was missed, particularly if studies were not published in peer-reviewed journals.

We applied strict selection criteria regarding study samples and interventions. We only included studies with participants with clinically diagnosed depression and one of four key NCDs. Other evidence is available and may be informative to the treatment of depressive symptoms in clinical practice, for example for people with subthreshold depression, those who have not received a formal diagnosis, or those with other chronic physical conditions. Interventions for which behavioural activation was a component but not the main part of the intervention were excluded, which means interventions with relevance for clinical practice, such as collaborative care without a substantial behavioural activation component, were not included.

We used dropout from the studies as an indicator of treatment acceptability. Although participants' dropout may be related to satisfaction with the treatment, this is a crude indicator. Other elements of treatment acceptability could be considered, such as satisfaction measured through questionnaires.

Agreements and disagreements with other studies or reviews

One recent Cochrane Review of behavioural activation in depression for adults included evidence from 53 studies. It showed that behavioural activation may be more effective than humanistic therapy, medication, and treatment as usual, and that it may be no less effective than CBT, psychodynamic therapy, or being placed on a waiting list (Uphoff 2020). Treatment acceptability was similar between behavioural activation and most comparison groups. This indirect evidence suggests that behavioural activation may be effective for the treatment of depression in people with NCDs, although we do not currently know whether evidence can be applied to this specific population, who may face different challenges in overcoming depression.

One trial of 705 older adults comparing collaborative care with a strong behavioural activation component to treatment as usual found benefits of behavioural activation for the treatment of subthreshold depression (Gilbody 2017). Among this study sample, physical comorbidities including diabetes, cancer, respiratory conditions, and heart disease were prevalent. However, this trial did not meet the selection criteria for this review as the population was selected based on age rather than presence of NCDs. One systematic review and meta-analysis of 18 trials of behavioural activation for the treatment of depression in older people, including Gilbody 2017, showed that behavioural activation reduced symptoms of depression more than treatment as usual (Orgeta 2017).

AUTHORS' CONCLUSIONS

Implications for practice

Various global and national organisations advise on the treatment of people with mental and physical health problems. The World Health Organization advises that care for people with mental disorders and physical comorbidities should be integrated and collaborative, with professionals in primary care, hospital, and mental health services all having a role to play (WHO 2017b). The American Psychological Association (APA) guideline for the treatment of depression recognises the importance of considering comorbidities for the treatment of depression in adults and older people. For older people with type 2 diabetes mellitus or chronic obstructive pulmonary disease, a combination of individual cognitive behavioural therapy (CBT) and usual care is recommended (APA 2019). The Association of American Family Physicians (AAFP) recommends antidepressant medication or CBT (or both) to treat depression following an acute coronary syndrome event (Frost 2019). The Cancer Care Ontario Program in Evidence-Based Care guideline advises psychosocial or pharmacological (or both) interventions for depression in people with cancer, with collaborative care including an element of behavioural activation therapy recommended for the treatment of major depression or persistent subthreshold symptoms (Li 2016).

Guidance from the UK on the treatment of depression in adults with a chronic physical health problem was last updated in 2009 (NICE 2009). Behavioural activation is recommended for the general population of adults with depression. For those with chronic physical health problems in addition to depression, the guideline recommends antidepressants and group-based CBT in the first instance. Depending on suitability and depression severity, individual CBT is also recommended.

The evidence from this review is not sufficient to draw conclusions on the treatment of depression with behavioural activation for people with NCDs in clinical practice. There was insufficient evidence for adults with moderate-to-severe depression poststroke or while receiving breast cancer treatment in the US. We found no evidence for other settings or countries, people with other NCDs, and formats of behavioural activation other than individual face-to-face delivery by specialists or specialists in training. We did not include any studies with participants with mild or subthreshold depression.

Before implementing behavioural activation as an alternative to other treatments for depression in this population, further research is required to establish the efficacy and acceptability of behavioural activation for the treatment of depression in adults with NCDs. It has been suggested that behavioural activation is less complicated than other psychological therapies to deliver and as such may be suited to wider dissemination (Ekers 2014). There may be the potential to implement behavioural activation in different healthcare settings and clinics attended by people with NCDs.

Implications for research

Behavioural activation is increasingly being evaluated for the treatment of depression or depressive symptoms in people with NCDs. It is likely that a future review will be able to provide more conclusive evidence on the efficacy and acceptability of behavioural activation in this population.

This review did not include studies with participants with symptoms of depression or subthreshold depression without a formal diagnosis. Such studies could add to the evidence base, as it is likely that many people with NCDs experience symptoms of depression without meeting the criteria for a diagnosis, or without receiving the formal clinical assessment required for a diagnosis. Future reviews of behavioural activation for people with NCDs may wish to include, or focus on, people with subthreshold depression or symptoms of depression. This would inform whether behavioural activation could be used to intervene early in this population, applying a preventive public health perspective, before depression develops or worsens.

Depression and NCDs such as diabetes, cancer, heart disease, and chronic respiratory illness are common in high-income countries as well as low- and middle-income countries. Given that behavioural activation is seen as a treatment which might successfully be delivered with fewer resources and less specialist training than established psychological therapies, evidence from low- and middle-income countries could establish whether behavioural activation can be an effective, acceptable, and feasible alternative in the treatment of depression among people with NCDs in settings where resources for mental health support are limited.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Hopko 2011

Study characteristics

Methods	**Study design:** RCT **Study grouping:** parallel group **Recruitment (how were participants recruited, where, when):** 80 adults with a principal diagnosis of major depression who were treated at the University of Tennessee Medical Center's Cancer Institute (Knoxville, TN). Recruited through clinic screening, clinic brochures, and oncologist referral.

Hopko 2011 *(Continued)*

Type of RCT (blind, double-blind, open): open

Participants	**Baseline characteristics** BA • *Gender (n and % men and women)*: 100% women • *Ethnic group (n and % in each group)*: 90% Caucasian, 10% African American • *Occupation/employment (n and % in categories)*: employed (full time) = 7 (17%); employed (part-time) = 9 (21%); unemployed = 11 (26%); retired = 15 (36%) • *Education level (n and % in categories)*: mean 15.1 years (SD 2.1) • *Comorbid anxiety (n and % of participants)*: generalised anxiety disorder = 21 (50%); social phobia = 4 (10%); post-traumatic stress disorder = 2 (5%); panic disorder = 2 (5%); specific phobia = 2 (5%); anxiety disorder NOS = 1 (3%) • *Depression severity (mean score at baseline or n and % in categories)*: moderate, mean HRSD 19.2 (SD 7.0) • *Age*: mean 56.4 (SD 11.1) years • *NCD:* breast cancer Problem-solving therapy • *Gender (n and % male and female)*: 100% women • *Ethnic group (n and % in each group)*: 95% Caucasian, 5% African American • *Occupation/employment (n and % in categories)*: employed (full time) = 10 (26%); employed (part-time) = 8 (21%); unemployed = 11 (29%); retired = 9 (24%) • *Education level (n and % in categories)*: mean 14.5 years (SD 2.4) • *Comorbid anxiety (n and % of participants)*: generalised anxiety disorder = 14 (37%); social phobia = 5 (13%); post-traumatic stress disorder = 3 (8%); panic disorder = 0 (0%); specific phobia = 1 (3%); anxiety disorder NOS = 0 (0%) • *Depression severity (mean score at baseline or n and % in categories)*: moderate, mean HRSD 20.1 (SD 5.9) • *Age*: mean 54.3 (SD 11.2) years • *NCD*: breast cancer **Included criteria:** breast cancer, diagnosis of major depressive disorder (DSM-IV), aged ≥ 18 years, moderate depressive symptoms **Excluded criteria:** recent antidepressant or antianxiety medication not stabilised before starting trial, bipolar disorder, psychosis, mental retardation, current alcohol or drug dependence, or principal diagnosis other than major depression. **Pretreatment:** baseline characteristics largely similar. BA group less likely to have a history of psychotherapy for depression, and more likely to have current antidepressant use and generalised anxiety disorder. Pretreatment depression scores similar.
Interventions	**Intervention characteristics** BA • *Type of intervention (BA or comparator)*: BA • *Description of intervention*: brief BA therapy for depression • *Dose (length of session)*: 1 hour per week • *Frequency*: once a week • *Duration*: 8 weeks • *Level of therapist (specialist or non-specialist)*: specialist in training • *Individual or group therapy*: individual • *Mode of delivery (face-to-face, telephone, online, combination)*: face-to-face • *Modifications to intervention*: participants were paid per session

Hopko 2011 *(Continued)*

	Problem-solving therapy • *Type of intervention (BA or comparator)*: comparator • *Description of intervention*: problem-solving therapy • *Dose (length of session)*: 1 hour per week • *Frequency*: once a week • *Duration*: 8 weeks • *Level of therapist (specialist or non-specialist)*: specialist in training • *Individual or group therapy*: individual • *Mode of delivery (face-to-face, telephone, online, combination)*: face-to-face • *Modifications to intervention*: participants were paid per session
Outcomes	*Depression symptoms (HRSD)* • **Outcome type**: continuous • **Scale**: HRSD • **Direction**: lower is better *Remission (HRSD)* • **Outcome type**: dichotomous • **Scale**: HRSD • **Direction**: higher is better • **Data value**: endpoint *Social functioning (physical component)* • **Outcome type**: continuous • **Scale**: SF-36 physical • **Direction**: higher is better *Quality of life* • **Outcome type**: continuous • **Scale**: QOLI • **Direction**: higher is better • **Data value**: endpoint *Anxiety symptoms* • **Outcome type**: continuous • **Scale**: BAI • **Direction**: lower is better • **Data value**: endpoint *Treatment acceptability (dropouts)* • **Outcome type**: dichotomous • **Reporting**: fully reported • **Direction**: lower is better • **Data value**: endpoint
Identification	**Sponsorship source:** research supported by Susan G. Komen for the Cure research grant awarded to Derek R. Hopko (BCTR0706709) **Country:** US **Setting:** recruitment at medical centre cancer institute in Tennessee, US

Hopko 2011 *(Continued)*

Comments: missing data imputed with multiple imputation.

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Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "If included following the comprehensive assessment, based on a preestablished randomization chart (Random Allocation Software, Version 1.0; Saghaei, 2004), patients were randomized to either BATD [behavioural activation therapy for depression] or PST [problem-solving therapy]." Comment: the study is described as randomised. Software used to randomise participants.
Allocation concealment (selection bias)	Unclear risk	Comment: unclear how sequence of allocation was concealed from researchers.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: blinding not possible due to nature of interventions. This may introduce bias, e.g. if participants prefer 1 treatment over the other.
Blinding of outcome assessment for the OBSERVER-RATED scale (detection bias)	Low risk	Quote: "Advanced doctoral students in clinical psychology conducted the comprehensive assessments. At the time of these assessments, examiners were unaware of the potential treatment condition of the patient if included in the study." Comment: outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: missing outcome data: 10/42 in BA group and 5/38 in problem-solving therapy group was imputed using multiple imputation. Although missing data were reported to be missing at random, imputing outcome data may have resulted in bias if attrition was related to satisfaction with the intervention or with the allocation.
Selective reporting (reporting bias)	Unclear risk	Comment: no reference to protocol or trial registration number.
Other bias	High risk	Comment: authors Derek R Hopko (principal investigator) and Carl W Lejuez developed BA therapy for depression intervention and manuals, and would, therefore, benefit from this intervention being successful. DR Hopko supervised the therapists.

Mitchell 2009

Study characteristics

Mitchell 2009 *(Continued)*

Methods	**Study design:** RCT **Study grouping:** parallel group **Recruitment (how were participants recruited, where, when):** people hospitalised in 4 acute care hospitals in Seattle, US. **Type of RCT (blind, double-blind, open):** open
Participants	**Baseline characteristics** BA + antidepressant • *Gender (n and % men and women)*: men 29 (60.4%) and women 19 (39.6%) • *Ethnic group (n and % in each group)*: Hispanic (intervention: 3 (6.3%); control: 2 (3.8%)); mixed race (12 (25%)); white (29 (60.4%)); black (3 (6.3%)); Japanese (3 (6.3%)); Pacific islander (0%); Korean (1 (2.1%)) • *Occupation/employment*: - • *Education level*: - • *Comorbid anxiety*: - • *Depression severity (mean score at baseline or n and % in categories)*: mean HRSD 20.0 (SD 4.53); range 10–29 • *Age*: mean 57 (range 25–88) years Treatment as usual + antidepressant • *Gender (n and % men and women)*: men 32 (60.4%) and women 21 (39.6%) • *Ethnic group (n and % in each group)*: Hispanic (2 (3.8%)); mixed race (10 (18.9%)); white (35, 66.0%); black (7 (13.2%)); Japanese (0%); Pacific islander (1 (1.9%)); Korean (0%) • *Occupation/ employment*: - • *Education level*: - • *Comorbid anxiety*: - • *Depression severity (mean score at baseline or N and % in categories)*: mean HRSD 19.8 (SD 4.15); range 11–29 • *Age*: mean 57 (range 29–88) years **Included criteria:** within 4 months of an ischaemic stroke, screened positive for depressive symptoms, diagnosis of clinical depression (DSM-IV). **Excluded criteria:** prior or current treatment for depression **Pretreatment:** similar baseline characteristics, stroke severity, and depression symptoms.
Interventions	**Intervention characteristics** BA + antidepressant • *Type of intervention (BA or comparator)*: BA • *Description of intervention*: Living Well with Stroke • *Dose (length of session)*: • *Frequency*: weekly (9 times in 8 weeks) • *Duration*: 8 weeks • *Level of therapist (specialist or non-specialist)*: specialist • *Individual or group therapy*: individual • *Mode of delivery (face-to-face, telephone, online, combination)*: face-to-face • *Modifications to intervention*: - Treatment as usual + antidepressant

Mitchell 2009 *(Continued)*

- *Type of intervention (BA or comparator)*: comparator
- *Description of intervention*: treatment as usual poststroke + antidepressant (sertraline first choice)
- *Dose (length of session)*: -
- *Frequency*: -
- *Duration*: 8 weeks
- *Level of therapist (specialist or non-specialist)*: -
- *Individual or group therapy*: individual
- *Mode of delivery (face-to-face, telephone, online, combination)*: face-to-face
- *Modifications to intervention*: -

Outcomes	*Depression symptoms* • **Outcome type**: continuous • **Reporting**: fully reported • **Scale**: HRSD • **Direction**: lower is better • **Data value**: change from baseline *Remission (perceived recovery)* • **Outcome type**: dichotomous • **Scale**: HRSD • **Direction**: higher is better • **Data value**: endpoint • **Notes**: HRSD ≤ 9 *Treatment acceptability (dropouts)* • **Outcome type**: dichotomous • **Reporting**: fully reported • **Direction**: lower is better • **Data value**: endpoint
Identification	**Sponsorship source:** National Institute of Nursing Research, National Institutes of Health grant R01N-R007755 **Country:** US **Setting:** 4 acute poststroke care hospitals in Seattle, Washington State, US **Comments:** - **Authors name:** Pamela H Mitchell **Institution:** University of Washington **Email:** pmitch@u.washington.edu **Address:** Box 357266, University of Washington, Seattle, WA 98195-7266, US
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "masking – randomization status was generated by a computerized adaptive randomization procedure after the method of Pocock and Simon."

Mitchell 2009 *(Continued)*

		Comment: computerised randomisation used.
Allocation concealment (selection bias)	Low risk	Comment: contacted author: allocation concealed from everyone except statistician and therapist. Therapist communicated allocation to participants.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding of participants and personnel possible due to nature of intervention. This may introduce bias, e.g. if some participants prefer psychotherapy over medication only.
Blinding of outcome assessment for the OBSERVER-RATED scale (detection bias)	Low risk	Quote: "All outcome assessors were masked to the participant's randomization status at each data collection point. We did not detect any breaches in masking." Comment: outcome assessors were blinding throughout study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: some reasons for dropout provided but not all. 4/48 in intervention group and 5/53 in control group.
Selective reporting (reporting bias)	Low risk	Quote: "http://www.clinicaltrials.gov/ct/show/NCT00194454?order=1" Comment: trial registration reported; outcomes match registration.
Other bias	High risk	Comment: authors reported no conflicts of interest. Dr Teri, last author on this publication, developed the intervention and, therefore, had an interest in it being successful. She also supervised therapists. This may have caused bias.

BA: behavioural activation; BAI: Beck Anxiety Inventory; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HRSD: Hamilton Rating Scale for Depression; n: number; NCD: non-communicable disease; NOS: not otherwise specified; QOLI: Quality Of Life Inventory; RCT: randomised controlled trial; SD: standard deviation; SF-36: 36-item Short Form.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cully 2014	No formal clinical diagnosis of depression.
Humphreys 2015	No formal clinical diagnosis of depression.
ISRCTN11290592	No formal clinical diagnosis of depression.
ISRCTN12715175	No formal clinical diagnosis of depression.
ISRCTN16242820	No formal clinical diagnosis of depression.
ISRCTN16601130	No formal clinical diagnosis of depression.
ISRCTN63855912	No formal clinical diagnosis of depression.
Jahoda 2015	Not key NCD.
Kaltman 2016	No formal clinical diagnosis of depression.
Kirkness 2017	No formal clinical diagnosis of depression.

Study	Reason for exclusion
McGregor 2011	No formal clinical diagnosis of depression.
Mehnert 2014	No formal clinical diagnosis of depression.
Morgan 2009	No formal clinical diagnosis of depression.
Naik 2019	No formal clinical diagnosis of depression.
NCT01506492	No formal clinical diagnosis of depression.
NCT01572389	No formal clinical diagnosis of depression.
NCT02121340	No formal clinical diagnosis of depression.
NCT02353546	No formal clinical diagnosis of depression.
NCT02382562	Not key NCD.
NCT02413840	No formal clinical diagnosis of depression.
NCT02846662	Not key NCD.
NCT03026426	Not key NCD.
NCT03233451	No formal clinical diagnosis of depression.
NCT03431493	No formal clinical diagnosis of depression.
Richards 2018	No formal clinical diagnosis of depression.
Sareh 2016	No formal clinical diagnosis of depression.
Thomas 2019	No formal clinical diagnosis of depression.
Tindle 2012	No formal clinical diagnosis of depression.

NCD: non-communicable disease.

Characteristics of studies awaiting classification *[ordered by study ID]*

NCT02185482

Methods	Unclear
Participants	150 participants with depression and type 2 diabetes in India.
Interventions	Physician-led counselling vs usual care
Outcomes	Change in depression (SCL-90), glycaemic control
Notes	Author could not be contacted.

SCL-90: Symptom Checklist-90.

Characteristics of ongoing studies *[ordered by study ID]*

NCT03688100

Study name	Personalized treatments for depressive symptoms in patients with advanced heart failure.
Methods	RCT
Participants	Adults with heart failure (II–IV) and depression
Interventions	Behavioural activation and medication management
Outcomes	Depression, generic health, cardiomyopathy, carer burden, emergency department visits, readmissions, days in hospital, mortality
Starting date	9 November 2018
Contact information	Vicki A Manoukian: vicki.manoukian@cshs.org
Notes	Completion planned for 2021.

RCT: randomised controlled trial.

DATA AND ANALYSES

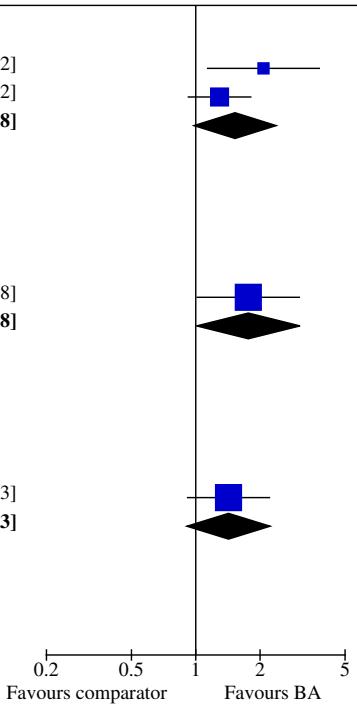
Comparison 1. Behavioural activation (BA) versus any comparator

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Treatment efficacy for depression (remission)	2		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1.1 Short-term (up to 6 months)	2	176	Risk Ratio (IV, Random, 95% CI)	1.53 [0.98, 2.38]
1.1.2 Medium-term (7–12 months)	1	92	Risk Ratio (IV, Random, 95% CI)	1.76 [1.01, 3.08]
1.1.3 Long-term (> 12 months)	1	67	Risk Ratio (IV, Random, 95% CI)	1.42 [0.91, 2.23]
1.2 Treatment acceptability (dropouts)	2		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.2.1 Short-term (up to 6 months)	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.2.2 Medium-term (7–12 months)	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.3 Improvement in depression symptoms	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.3.1 Short-term (up to 6 months)	2	176	Mean Difference (IV, Random, 95% CI)	-1.15 [-2.71, 0.41]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3.2 Medium-term (7–12 months)	2	172	Mean Difference (IV, Random, 95% CI)	-1.51 [-4.14, 1.12]
1.3.3 Long-term (> 12 months)	1	67	Mean Difference (IV, Random, 95% CI)	-2.00 [-4.71, 0.71]
1.4 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4.1 Short-term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4.2 Medium-term (7–12 months)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.5 Social adjustment and functioning	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.5.1 Short-term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.5.2 Medium-term (7–12 months)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.6 Improvement in anxiety symptoms	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.6.1 Short-term (up to 6 months)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.6.2 Medium-term (7–12 months)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.7 Treatment efficacy for depression – sensitivity analyses	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.7.1 Medium-term (up to 6 months) ITT	1	101	Risk Ratio (M-H, Random, 95% CI)	1.78 [1.01, 3.16]
1.7.2 Medium-term (up to 6 months) – best case	1	106	Risk Ratio (M-H, Random, 95% CI)	2.32 [1.34, 4.03]
1.7.3 Medium-term (up to 6 months) – worst case	1	101	Risk Ratio (M-H, Random, 95% CI)	1.29 [0.79, 2.11]

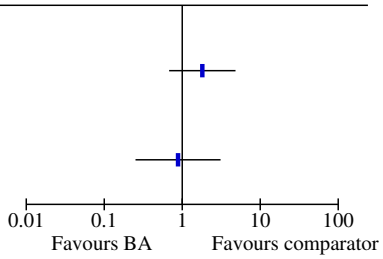
Analysis 1.1. Comparison 1: Behavioural activation (BA) versus any comparator, Outcome 1: Treatment efficacy for depression (remission)

Study or Subgroup	Behavioural activation Events	Total	Comparator Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Short-term (up to 6 months)						
Mitchell 2009	21	46	11	50	35.3%	2.08 [1.13 , 3.82]
Hopko 2011	30	42	21	38	64.7%	1.29 [0.92 , 1.82]
Subtotal (95% CI)		**88**		**88**	**100.0%**	**1.53 [0.98 , 2.38]**
Total events:	51		32			
Heterogeneity: Tau² = 0.05; Chi² = 1.76, df = 1 (P = 0.19); I² = 43%						
Test for overall effect: Z = 1.87 (P = 0.06)						
1.1.2 Medium-term (7–12 months)						
Mitchell 2009	21	44	13	48	100.0%	1.76 [1.01 , 3.08]
Subtotal (95% CI)		**44**		**48**	**100.0%**	**1.76 [1.01 , 3.08]**
Total events:	21		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.99 (P = 0.05)						
1.1.3 Long-term (> 12 months)						
Mitchell 2009	22	34	15	33	100.0%	1.42 [0.91 , 2.23]
Subtotal (95% CI)		**34**		**33**	**100.0%**	**1.42 [0.91 , 2.23]**
Total events:	22		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.54 (P = 0.12)						
Test for subgroup differences: Chi² = 0.34, df = 2 (P = 0.84), I² = 0%						



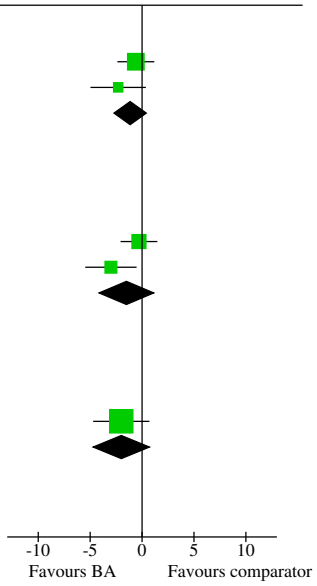
Analysis 1.2. Comparison 1: Behavioural activation (BA) versus any comparator, Outcome 2: Treatment acceptability (dropouts)

Study or Subgroup	Behavioural activation Events	Total	Comparator Events	Total	Risk Ratio IV, Random, 95% CI
1.2.1 Short-term (up to 6 months)					
Hopko 2011	10	42	5	38	1.81 [0.68 , 4.82]
1.2.2 Medium-term (7–12 months)					
Mitchell 2009	4	48	5	53	0.88 [0.25 , 3.10]



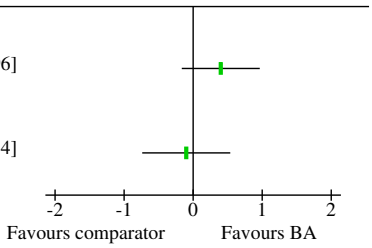
Analysis 1.3. Comparison 1: Behavioural activation (BA) versus any comparator, Outcome 3: Improvement in depression symptoms

Study or Subgroup	Behavioural activation Mean	SD	Total	Comparator Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 Short-term (up to 6 months)								
Hopko 2011	5.7	3.2	42	6.3	4.7	38	67.7%	-0.60 [-2.38 , 1.18]
Mitchell 2009	-8.3	6.8	46	-6	6.5	50	32.3%	-2.30 [-4.97 , 0.37]
Subtotal (95% CI)			**88**			**88**	**100.0%**	**-1.15 [-2.71 , 0.41]**
Heterogeneity: Tau² = 0.11; Chi² = 1.08, df = 1 (P = 0.30); I² = 7%								
Test for overall effect: Z = 1.45 (P = 0.15)								
1.3.2 Medium-term (7–12 months)								
Hopko 2011	4.5	3.6	42	4.8	4.4	38	55.3%	-0.30 [-2.07 , 1.47]
Mitchell 2009	-9.2	5.7	44	-6.2	6.4	48	44.7%	-3.00 [-5.47 , -0.53]
Subtotal (95% CI)			**86**			**86**	**100.0%**	**-1.51 [-4.14 , 1.12]**
Heterogeneity: Tau² = 2.44; Chi² = 3.03, df = 1 (P = 0.08); I² = 67%								
Test for overall effect: Z = 1.12 (P = 0.26)								
1.3.3 Long-term (> 12 months)								
Mitchell 2009	-11.3	6.5	34	-9.3	4.7	33	100.0%	-2.00 [-4.71 , 0.71]
Subtotal (95% CI)			**34**			**33**	**100.0%**	**-2.00 [-4.71 , 0.71]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.45 (P = 0.15)								



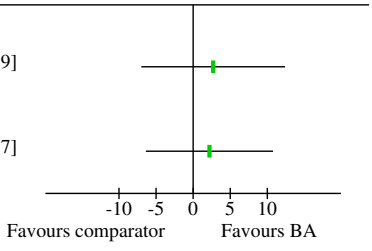
Analysis 1.4. Comparison 1: Behavioural activation (BA) versus any comparator, Outcome 4: Quality of life

Study or Subgroup	Behavioural activation Mean	SD	Total	Comparator Mean	SD	Total	Mean Difference IV, Random, 95% CI
1.4.1 Short-term (up to 6 months)							
Hopko 2011	2.6	1	42	2.2	1.5	38	0.40 [-0.16 , 0.96]
1.4.2 Medium-term (7–12 months)							
Hopko 2011	2.1	1.4	42	2.2	1.5	38	-0.10 [-0.74 , 0.54]



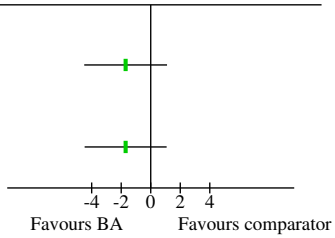
Analysis 1.5. Comparison 1: Behavioural activation (BA) versus any comparator, Outcome 5: Social adjustment and functioning

Study or Subgroup	Behavioural activation Mean	SD	Total	Comparator Mean	SD	Total	Mean Difference IV, Random, 95% CI
1.5.1 Short-term (up to 6 months)							
Hopko 2011	62.2	23.3	42	59.5	20.9	38	2.70 [-6.99 , 12.39]
1.5.2 Medium-term (7–12 months)							
Hopko 2011	63.9	17.9	42	61.7	20.9	38	2.20 [-6.37 , 10.77]



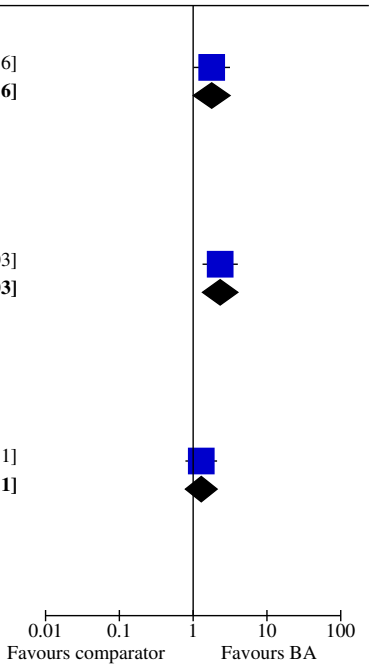
Analysis 1.6. Comparison 1: Behavioural activation (BA) versus any comparator, Outcome 6: Improvement in anxiety symptoms

Study or Subgroup	Behavioural activation Mean	SD	Total	Comparator Mean	SD	Total	Mean Difference IV, Random, 95% CI
1.6.1 Short-term (up to 6 months)							
Hopko 2011	9	5.5	42	10.7	7.1	38	-1.70 [-4.50 , 1.10]
1.6.2 Medium-term (7–12 months)							
Hopko 2011	7.5	5.2	42	9.2	7.2	38	-1.70 [-4.48 , 1.08]



Analysis 1.7. Comparison 1: Behavioural activation (BA) versus any comparator, Outcome 7: Treatment efficacy for depression – sensitivity analyses

Study or Subgroup	Behavioural activation Events	Total	Comparator Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Medium-term (up to 6 months) ITT						
Mitchell 2009	21	48	13	53	100.0%	1.78 [1.01 , 3.16]
Subtotal (95% CI)		**48**		**53**	**100.0%**	**1.78 [1.01 , 3.16]**
Total events:	21		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.99 (P = 0.05)						
1.7.2 Medium-term (up to 6 months) – best case						
Mitchell 2009	25	48	13	58	100.0%	2.32 [1.34 , 4.03]
Subtotal (95% CI)		**48**		**58**	**100.0%**	**2.32 [1.34 , 4.03]**
Total events:	25		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.00 (P = 0.003)						
1.7.3 Medium-term (up to 6 months) – worst case						
Mitchell 2009	21	48	18	53	100.0%	1.29 [0.79 , 2.11]
Subtotal (95% CI)		**48**		**53**	**100.0%**	**1.29 [0.79 , 2.11]**
Total events:	21		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.01 (P = 0.31)						
Test for subgroup differences: Chi² = 2.48, df = 2 (P = 0.29), I² = 19.3%						



APPENDICES

Appendix 1. Categories of psychological therapies

Categories	Abbreviation	Subcategories	Abbreviation
1. Behavioural therapies	BT	Behavioural therapy (Lewinsohn)	—
		Behavioural activation (original model) (Jacobson)	BA

(Continued)

		Social skills training/assertiveness training	SST/assertion
		Relaxation therapy	—
		Other behavioural therapies	—
2. Cognitive behavioural therapies	CBT	Cognitive therapy	—
		Rational emotive behaviour therapy	—
		Problem-solving therapy	—
		Self-control therapy	—
		Coping with depression course	—
		Other cognitive behavioural therapies	—
3. Mindfulness-based 'third-wave' cognitive and behavioural therapies	Third-wave CBT	Acceptance and commitment therapy	ACT
		Compassionate mind training	—
		Functional analytic psychotherapy	—
		Extended behavioural activation	eBA
		Metacognitive therapy	—
		Mindfulness-based cognitive therapy	—
		Dialectical behaviour therapy	—
		Other third-wave cognitive and behavioural therapies (other third-wave CBT)	—
4. Psychodynamic therapies	—	Drive/structural model (Freud)	—
		Relational model (Strupp, Luborsky)	—
		Integrative analytic model (Mann)	—
		Other psychodynamic therapies	—
5. Humanistic therapies	—	Person-centred therapy (Rogerian)	—
		Gestalt therapy	—
		Experiential therapies	—
		Transactional analysis	—
		Existential therapy	—
		Non-directive/supportive therapies	—

(Continued)

		Other humanistic therapies	—
6. Interpersonal, cognitive analytic, and other integrative therapies	—	Interpersonal therapy	IPT
		Cognitive analytic therapy	CAT
		Psychodynamic interpersonal therapy	—
		Cognitive behavioural analysis system of psychotherapy	—
		Counselling	—
		Motivational interviewing	—
		Other integrative therapy approaches	—

Appendix 2. Full search strategy

CCMD Trials Register Search (current to 14 June 2016 only)

03/10/2019

#1 (depression or depressive disorder):mh,emt,kw,ky AND INREGISTER 20650

#2 (depress* adj3 (acute or clinical* or diagnos* or disorder* or major or unipolar or illness or scale* or score* or adult* or patient* or participant* or people or inpatient* or in-patient* or outpatient* or out-patient*)):ab AND INREGISTER 15685

#3 (depress* and (Beck* or BDI* or DSM* or (Statistical Manual adj2 Mental Disorders) or Hamilton or HAM-D or HAMD or MADRS or (International Classification adj2 Disease?) or ICD-10 or ICD-9)):ab AND INREGISTER 8670

#4 “with depressi*”:ab AND INREGISTER 2339

#5 (depressi* or depressed):ti AND INREGISTER 14828

#6 #1 OR #2 OR #3 OR #4 OR #5 24421

#7 ((behavio* adj1 activat*) or BATD) AND INREGISTER 197

#8 (behavio* and (self adj (evaluat* or monitor*))) AND INREGISTER 481

#9 (behavio* adj2 (contracting or modification or modify*)) AND INREGISTER 453

#10 reinforc* AND INREGISTER 311

#11 (activit* adj2 schedul*) AND INREGISTER 26

#12 ((pleas* or enjoy* or reward*) adj4 (activit* or event*)) AND INREGISTER 110

#13 ((operant or instrumental) adj (conditioning or learning)) AND INREGISTER 26

#14 (positive interaction* or avoida* coping or environmental contingenc* or contigency management) AND INREGISTER 50

#15 functional analysis AND INREGISTER 10

#16 ((gain or gains or reapprais*) adj2 focus*) AND INREGISTER 2

#17 ((psychoeducat* or psycho-educat*) and (behavi* or coping or self manag*)) AND INREGISTER 699

#18 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 (2142)

#19 #6 AND #18 (1051)

#20 (behavio* adj (counsel* or intervention or train* or treatment or therapy or psychotherapy)) AND INREGISTER 9331

#21 #20 AND #6 (4402)

#22 ((long-term or longterm or chronic* or occupational) next (condition* or disease* or symptom* or problem* or failure*)) AND INREGISTER 999

#23 (asthma* or bronchitis or chronic obstructive or emphysema or hypertension or lung or pulmonary or respiratory) AND INREGISTER 1053

#24 (obstruct* NEAR (airway* or airflow*)) AND INREGISTER 13

#25 ((hyper responsiveness or hyper-responsiveness or allergy or allergi* or hypersensitiv*) NEAR (airway*)) AND INREGISTER 0

#26 (COPD or COAD or COBD or AECB) AND INREGISTER 133

#27 diabet* or IDDM or NIDDM or MODY or T1DM or T2DM or T1D or T2D AND INREGISTER 521

#28 (cardio* or cardia* or CVD or heart* or coronary* or angina* or ventric* or myocard* or pericard* or ischem* or ischaem* cerebrovasc* or stroke or strokes or poststroke or apoplexy or (brain NEAR (accident* or trauma*)) or ((brain* or cerebral or lacunar) NEAR infarct*)) AND INREGISTER 3439

#29 hypertensi* or hyperlip* or hypercholester* or hypertriglycerid* or hyper-tensi* or hyper-lip* or hyper-cholester* or hyper-triglycerid* or arteriosclerosis AND INREGISTER 386

#30 (emboli* or arrhythmi* or arteriosclero* or atherosclero* or peripheral arter* disease* or thrombo* or atrial fibrillat* or tachycardi* or endocardi* or sick sinus) AND INREGISTER 391

#31 (cancer* or neoplas* or tumo* or carcinoma* or hodgkin* or nonhodgkin* or adenocarcinoma* or leukemia* or leukaemia* or metasta* or malignan* or lymphoma* or sarcoma* or melanoma* or myeloma* or oncolog* or psychooncology or psycho-oncology) AND INREGISTER 1215

#32 #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 (6284)

#33 (#32 AND #19) 191

#34 (#21 AND #32) 676

#35 (#33 OR #34) 755

#36 (cholesterol* or “blood pressure”) AND INREGISTER 1223

#37 (#36 AND #19) 22

#38 (#36 AND #21) 63

#39 (#37 OR #38 OR #35) 779

#40 (CBT OR "cogniti* behavio*"):ti AND INREGISTER 2790

#41 (activat* or BATD or (self NEXT (evaluat* or monitor*)) or contracting or modification or modify* or (activit* and schedul*) or ((pleas* or enjoy* or reward*) and (activit* or event*)) or ((operant or instrumental) and (conditioning or learning)) or positive interaction* or avoida* coping or environmental contingenc* or contigency management or functional analysis or ((gain or gains or reapprais*) and focus*) or ((psychoeducat* or psycho-educat*) and (behavi* or coping or self manag*))):ti AND INREGISTER 447

#42 (#40 NOT #41) 2732

#43 (#39 NOT #42) 577

ClinicalTrials.gov

25/09/2019

Search 1

Condition or disease: Depression

Other terms: diabetes OR cancer or neoplasm OR tumor OR tumour OR asthma OR stroke or hypertension

Study Type: Interventional Studies

Study results: All studies

Age group – Adult plus Older adult

Intervention: behaviour activation OR behavior activation OR behavioural activation OR behavioral activation

21 hits

Search 2

Condition or disease: Depression

Other terms: CVD OR cardiovascular OR cardiac OR heart OR coronary OR angina OR ventricular OR myocardial

Study Type: Interventional Studies

Study results: All studies

Age group – Adult plus Older adult

Intervention: behaviour activation OR behavior activation OR behavioural activation OR behavioral activation

25 hits

Search 3

Condition or disease: Depression

Other terms: ischemia OR ischaemia OR cerebrovascular OR COPD OR pulmonary OR lung OR respiratory OR bronchitis

Study Type: Interventional Studies

Study results: All studies

Age group – Adult plus Older adult

Intervention: behaviour activation OR behavior activation OR behavioural activation OR behavioral activation

10 studies

Search 4

Condition or disease: Depression

Other terms: diabetes OR cancer or neoplasm OR tumor OR tumour OR asthma OR stroke or hypertension

Study Type: Interventional Studies

Study results: All studies

Age group – Adult plus Older adult

Intervention: behaviour therapy OR behavior therapy OR behavioural therapy OR behavioral therapy

109 hits

Search 5

Condition or disease: Depression

Other terms: CVD OR cardiovascular OR cardiac OR heart OR coronary OR angina OR ventricular OR myocardial

Study Type: Interventional Studies

Study results: All studies

Age group – Adult plus Older adult

Intervention: behaviour therapy OR behavior therapy OR behavioural therapy OR behavioral therapy

113

Search 6

Condition or disease: Depression

Other terms: ischemia OR ischaemia OR cerebrovascular OR COPD OR pulmonary OR lung OR respiratory OR bronchitis

Study Type: Interventional Studies

Study results: All studies

Age group – Adult plus Older adult

Intervention: behaviour therapy OR behavior therapy OR behavioural therapy OR behavioral therapy

51 hits

Cochrane Central Register of Controlled Trials Issue 9 of 12, September 2019

03/10/2019

ID Search Hits

#1 (((behavio* Near/1 activat*) or BATD)):ti,ab,kw 737

#2 behavio* and (self NEXT (evaluat* or monitor*)):ti,ab,kw 1978

#3 (behavio* near/2 (contracting or modification or modify*)):ti,ab,kw 1490

#4 reinforc*:ti,kw 2608

#5 (reinforce or reinforcer or reinforcement or reinforcements or re-inforcement or re-inforcements):ab 3988

#6 (reinforc* near/3 (behavio* or environment* or experience*)):ti,ab,kw 356

#7 (reinforc* near/1 (positive or contingent)):ti,ab,kw 319

#8 (activit* near/2 schedul*):ti,ab,kw 190

#9 ((pleas* or enjoy* or reward*) near/4 (activit* or event*)):ti,ab,kw 702

#10 ((operant or instrumental) NEXT (conditioning or learning)):ti,ab,kw 193

#11 ("positive interaction" or "positive interactions" or "avoidance coping" or "environmental contingency" or "environmental contingencies" or "contingency management"):ti,ab,kw 938

#12 "functional analysis":ti,ab,kw 204

#13 ((gain* or reapprais*) near/2 focus*):ti,ab,kw 44

#14 ((psychoeducat* or psycho-educat*) and (behavi* or coping or (self and manage))):ti,ab,kw 2168

#15 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 13058

#16 MeSH descriptor: [Depression] this term only 10565

#17 MeSH descriptor: [Depressive Disorder] this term only 6862

#18 MeSH descriptor: [Depressive Disorder, Major] this term only 4338

#19 (depressi* or depressed):ti 27584

#20 (depress* near/3 (acute or clinical* or diagnos* or disorder* or major or unipolar or illness or scale* or score* or adult* or patient* or participant* or people or inpatient* or outpatient*)):ab 32686

#21 (depress* near/3 ("in-patient*" or "out-patient*")):ab 54

#22 (depress* and (Beck* or BDI* or DSM* or (Statistical Manual near/2 Mental Disorders) or Hamilton or HAM-D or HAMD or MADRS or (International Classification near/2 Disease*) or ICD-10 or ICD-9)):ab 15159

#23 ("with depression" or "with depressive"):ab 3716

#24 #16 or #17 or #18 or #19 or #20 or #21 or #21 or #22 or #23 50806

#25 #15 and #24 1795

#26 MeSH descriptor: [Behavior Therapy] this term only 4354

#27 (behavio* next (counsel* or intervention or train* or treatment or therapy or psychotherapy)):ti,ab,kw 25050

#28 #26 or #27 25050

#29 #24 and #28 5948

#30 #25 or #29 6963

#31 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] this term only 4575

#32 MeSH descriptor: [Bronchitis, Chronic] this term only 148

#33 MeSH descriptor: [Pulmonary Emphysema] this term only 266

#34 MeSH descriptor: [Lung Diseases, Obstructive] this term only 2532

#35 MeSH descriptor: [Asthma] explode all trees 11043

#36 MeSH descriptor: [Respiratory Hypersensitivity] explode all trees 13717

#37 MeSH descriptor: [Hypertension, Pulmonary] this term only 867

#38 asthma*:ti,ab,kw 32702

#39 ((long-term or longterm or chronic*) near/5 (bronchitis or respirat*)):ti,ab,kw 4205

#40 emphysema*:ti,ab,kw 1435

#41 (obstruct* near/3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)):ti,ab,kw 18195

#42 (("hyper responsiveness" or hyper-responsiveness or allergy or allergi* or hypersensitiv*) near/5 (airway* or respirat*)):ti,ab,kw 1385

#43 ((long-term or longterm or "long term" or Chronic* or occupational) near/2 lung* near/5 (condition* or disease* or symptom* or problem* or failure*)):ti,ab,kw 7277

#44 (respirat* near/2 (condition* or disease* or symptom* or problem*)):ti,ab,kw 8212

#45 ("pulmonary hypertension"):ti,ab,kw 2830

#46 (COPD or COAD or COBD or AECB):ti,ab,kw 15065

#47 #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 66364

#48 MeSH descriptor: [Diabetes Mellitus] explode all trees 27785

#49 MeSH descriptor: [Glucose Tolerance Test] this term only 1966

#50 MeSH descriptor: [Glycated Hemoglobin A] this term only 5423

#51 diabet*:ti,ab,kw 85787

#52 (noninsulin* or "non*insulin*" or "non*insulin*" AND depend*):ti,ab,kw 15762

#53 ("fasting glucose" or "plasma glucose" or "glucose tolerance test" or "glucose tolerance tests" or "glucose tolerance testing" or (glyc*emic near/2 control*)):ti,ab,kw 25536

#54 (HbA1c or A1C or A1c or Hb1c or ((glycated or glycosylated) near h*emoglobin*)):ti,ab,kw 24356

#55 (NIDDM or T2D or T2DM):ti,ab,kw 8929

#56 #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 93958

#57 MeSH descriptor: [Diabetes Insipidus] explode all trees 62

#58 "diabetes insipidus":ti,ab,kw 141

#59 #57 or #58 142

#60 #54 not #58 24356

#61 MeSH descriptor: [Cardiovascular Diseases] explode all trees 98577

#62 (cardio* or cardia* or CVD):ti,ab,kw 137734

#63 (heart* or coronary*):ti,ab,kw 163233

#64 (angina* or ventric*):ti,ab,kw 42095

#65 (myocard* or pericard*):ti,ab,kw 43303

#66 (isch*em* or cerebrovasc*):ti,ab,kw 56095

#67 MeSH descriptor: [Stroke] explode all trees 8541

#68 (stroke or strokes or poststroke):ti,ab,kw 52250

#69 apoplexy:ti,ab,kw 325

#70 (brain near/2 accident*):ti,ab,kw 215

#71 ((brain* or cerebral or lacunar) near/2 infarct*):ti,ab,kw 4674

#72 MeSH descriptor: [Hypertension] explode all trees 16863

#73 (hypertensi* or hyperlip*):ti,ab,kw 67411

#74 (hypercholester* or hypertriglycerid*):ti,ab,kw 9436

#75 MeSH descriptor: [Arteriosclerosis] explode all trees 9205

#76 (arteriosclero* or atherosclero* or "peripheral arter* disease*"):ti,ab,kw 12614

#77 MeSH descriptor: [Cholesterol] explode all trees 9952

#78 cholesterol:ti,ab,kw 34711

#79 MeSH descriptor: [Blood Pressure] this term only 26032

#80 "blood pressure":ti,ab,kw 84592

#81 (emboli* or arrhythmi*):ti,ab,kw 21574

#82 (thrombo* or "atrial fibrillation"):ti,ab,kw 58813

#83 (tachycardi* or endocardi* or "sick sinus"):ti,ab,kw 9537

#84 #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 386929

#85 MeSH descriptor: [Neoplasms] explode all trees 71857

#86 (cancer* or neoplas* or tumo* or carcinoma* or hodgkin* or nonhodgkin* or adenocarcinoma* or leuk*emia* or metasta* or malignan* or lymphoma* or sarcoma* or melanoma* or myeloma* or oncolog* or psychooncology or psycho-oncology):ti,ab,kw 222547

#87 #85 or #86 225813

#88 #47 or #60 or #84 or #87 640341

#89 #30 and #88 1007

990 trials in CENTRAL

DART-Europe E-theses Portal (www.dart-europe.eu/)

25/09/2019

*really hard to search- the 'refine' option doesn't work. I can only do a search in 1 line that works properly.

"behavioural activation" OR "behavioral activation" OR "behavior activation" OR "behaviour activation"

29 hits

(behaviour OR behavior) AND therapy AND Depression AND (Trial* OR random* OR RCT OR placebo* OR review*)

56 hits

Embase Classic+Embase 1947 to 2019 September 24

25/09/2019

1 ((behavio* adj1 activat*) or BATD).tw,kw. (2705)

2 behavio*.mp. and (self adj (evaluat* or monitor*)).tw,kw. (4865)

3 (behavio* adj2 (contracting or modification or modify*)).tw,kw. (8869)

4 reinforc*.ti,kw. (21802)

5 (reinforce or reinforcer or reinforcement or reinforcements or re-inforcement or re-inforcements).ab. /freq=2 (12814)

6 (reinforc* adj3 (behavio* or environment* or experience*)).tw,kw. (4620)

7 (reinforc* adj1 (positive or contingent)).tw,kw. (3282)

8 (activit* adj2 schedul*).tw,kw. (775)

9 ((pleas* or enjoy* or reward*) adj4 (activit* or event?)).tw,kw. (4952)

10 ((operant or instrumental) adj (conditioning or learning)).tw,kw. (4383)

11 (positive interaction* or avoida* coping or environmental contingenc* or contingency management).tw,kw. (5673)

12 functional analysis.tw,kw. (28567)

13 ((gain? or reapprais*) adj2 focus*).tw,kw. (182)

14 ((psychoeducat* or psycho-educat*) and (behavi* or coping or self manag*)).ti,ab,kw. (4345)

15 or/1-14 [Behavioural Activation] (95541)

16 exp depression/ (462857)

17 (depressi* or depressed).tw,kw. (604971)

18 dysthymi*.tw,kw. (4289)

19 distress*.ti,kw. (44962)

20 (mood? or mental health).tw,kw. (277403)

21 ((emotion* or psychological) adj (trauma* or distress*)).tw,kw. (34773)

22 "common mental disorder*".tw,kw. (2757)

23 or/16-22 [Depression - Cochrane terms] (980385)

24 15 and 23 [BA and Depression] (8762)

25 behavior therapy/ (43569)

26 (behavio* adj (counsel* or intervention or train* or treatment or therapy or psychotherapy)).tw,kw. (44197)

27 25 or 26 (73524)

28 23 and 27 [Behaviour Therapy and Depression] (21614)

29 24 or 28 [BA or Behaviour Therapy AND Depression] (28601)

30 chronic obstructive lung disease/ (126011)

31 chronic bronchitis/ (14926)

32 exp lung emphysema/ (26142)

33 exp asthma/ (266419)

34 exp respiratory tract allergy/ (305469)

35 pulmonary hypertension/ (82989)

36 asthma*.tw,kw. (234792)

37 ((long-term or longterm or chronic*) adj5 (bronchitis or respirat*)).tw,kw. (41118)

38 emphysema*.tw,kw. (42290)

39 (obstruct* adj3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)).tw,kw. (127460)

40 ((hyper responsiveness or hyper-responsiveness or allergy or allergi* or hypersensitiv*) adj5 (airway? or respirat*)).tw,kw. (19564)

41 ((long-term or longterm or Chronic* or occupational) adj2 lung* adj5 (condition* or disease* or symptom* or problem* or failure*)).tw,kw. (22365)

42 (respirat* adj2 (condition* or disease* or symptom* or problem*)).tw,kw. (83660)

43 pulmonary hypertension.tw,kw. (60555)

44 (COPD or COAD or COBD or AECB).tw,kw. (83692)

45 or/30-44 [Chronic Respiratory Diseases] (700497)

46 exp diabetes mellitus/ (960552)

47 exp glucose tolerance test/ (64609)

48 exp glycosylated hemoglobin/ (118751)

49 diabet*.tw,kw. (941196)

50 (noninsulin*-depend* or non-insulin*-depend* or noninsulin*depend* or non-insulin*depend*).tw,kw. (14890)

51 (fasting glucose or plasma glucose or glucose tolerance test* or (glyc?emic adj2 control*)).tw,kw. (145120)

52 (HbA1c or A1C or A1c or Hb1c or ((glycated or glycosylated) adj h?emoglobin?)).tw,kw. (98665)

53 (NIDDM or T2D or T2DM).tw,kw. (85587)

54 or/46-53 (1196262)

55 exp diabetes insipidus/ (16453)

56 diabet* insipidus.tw,kw. (12361)

57 55 or 56 (18000)

58 54 not 57 [Diabetes] (1182119)

59 exp cardiovascular disease/ (4289589)

60 (cardio* or cardia* OR cvd).tw,kw. (1761464)

61 (heart* or coronary*).tw,kw. (1618428)

62 (angina* or ventric*).tw,kw. (680155)

63 (myocard* or pericard*).tw,kw. (614219)

64 (isch?em* or cerebrovasc*).tw,kw. (623781)

65 exp cerebrovascular accident/ (201090)

66 (stroke or strokes or poststroke).tw,kw. (387374)

67 apoplexy.tw,kw. (4279)

68 (brain adj2 accident*).tw,kw. (257)

69 ((brain* or cerebral or lacunar) adj2 infarct*).tw,kw. (40499)

70 elevated blood pressure/ or exp hypertension/ or exp blood pressure/ (1170153)

71 blood pressure.tw,kw. (438440)

72 (hypertensi* or hyperlip*).tw,kw. (719324)

73 (hypercholester* or hypertriglycerid*).tw,kw. (68908)

74 exp arteriosclerosis/ (267676)

75 exp cholesterol/ (325632)

76 (cholesterol or arteriosclero* or atherosclero* or peripheral arter* disease*).tw,kw. (330448)

77 (emboli* or arrhythmi*).tw,kw. (333497)

78 (thrombo* or "atrial fibrillat*").tw,kw. (657257)

79 (tachycardi* or endocardi* or "sick sinus").tw,kw. (166058)

80 or/59-79 [CVD] (6028103)

81 exp neoplasm/ (4693885)

82 (cancer* or neoplas* or tumo* or carcinoma* or hodgkin* or nonhodgkin* or adenocarcinoma* or leuk?emia* or metasta* or malignan* or lymphoma* or sarcoma* or melanoma* or myeloma* or oncolog* or psychoongology or psycho-oncology).tw,kw. (5006829)

83 81 or 82 [Cancer] (5875965)

84 45 or 58 or 80 or 83 [COPD Diabetes CVD or Cancer] (12099598)

85 exp randomized controlled trial/ (576165)

86 exp double-blind procedure/ (169084)

87 exp single-blind procedure/ (36791)

88 exp crossover-procedure/ (61344)

89 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw. (236321)

90 placebo/ (353710)

91 placebo*.tw. (303376)

92 randomization/ (84704)

93 trial.ti. (290797)

94 clinical trial*.tw. (497341)

95 (randomly or randomis* or randomiz*).tw,kw. (1206723)

96 controlled clinical trial/ (465844)

97 or/85-96 [RCT or CCT] (2106740)

98 exp animals/ not exp humans/ (5315473)

99 exp nonhuman/ not exp human/ (4490184)

100 exp experimental animal/ (673589)

101 exp veterinary medicine/ (45399)

102 animal experiment/ (2442893)

103 or/98-102 [Animal studies] (7516518)

104 97 not 103 [Final RCT search] (1874512)

105 29 and 84 and 104 [BA or Behaviour therapy and CMDs and COPD Diabetes CVD and RCTs] (1984)

106 29 and 84 (4855)

107 limit 106 to (meta analysis or "systematic review") (363)

108 ((systematic adj2 review*) or scoping review* or synthesis or meta-analys* or "meta analysis").ti. (623967)

109 106 and 108 (157)

110 ("Search filter*" or "search strateg*" or "literature search*").ab. (75378)

111 106 and 110 (57)

112 107 or 109 or 111 (417)

113 105 or 112 [BA or Behaviour Therapy and CMDs and COPD Diabetes CVD and RCTs OR systematic reviews] (2165)

114 exp juvenile/ not exp adult/ (2455191)

115 113 not 114 (2045)

EThOS - the British Libraries e-theses online service (ethos.bl.uk/) – Advanced search]

25/09/2019

6 separate searches to run then combine results, remove duplicates…

Search 1

"behavioural activation" Any word

OR

"behaviour therapy" Title

AND

Depression

AND

Trial

16 hits

Search 2

"behavioural activation" Any word

OR

"behaviour therapy" Title

AND

Depression

AND

RCT

7 hits

Search 3

"behavioural activation" Any word

OR

"behaviour therapy" Title

AND

Depression

AND

Randomised

14 hits

Search 4

"behavioural activation" Any word

OR

"behaviour therapy" Title

AND

Depression

AND

“Systematic Review”

9 hits

Search 5

"behavioural activation" Any word

OR

"behaviour therapy" Title

AND

Depression

AND

Meta-analysis

6 hits

Global Health 1910 to 2019 Week 36

25/09/2019

1 ((behavio* adj1 activat*) or BATD).tw,id. (106)

2 behavio*.mp. and (self adj (evaluat* or monitor*)).tw,id. (668)

3 (behavio* adj2 (contracting or modification or modify*)).tw,id. (2946)

4 reinforc*.ti,id. (733)

5 (reinforce or reinforcer or reinforcement or reinforcements or re-inforcement or re-inforcements).ab. /freq=2 (554)

6 (reinforc* adj3 (behavio* or environment* or experience*)).tw,id. (349)

7 (reinforc* adj1 (positive or contingent)).tw,id. (195)

8 (activit* adj2 schedul*).tw,id. (75)

9 ((pleas* or enjoy* or reward*) adj4 (activit* or event?)).tw,id. (441)

10 ((operant or instrumental) adj (conditioning or learning)).tw,id. (119)

11 (positive interaction* or avoida* coping or environmental contingenc* or contingency management).tw,id. (618)

12 functional analysis.tw,id. (1585)

13 ((gain? or reapprais*) adj2 focus*).tw,id. (28)

14 ((psychoeducat* or psycho-educat*) and (behavi* or coping or self manag*)).ti,ab,id. (185)

15 or/1-14 [Behavioural Activation] (8115)

16 depression/ (20888)

17 (depressi* or depressed).tw,id. (49196)

18 dysthymi*.tw,id. (202)

19 distress*.tw,id. (13076)

20 (mood? or mental health or ((emotion* or psychological) adj trauma*)).tw,id. (32705)

21 "common mental disorder*".tw,id. (660)

22 or/16-21 [Depression] (82061)

23 15 and 22 [BA and Depression] (560)

24 psychotherapy/ (1351)

25 (behavio* adj (counsel* or intervention or train* or treatment or therapy or psychotherapy)).tw,id. (4535)

26 24 or 25 [Behaviour therapy] (5449)

27 22 and 26 [Behaviour Therapy and Depression] (1085)

28 23 or 27 [BA or Behaviour Therapy AND Depression] (1557)

29 respiratory diseases/ or allergic bronchopulmonary aspergillosis/ or asthma/ or bronchitis/ or chronic obstructive pulmonary disease/ or pulmonary emphysema/ (85849)

30 asthma*.tw,id. (29430)

31 ((long-term or longterm or chronic*) adj5 (bronchitis or respirat*)).tw,id. (5484)

32 emphysema*.tw,id. (2674)

33 (obstruct* adj3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)).tw,id. (10440)

34 ((hyper responsiveness or hyper-responsiveness or allergy or allergi* or hypersensitiv*) adj5 (airway? or respiratory)).tw,id. (5594)

35 ((long-term or longterm or Chronic* or occupational) adj2 lung* adj5 (condition* or disease* or symptom* or problem* or failure*)).tw,id. (1991)

36 (respiratory adj2 (condition* or disease* or symptom* or problem*)).tw,id. (72584)

37 pulmonary hypertension.tw,id. (1285)

38 (COPD or COAD or COBD or AECB).tw,id. (5071)

39 or/29-38 [Chronic Respiratory Diseases] (102992)

40 diabetes/ or diabetes mellitus/ or glucose tolerance test/ (84582)

41 diabetes/ or diabetes mellitus/ (83522)

42 glucose tolerance test/ (1958)

43 blood sugar/ (47205)

44 diabet*.tw,id. (130275)

45 (noninsulin*-depend* or non-insulin*-depend* or noninsulin*depend* or non-insulin*depend*).tw,id. (2029)

46 (fasting glucose or plasma glucose or glucose tolerance test* or (glyc?emic adj2 control*)).tw,id. (26556)

47 (HbA1c or A1C or A1c or Hb1c or ((glycated or glycosylated) adj h?emoglobin?)).tw,id. (10369)

48 (NIDDM or T2D or T2DM).tw,id. (9180)

49 or/40-48 [Diabetes] (156940)

50 exp cardiovascular diseases/ (121130)

51 (cardio* or cardia* or cvd).tw,id. (133892)

52 (heart* or coronary*).tw,id. (117744)

53 (angina* or ventric*).tw,id. (17400)

54 (myocard* or pericard*).tw,id. (31877)

55 (isch?em* or cerebrovasc*).tw,id. (26569)

56 exp stroke/ (11434)

57 (stroke or strokes or poststroke).tw,id. (18935)

58 apoplexy.tw,id. (166)

59 (brain adj2 accident*).tw,id. (5)

60 ((brain* or cerebral or lacunar) adj2 infarct*).tw,id. (2156)

61 exp hypertension/ (40299)

62 (hypertensi* or hyperlip*).tw,id. (67458)

63 (hypercholester* or hypertriglycerid*).tw,id. (15474)

64 exp atherosclerosis/ (18021)

65 cholesterol/ (62723)

66 (cholesterol or arteriosclero* or atherosclero* or peripheral arter* disease*).tw,id. (90502)

67 blood pressure/ (36160)

68 blood pressure.tw,id. (69564)

69 (emboli* or arrhythmi*).tw,id. (8651)

70 (thrombo* or "atrial fibrillat*").tw,id. (30155)

71 (tachycardi* or endocardi* or "sick sinus").tw,id. (10719)

72 or/50-71 [CVD] (360573)

73 exp neoplasms/ (225495)

74 (cancer* or neoplas* or tumo* or carcinoma* or hodgkin* or nonhodgkin* or adenocarcinoma* or leuk?emia* or metasta* or malignan* or lymphoma* or sarcoma* or melanoma* or myeloma* or oncolog* or psychoongology or psycho-oncology).tw,id. (435173)

75 73 or 74 [Cancer] (437583)

76 39 or 49 or 72 or 75 [COPD Diabetes CVD or Cancer] (916371)

77 clinical trials/ or randomized controlled trials/ (54715)

78 placebos/ (2370)

79 trial.ti. (32112)

80 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw. (26857)

81 placebo*.tw. (35290)

82 (random* not (random sampl* or random digit* or random effect* or random survey or random regression)).tw. (183238)

83 or/77-82 [RCT] (215375)

84 28 and 76 and 83 [BA or Behaviour therapy and CMDs and COPD Diabetes CVD and RCTs] (93)

85 ((systematic adj2 review*) or scoping review* or synthesis or meta-analys* or "meta analysis").ti. (54215)

86 ("Search filter*" or "search strateg*" or "literature search*").ab. (8107)

87 85 or 86 (58255)

88 28 and 76 and 87 [Systematic Reviews] (8)

89 84 or 88 [BA or Behaviour Therapy and CMDs and COPD Diabetes CVD and RCTs OR systematic reviews] (98)

Global Index Medicus

25/09/2019

(behavio* AND (activat* OR activity OR "self evaluation" OR "self monitor*" OR modification OR modify* OR contracting OR reinforc* OR psycho-education OR psychoeduction)) OR ("behavio* therapy") [in Title, abstract, subject]

AND

trial or trials or placebo* or rct or random* or review* or overview or meta-analysis [in Title, abstract, subject]

AND

diabet* OR cancer* or neoplas* OR tumor* OR tumour* OR asthma* OR stroke or hypertensi* OR CVD or cardio* OR cardia* OR heart* OR coronary* OR angina* OR ventric* OR myocard* OR ischemi* OR r ischaemi* OR cerebrovasc OR COPD OR pulmonary OR lung* OR bronch* OR respirat* [in Title, abstract, subject]

AND

depress* or "low mood*" or dysthymi* [in Title, abstract, subject]

115 hits

WPRIM (Western Pacific) (63)

LILACS (Americas) (35)

IMEMR (Eastern Mediterranean) (15)

IMSEAR (South-EastAsia) (2)

IRIS (WHO) – Use Advanced Filters mode.

25/09/2019

apps.who.int/iris/discover?query=trial+or+trials+or+rct+or+random+or+randomised+or+randomized+or+randomly

All of IRIS: trial or trials or rct or random or randomised or randomized or randomly

AND

Subject: Depression

AND

Subject: Behavior or behaviour or behavioral or behavioural

0 hits

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to September 23, 2019

25/09/2019

1 ((behavio* adj1 activat*) or BATD).tw,kf. (2217)

2 behavio*.mp. and (self adj (evaluat* or monitor*)).tw,kf. (3556)

3 (behavio* adj2 (contracting or modification or modify*)).tw,kf. (6565)

4 reinforc*.ti,kf. (19262)

5 (reinforce or reinforcer or reinforcement or reinforcements or re-inforcement or re-inforcements).ab. /freq=2 (11015)

6 (reinforc* adj3 (behavio* or environment* or experience*)).tw,kf. (3798)

7 (reinforc* adj1 (positive or contingent)).tw,kf. (2505)

8 (activit* adj2 schedul*).tw,kf. (530)

9 ((pleas* or enjoy* or reward*) adj4 (activit* or event?)).tw,kf. (3574)

10 ((operant or instrumental) adj (conditioning or learning)).tw,kf. (3244)

11 (positive interaction* or avoida* coping or environmental contingenc* or contingency management).tw,kf. (4534)

12 functional analysis.tw,kf. (22895)

13 ((gain? or reapprais*) adj2 focus*).tw,kf. (158)

14 ((psychoeducat* or psycho-educat*) and (behavi* or coping or self manag*)).ti,ab,kf. (2601)

15 or/1-14 [Behavioural Activation] (76489)

16 Depression/ (111569)

17 exp depressive disorder/ (105157)

18 (depressi* or depressed).tw,kf. (421697)

19 dysthymi*.tw,kf. (3109)

20 distress*.tw,kf. (116243)

21 (mood? or mental health or ((emotion* or psychological) adj trauma*)).tw,kf. (207320)

22 "common mental disorder*".tw,kf. (2311)

23 or/16-22 [Depression - Cochrane terms] (694602)

24 15 and 23 [BA and Depression] (5868)

25 Behavior Therapy/ (27103)

26 (behavio* adj (counsel* or intervention or train* or treatment or therapy or psychotherapy)).tw,kf. (29894)

27 25 or 26 [Behaviour therapy] (51473)

28 23 and 27 [Behaviour Therapy and Depression] (12629)

29 24 or 28 [BA or Behaviour Therapy AND Depression] (17366)

30 Pulmonary disease, chronic obstructive/ (36943)

31 Bronchitis, chronic/ or Pulmonary emphysema/ (17095)

32 Lung diseases, obstructive/ (18142)

33 exp Asthma/ (124320)

34 exp Respiratory Hypersensitivity/ (150812)

35 Hypertension, Pulmonary/ (33256)

36 asthma*.tw,kf. (153407)

37 ((long-term or longterm or chronic*) adj5 (bronchitis or respirat*)).tw,kf. (25995)

38 emphysema*.tw,kf. (26832)

39 (obstruct* adj3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)).tw,kf. (83455)

40 ((hyper responsiveness or hyper-responsiveness or allergy or allergi* or hypersensitiv*) adj5 (airway? or respirat*)).tw,kf. (12659)

41 ((long-term or longterm or Chronic* or occupational) adj2 lung* adj5 (condition* or disease* or symptom* or problem* or failure*)).tw,kf. (14417)

42 (respirat* adj2 (condition* or disease* or symptom* or problem*)).tw,kf. (56825)

43 pulmonary hypertension.tw,kf. (34943)

44 (COPD or COAD or COBD or AECB).tw,kf. (43789)

45 or/30-44 [Chronic Respiratory Diseases] (409808)

46 exp Diabetes mellitus/ (407656)

47 Glucose Tolerance Test/ (33774)

48 Glycated Hemoglobin A/ (33142)

49 diabet*.tw,kf. (601034)

50 (noninsulin*-depend* or non-insulin*-depend* or noninsulin*depend* or non-insulin*depend*).tw,kf. (12152)

51 (fasting glucose or plasma glucose or glucose tolerance test* or (glyc?emic adj2 control*)).tw,kf. (92016)

52 (HbA1c or A1C or A1c or Hb1c or ((glycated or glycosylated) adj h?emoglobin?)).tw,kf. (50626)

53 (NIDDM or T2D or T2DM).tw,kf. (48996)

54 or/46-53 (698768)

55 exp Diabetes Insipidus/ (7771)

56 diabet* insipidus.tw,kf. (8651)

57 55 or 56 (10648)

58 54 not 57 [Diabetes] (689642)

59 exp Cardiovascular Diseases/ (2304392)

60 (cardio* or cardia* or cvd).tw,kf. (1148831)

61 (heart* or coronary*).tw,kf. (1096235)

62 (angina* or ventric*).tw,kf. (443815)

63 (myocard* or pericard*).tw,kf. (412274)

64 (isch?em* or cerebrovasc*).tw,kf. (407127)

65 exp Stroke/ (125438)

66 (stroke or strokes or poststroke).tw,kf. (235050)

67 apoplexy.tw,kf. (3021)

68 (brain adj2 accident*).tw,kf. (161)

69 ((brain* or cerebral or lacunar) adj2 infarct*).tw,kf. (25996)

70 exp Hypertension/ (247564)

71 (hypertensi* or hyperlip*).tw,kf. (449183)

72 (hypercholester* or hypertriglycerid*).tw,kf. (46305)

73 exp Arteriosclerosis/ (170257)

74 exp Cholesterol/ (156627)

75 (cholesterol or arteriosclero* or atherosclero* or peripheral arter* disease*).tw,kf. (235241)

76 Blood Pressure/ (269165)

77 blood pressure.tw,kf. (293222)

78 (emboli* or arrhythmi*).tw,kf. (212813)

79 (thrombo* or "atrial fibrillat*").tw,kf. (414307)

80 (tachycardi* or endocardi* or "sick sinus").tw,kf. (108374)

81 or/59-80 [CVD] (3931951)

82 exp Neoplasms/ (3218192)

83 (cancer* or neoplas* or tumo* or carcinoma* or hodgkin* or nonhodgkin* or adenocarcinoma* or leuk?emia* or metasta* or malignan* or lymphoma* or sarcoma* or melanoma* or myeloma* or oncolog* or psychoongology or psycho-oncology).tw,kf. (3581527)

84 82 or 83 [Cancer] (4249796)

85 45 or 58 or 81 or 84 [COPD Diabetes CVD or Cancer] (8430805)

86 randomized controlled trial.pt. (489727)

87 controlled clinical trial.pt. (93263)

88 randomized.ab. (454879)

89 placebo.ab. (200744)

90 clinical trials as topic.sh. (188454)

91 randomly.ab. (318349)

92 trial.ti. (204932)

93 86 or 87 or 88 or 89 or 90 or 91 or 92 (1239133)

94 exp animals/ not humans.sh. (4617436)

95 93 not 94 (1139614)

96 29 and 85 and 95 [BA or Behaviour therapy and CMDs and COPD Diabetes CVD and RCTs] (867)

97 29 and 85 (2140)

98 limit 97 to "systematic review" (82)

99 96 or 98 [BA or Behaviour Therapy and CMDs and COPD Diabetes CVD and RCTs OR systematic reviews] (917)

100 (exp Child/ or Adolescent/ or exp Infant/) not exp Adult/ (1821899)

101 99 not 100 (869)

Open Grey (www.opengrey.eu/)

25/09/2019

(behavio* NEAR/5 (activation OR activity OR therapy OR "self evaluation" OR "self monitor*" OR modification OR modify* OR contracting OR reinforc* OR psycho-education OR psychoeducation)) AND depression AND (trial OR trial OR trials OR placebo* OR rct OR random* OR review* OR overview OR meta-analysis)

23 hits

Open Access Theses and Dissertations (oatd.org)

25/09/2019

Unable to run a simple search for ‘depression’ in this database without it timing out (tried in Google Chrome and Explorer)

ProQuest Dissertations & Theses

25/09/2019

S1 noft("clinical trial*" or "controlled trial*" or random* or "single blind*" or "double blind*" or "research design" or "comparative stud*" or "evaluation stud*" or "follow-up stud*" or "prospective stud*") 217416

S2 noft(cardio* or cardia* or heart* or coronary* or angina* or ventric* or myocard* or pericard*) OR noft(ischemi* or ischaemi* or cerebrovasc* or stroke or strokes or apoplexy) OR noft((brain n/2 accident)) OR noft(((brain* or cerebral or lacunar) n/2 infarct*)) OR noft(hypertensi* or hyperlip* or hypercholester* or hypertriglycerid* or cholesterol or "blood pressure") OR noft(emboli* or arrhythmi* or thrombo* or "atrial fibrillat*" or tachycardi* or endocardi* or "sick sinus") 114420

S3 noft(cancer* or neoplas* or tumo* or carcinoma* or hodgkin* or nonhodgkin* or adenocarcinoma* or leukemia* or leukaemia* or metasta*) OR noft(malignan* or lymphoma* or sarcoma* or melanoma* or myeloma* or oncolog*) OR noft(diabet* or asthma or emphysema* or COPD) OR noft((obstruct* n/3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*))) OR noft(((hyper* or allerg*) n/5 (airway* or respiratory))) OR noft((long-term or longterm or Chronic* or occupational) n/2 (bronchitis or respirat* or lung*)) OR noft((respiratory n/2 (condition* or disease* or symptom* or problem*))) OR noft("pulmonary hypertension") 156037

S4 S2 OR S3 256439

S5 noft(((behavio* n/1 activat*) or BATD)) OR noft(behavio* and self and (evaluat* or monitor*)) OR noft(reinforc*) OR noft((activit* n/2 schedul*)) OR noft(((pleas* or enjoy* or reward*) n/4 (activit* or event*))) OR noft(((operant or instrumental) n/1 (conditioning or learning))) OR noft(("positive interaction" OR "positive interactions") or "avoida* coping" or "functional analysis") OR noft(((gain* or reapprais*)

n/2 focus)) OR noft((psychoeducat* or psycho-educat*) and (behavi* or coping or self manag*)) OR noft("environmental contingenc*" or "contingency management") 86000

S6 noft(behavio* n/1 (counsel* or intervention or train* or treatment or therapy or psychotherapy)) 11146

S7 s5 or s6 94997

S8 noft(depressi* or depressed or dysthymi* or distress* or trauma* or mood*) OR noft("mental health" or "common mental disorder*") 141230

S9 S7 AND S8 AND S1 AND S4 205

PsycINFO 1806 to September Week 2 2019

25/09/2019

1 ((behavio* adj1 activat*) or BATD).tw,id. (2286)

2 behavio*.mp. and (self adj (evaluat* or monitor*)).tw,id. (5812)

3 (behavio* adj2 (contracting or modification or modify*)).tw,id. (8179)

4 reinforc*.ti,id. (26727)

5 (reinforce or reinforcer or reinforcement or reinforcements or re-inforcement or re-inforcements).ab. /freq=2 (15839)

6 (reinforc* adj3 (behavio* or environment* or experience*)).tw,id. (6747)

7 (reinforc* adj1 (positive or contingent)).tw,id. (4594)

8 (activit* adj2 schedul*).tw,id. (587)

9 ((pleas* or enjoy* or reward*) adj4 (activit* or event?)).tw,id. (4210)

10 ((operant or instrumental) adj (conditioning or learning)).tw,id. (5971)

11 (positive interaction* or avoida* coping or environmental contingenc* or contingency management).tw,id. (5673)

12 functional analysis.tw,id. (3141)

13 ((gain? or reapprais*) adj2 focus*).tw,id. (127)

14 ((psychoeducat* or psycho-educat*) and (behavi* or coping or self manag*)).ti,ab,id. (4695)

15 behavioral activation system/ (346)

16 or/1-15 [Behavioural Activation] (72175)

17 exp major depression/ (124956)

18 "depression (emotion)"/ (25075)

19 (depressi* or depressed).tw,id. (293646)

20 dysthymi*.tw,id. (3861)

21 distress*.tw,id. (70073)

22 (mood? or mental health or ((emotion* or psychological) adj trauma*)).tw,id. (249686)

23 "common mental disorder*".tw,id. (1760)

24 or/17-23 [Depression - Cochrane terms] (527922)

25 16 and 24 [BA and Depression] (8228)

26 behavior therapy/ (13633)

27 (behavio* adj (counsel* or intervention or train* or treatment or therapy or psychotherapy)).tw,id. (45892)

28 26 or 27 [Behaviour therapy] (51482)

29 24 and 28 [Behaviour Therapy and Depression] (15673)

30 25 or 29 [BA or Behaviour Therapy AND Depression] (22301)

31 chronic obstructive pulmonary disease/ (1123)

32 bronchial disorders/ or pulmonary emphysema/ (220)

33 asthma/ (4549)

34 lung disorders/ (1658)

35 asthma*.tw,id. (7664)

36 ((long-term or longterm or chronic*) adj5 (bronchitis or respirat*)).tw,id. (675)

37 emphysema*.tw,id. (251)

38 (obstruct* adj3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)).tw,id. (2746)

39 ((hyper responsiveness or hyper-responsiveness or allergy or allergi* or hypersensitiv*) adj5 (airway? or respirat*)).tw,id. (144)

40 ((long-term or longterm or Chronic* or occupational) adj2 lung* adj5 (condition* or disease* or symptom* or problem* or failure*)).tw,id. (385)

41 (respirat* adj2 (condition* or disease* or symptom* or problem*)).tw,id. (2102)

42 pulmonary hypertension.tw,id. (188)

43 (COPD or COAD or COBD or AECB).tw,id. (1534)

44 or/31-43 [Chronic Respiratory Diseases] (13524)

45 diabetes mellitus/ or exp type 2 diabetes/ (7872)

46 diabet*.tw,id. (30243)

47 (noninsulin*-depend* or non-insulin*-depend* or noninsulin*depend* or non-insulin*depend*).tw,id. (284)

48 (fasting glucose or plasma glucose or glucose tolerance test* or (glyc?emic adj2 control*)).tw,id. (3844)

49 (HbA1c or A1C or A1c or Hb1c or ((glycated or glycosylated) adj h?emoglobin?)).tw,id. (2901)

50 (NIDDM or T2D or T2DM).tw,id. (2051)

51 or/45-50 [Diabetes] (32309)

52 exp cardiovascular disorders/ (59835)

53 (cardio* or cardia* or cvd).tw,id. (49352)

54 (heart* or coronary*).tw,id. (62799)

55 (angina* or ventric*).tw,id. (10534)

56 (myocard* or pericard*).tw,id. (5852)

57 (isch?em* or cerebrovasc*).tw,id. (23405)

58 cerebrovascular accidents/ or exp cerebral ischemia/ (23090)

59 (stroke or strokes or poststroke).tw,id. (33557)

60 apoplexy.tw,id. (146)

61 (brain adj2 accident*).tw,id. (68)

62 ((brain* or cerebral or lacunar) adj2 infarct*).tw,id. (2733)

63 exp hypertension/ (6968)

64 (hypertensi* or hyperlip*).tw,id. (17842)

65 (hypercholester* or hypertriglycerid*).tw,id. (1093)

66 arteriosclerosis/ (121)

67 cholesterol/ (2100)

68 (cholesterol or arteriosclero* or atherosclero* or peripheral arter* disease*).tw,id. (7869)

69 exp blood pressure disorders/ (7952)

70 blood pressure.tw,id. (19309)

71 (emboli* or arrhythmi*).tw,id. (4531)

72 (thrombo* or "atrial fibrillat*").tw,id. (5145)

73 (tachycardi* or endocardi* or "sick sinus").tw,id. (1694)

74 or/52-73 [CVD] (171715)

75 exp neoplasms/ (49460)

76 (cancer* or neoplas* or tumo* or carcinoma* or hodgkin* or nonhodgkin* or adenocarcinoma* or leuk?emia* or metasta* or malignan* or lymphoma* or sarcoma* or melanoma* or myeloma* or oncolog* or psychoongology or psycho-oncology).tw,id. (82444)

77 75 or 76 [Cancer] (83722)

78 44 or 51 or 74 or 77 [COPD Diabetes CVD or Cancer] (273613)

79 exp clinical trials/ or experimental design/ (22409)

80 exp treatment effectiveness evaluation/ (23866)

81 exp mental health program evaluation/ (2075)

82 exp random sampling/ (824)

83 randomi*.tw. (81401)

84 (clinic* adj4 trial*).tw. (35781)

85 (random* adj5 (assign* or allocat* or assort*)).tw. (42856)

86 (crossover or cross-over).tw. (9898)

87 ((singl* or doubl* or tripl* or trebl*) adj (blind* or mask*)).tw. (25366)

88 exp placebo/ (5351)

89 placebo*.tw. (39516)

90 or/79-89 [Trials] (188622)

91 30 and 78 and 90 [BA or Behaviour therapy and CMDs and COPD Diabetes CVD and RCTs] (468)

92 30 and 78 (1558)

93 limit 92 to ("0830 systematic review" or 1200 meta analysis or 1300 metasynthesis) (58)

94 ((systematic adj2 review*) or scoping review* or synthesis or meta-analys* or "meta analysis").ti. (37108)

95 92 and 94 (44)

96 ("Search filter*" or "search strateg*" or "literature search*").ab. (9274)

97 92 and 96 (13)

98 91 or 93 or 95 or 97 [BA or Behaviour Therapy and CMDs and COPD Diabetes CVD and RCTs OR systematic reviews] (498)

99 ((child* or adolescen*) not adult*).ag. (492563)

100 98 not 99 (483)

World Health Organization trials portal (ICTRP)

25/09/2019

Title: diabet* OR cancer* or neoplas* OR tumor* OR tumour* OR asthma* OR stroke or hypertensi* OR CVD or cardio* OR cardia* OR heart* OR coronary* OR angina* OR ventric* OR myocard* OR ischemi* OR r ischaemi* OR cerebrovasc OR COPD OR pulmonary OR lung* OR bronch* OR respirat*

AND

Condition: Depress*

AND

Intervention: behavio* OR reinforc* OR psycho-education OR psychoeduction

Recruitment status: ALL

302 hits

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HISTORY

Protocol first published: Issue 10, 2019
Review first published: Issue 8, 2020

CONTRIBUTIONS OF AUTHORS

EU and NS conceived the idea for this review.

MP led the adaption of the review protocol (Uphoff 2019) from the protocol of the review 'Behavioural activation therapies for depression in adults' (Uphoff 2020).

EU, MP, DB, DC, PM, MP, and RR participated in screening, data extraction of studies, and risk of bias assessments.

JW designed and performed the searches and revised the 'search strategy' sections of the review.

EU performed the analyses and GRADE assessments.

All authors contributed to the writing of the manuscript.

DECLARATIONS OF INTEREST

EU: none.

MP: none.

CB: none.

DB: none.

RC: leads and has responsibility for Cochrane Common Mental Disorders, which has supported parts of the review process and is largely funded by a grant from the National Institute of Health and Research (NIHR) in the UK.

DC: none.

DE: in his role of Chief Investigator, is responsible for the conduct of the ongoing CHEMIST and MODS trials in which behavioural activation therapies are evaluated. He is the author of several publications reporting on trials of behavioural activation.

EF: co-investigator of "Developing and evaluating an adapted behavioural activation intervention for people with depression and diabetes in South Asia". Funded by the NIHR in the UK; ref. NIHR200806.

PM: none.

MP: none.

RR: none.

JW: none.

NS: co-investigator of "Developing and evaluating an adapted behavioural activation intervention for people with depression and diabetes in South Asia". Funded by the NIHR in the UK; ref. NIHR200806.

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- University of Exeter, UK

External sources

- National Institute for Health Research (NIHR), UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol (Uphoff 2019), we stated that GRADE assessments would be performed by two review authors independently. As this is not a requirement of Cochrane Reviews, we decided instead that one experienced review author would perform the assessments (EU) and other review authors would check. Any disagreements were discussed between the review authors.

We had planned to conduct meta-analyses for our prespecified outcomes, but this was not possible for all, but the treatment efficacy outcome given the small amount of data available from the two included studies. Results were synthesised narratively instead. No subgroup analyses or sensitivity analyses were performed, except for sensitivity analyses exploring the influence of missing data on the results.

One study reported multiple outcome domains of the SF-36 relevant to social adjustment and functioning. Given the importance of the interaction between depression and physical health for the population of this review, we reported the SF-36 physical component.