Behavioural activation for the treatment of unipolar depressive disorders in patients with a chronic physical illness: Protocol for a systematic review and meta-analysis

Lydia Brown,1 Stav Amichai Hillel,2 Richard Gray,3 Steven Chang2

1University of Melbourne

2College of Science, Health & Engineering, La Trobe University

3School of Nursing & Midwifery, La Trobe University

**1. Introduction & Rationale**

Those with a chronic psychical illness are at an elevated risk of suffering from unipolar depressive disorders. Behavioural activation is a promising intervention that has been found to be effective in alleviating symptoms of unipolar depressive disorders in non-medical populations, but to date no study has systematically reviewed the evidence for behavioural activation as a treatment for depressed patients with a co-morbid physical illness.

**2. Research Question**

Is behavioural activation efficacious in the treatment of unipolar depressive disorders in patients with a chronic physical illness?

**P** Patients with unipolar depressive disorder and a chronic physical illness

**I** Behavioural Activation

**C** Ø

**O** Symptom alleviation

**R** Randomised controlled trial

**3. Methodology**

A systematic review of randomised controlled trials with two co-occurring components: (i) behavioural activation as intervention (where behavioural activation includes activity scheduling and self-monitoring as core components following Ekers et al. (2014)); and (ii) an objective measure of a unipolar depressive disorder (symptom severity or diagnostic status measured via the Patient Health Questionnaire (PHQ-9) or a clinician respectively).

The systematic review will follow the PRIMSA guidelines ([Moher, Liberati, Tetzlaff, Altman, & Group, 2009](#_ENREF_4)).

*3.1 Data sources*

The Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Education Resources Information Center (ERIC), Excerpta Medica database (Embase), MEDLINE via Ovid, and PsychInfo via Ovid will be searched for eligible studies. Further, we will supplement these sources by searching on ClinicalTrials.gov for unpublished studies.

*3.2 Eligibility criteria*

*3.2.1 Types of participants*

As study is eligible if its sample:

* is 18+ of any sex;
* has a primary diagnosis of a unipolar depressive disorder and has a chronic physical illness.

A unipolar depressive disorder is any disorder that falls under the rubric ‘depressive disorders’ as in DSM-5 (American Psychiatric Association, 2013). Despite subclinical symptoms of depression being a risk factor for poor patient outcomes, studies that report on subclinical symptoms of depression will not be included in the systematic review, so as to control for heterogeneity of the sample. Accordingly, study samples must minimally either: score 10 > on PHQ-9, or be diagnosed with minor depression >.

*3.2.2 Types of studies*

As study is eligible if it:

* is a randomised controlled trial whose arms (at least two) are behavioural activation delivered via any medium (e.g. individual, group, telephone or online) and any comparator(s);
* provides sufficient statistics (group means and standard deviations) to be included in the meta-analysis. (If such statistics are not published or available via contacting the authors, the study will be included only in the systematic review, and not in its meta-analysis component);
* is published in any language;
* is peer-reviewed.

A study is ineligible if it:

* fails to include the core components of behavioural activation (activity scheduling and self-monitoring);
* includes cognitive restructuring or a counselling component as part of the intervention (Ekers et al., 2014).

In the event that two studies partially or completely share a common dataset, the study with the larger sample size (or the first published study if sample sizes are equal) will be included in the analysis.

**4. Search strategy**

The search will be conducted with the support of an information scientist, in order to tailor the search strategy to the requirements of each electronic database. Keywords will include*:*

*'behavi?r\* activation' 'behavi?r therap\*' 'third generation behavi?r\* therap\*' 'clinical behavi?r\*analys?s' 'activit\* schedul\*' 'self monitor\*' 'positive replac\* behavi?r\*''major depressive disorder' 'Clinical depression' 'major depression' 'unipolar depression' 'unipolar disorder' 'recurrent depression'*

Keywords will be associated with comparable subject headings in a highly-sensitive syntax.

No search terms of sufficient sensitivity and specify are available to identify studies pertaining to patients with a chronic medical illness ([Harris, Farrand, & Dickens, 2013](#_ENREF_2)).

To ensure no studies are missed, a manual review of reference lists of included studies and relevant review papers will also be conducted. Key researchers in the field of behavioural activation will also be contacted to ensure that no relevant studies are missed.

Finally, in order to minimise publication bias, we will search on ClinicalTrials.gov and the International Clinical Trials Registry Platform (ICTRP) for unpublished studies. In the absence of controlled subject heading fields, we will perform an advanced faceted search using keywords. See Appendix 1 for the complete search strategy.

**5. Election of studies**

All studies generated from the search strategies described above will be screened on Covidence, a screening tool ([https://www.covidence.org](https://www.covidence.org/)), after duplicates are removed. Studies will be screened against the inclusion and exclusion criteria by LB, SAH, and RG. The full-text of relevant articles will then be assessed for eligibility by two independent reviewers (LB, SAH). Inter-rater reliability will be assessed, and disagreements will be resolved by consensus (RG).

**6. Quality assessment**

Study quality will be assessed using Cochrane Collaboration’s tool for assessing risk of bias in RCTs. Study quality will be assessed by two independent authors. Inter-rater reliability will be assessed, and disagreements resolved by consensus.

**7. Quantitative data synthesis**

For studies that include a control condition, hedges’ *g* and its 95% confidence interval will be used to quantify between-group differences. Standardised group differences at follow-up (Hedges’ *g*) will be used if groups are equivalent in depressive symptoms at baseline, or group differences in pre-post change scores will be used if groups are not equivalent at baseline. This has been done in prior meta-analyses (e.g. Boiler et al., 2013). For studies not equivalent at baseline, the calculation of pre-post treatment differences requires the intra-individual correlation between pre- and post- treatment depressive symptoms to be reported. If this is not available, a conservative estimate of *r*=.7 will be assumed, following the recommendations of Rosenthal (1993). This rule of thumb has been used in previous meta analyses ([Hofmann, Sawyer, Witt, & Oh, 2010](#_ENREF_3)).

Single arm pre-post studies will be collated by examining pre-post difference scores, whilst taking into account the intra-individual correlation between scores at time 1 and 2 ([Cuijpers, Weitz, Cristea, & Twisk, 2017](#_ENREF_1)).

The conservative random effects model will be used in our calculations, given the expected heterogeneity in study designs and protocols. Data analysis will be conducted using the *metafor* package in R.

**8. Study level moderators**

If our meta-analysis finds evidence of heterogeneity in effect sizes, a meta-regression will be conducted to consider the role of the following moderators (assuming sufficient data) in explaining between-study variance in effect sizes:

* Study quality
* Medical condition
* Level of therapist qualification/training
* Number of sessions
* Group/individual therapy
* BA Intervention type: simple versus complex (including functional analysis and/or values focussed activity)

**References**

American Psychiatric Association. (2013). *Diagnostic and statistical manual of*

*mental disorders*(5th ed.). Arlington, VA: American Psychiatric Publishing.

Cuijpers, P., Weitz, E., Cristea, I., & Twisk, J. (2017). Pre-post effect sizes should be avoided in

meta-analyses. *Epidemiology and psychiatric sciences, 26*(4), 364-368.

Harris, S., Farrand, P., & Dickens, C. (2013). Behavioural activation interventions for depressed

individuals with a chronic physical illness: a systematic review protocol. *Systematic reviews, 2*(1), 105.

Hofmann, S. G., Sawyer, A. T., Witt, A. A., & Oh, D. (2010). The effect of mindfulness-based

therapy on anxiety and depression: A meta-analytic review. *Journal of consulting and clinical psychology, 78*(2), 169.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Group, P. (2009). Preferred reporting items for

systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine, 6*(7), e1000097.

PHQ-9. (2018). In *American Psychological Association, Public Intere3st Directorate Reports*.

Retrieved from <http://www.apa.org/pi/about/publications/caregivers/practice-settings/assessment/tools/patient-health.aspx>