

Effects of interpersonal psychotherapy in depressed patients with or without personality disorder. A systematic review of randomized clinical trials with meta-analysis.

By

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Background

According to the WHO, major depressive disorder is the second largest healthcare problem worldwide in terms of illness induced disability.¹ It afflicts an estimated of 17% of individuals during their lifetimes at tremendous cost to the individual and society,^{2 3} and roughly a third of all depressive disorders take a chronic course.^{4 5} Compared to other medical disorders, depressive illness causes the most significant deterioration in individual quality of life.⁶ Approximately 15% of depressive patients will commit suicide over a 10-20 year period.⁷

Close to 10% of the population would, at any given time, meet the criteria for a personality disorder.⁸ It is often stated in the literature that comorbid personality disorder with depression predicts a poor outcome for depression compared with depression alone.⁹ So forth, one meta-analysis finds that depressed patients with a comorbid personality disorder have a poorer response to all antidepressant treatments (excluding electric convulsive treatment (ECT)) compared with patients with a diagnosis of depression alone.¹⁰ Another meta-analysis finds that comorbid personality disorder in depressive patients is not a predictor of treatment efficacy in standard antidepressant therapy.¹¹ The findings are therefore conflicting.

Objective

To evaluate the benefits and harms of interpersonal psychotherapy for major depressive disorder in patients with or without personality disorder.

Criteria for trials included

Study design

Randomized clinical trials comparing the effect of interpersonal psychotherapy versus 'no intervention' or 'treatment as usual' for major depressive disorder. Trials will also have to assess personality and will be included irrespective of language, publication status, publication year, and publication type.

Participants

Participants must be over 17 years, and the primary diagnosis must be major depressive disorder.

The diagnosis of major depressive disorder must be made based on one of the standardized criteria, such as DSM IV,¹² ICD 10,¹³ DSM III,¹⁴ or DSM III-R,¹⁵ or Feighner criteria.¹⁶ The diagnoses of personality disorder must also be made based on standardized criteria such as DSM IV,¹² ICD 10,¹³ DSM III,¹⁷ or DSM III-R.¹⁵ Comorbidity with other psychiatric diagnoses will not be exclusion criteria. Participants suffering from serious somatic illness or depression during or after pregnancy will be excluded. Trials focusing on 'late life' depression or depression in participants with a drug or alcohol dependence will also be excluded. This is done because we expect participants in such trials to respond differently to standardized psychotherapy

than other depressed patients, and these types of depressed patients are traditionally examined in separate trials.

Interventions

Interpersonal psychotherapy

Interpersonal psychotherapy (IPT) is a structured form of psychotherapy that addresses interpersonal issues in depression.¹⁸⁻²¹ In order for the intervention to be classified as 'interpersonal psychotherapy' the intervention had to be:

- Aimed specifically to intervene on interpersonal disputes, role transitions, grief, and interpersonal deficits.¹⁸⁻²¹
- Undertaken face-to-face either individually or in a group.

Psychodynamic-interpersonal therapy is a modified form of interpersonal psychotherapy,²² but due to its similar characteristics to interpersonal psychotherapy,¹⁸⁻²² we have chosen also to include trials assessing psychodynamic-interpersonal therapy.

Co-interventions

Trials comparing interpersonal psychotherapy versus 'no intervention' or 'treatment as usual' as add-on therapy to antidepressant medication will be included.

Trials comparing interpersonal psychotherapy as add-on therapy to electroconvulsive therapy (ECT) will be excluded. This is done because ECT cause short-term memory loss and therefore may minimize the potential effect of interpersonal psychotherapy.

All other trials comparing interpersonal psychotherapy versus 'no intervention' or 'treatment as usual' as add-on therapy to any kind of therapy will be

included, but only if this therapy is described and delivered similarly in the different intervention groups.

Outcome measures

All outcomes will be assessed for patients with or without personality disorder separately, and these two patient groups will be compared on the following list of outcomes.

All responses will be calculated based on the total number of randomized patients - if at all possible (intention-to-treat analysis).

Primary outcome measures

1. The mean value on follow-up using Hamilton Rating Scale for Depression (HDRS),²³ Becks Depression Inventory (BDI),²⁴ or Montgomery-Asberg Depression Rating Scale (MADRS).²⁵

We will estimate therapeutic responses at two time points:

- Response at cessation of treatment. Often after 6-18 weeks of treatment. The trials original primary choice of completion date will be used.
- Response at follow-up: response at maximum follow-up.

2. We will classify adverse events as serious or non-serious. Serious adverse events will be defined as medical events that are life threatening; result in death, disability, or significant loss of function; that cause hospital admission or prolonged hospitalization; a hereditary anomaly; or fetal injury.²⁶ All other adverse events (that is, events that have not necessarily had a causal relationship with the treatment, but that resulted in a change in- or cessation of the treatment) will be considered as non-serious events.

3. Quality of life. We will accept any measure of quality of life, noting each definition.

Secondary outcome measures

1. The proportion of patients achieving remission is calculated based on the total number of randomized patients. We have, pragmatically, defined remission as a score on HDRS of less than 8, MADRS less than 10, or BDI less than 10 in that prioritized order.²³⁻²⁵

2. Number of suicides, suicide attempts or suicide inclination

Search methods

We have chosen to search Psyk Info, the Cochrane Library's CENTRAL, MEDLINE via PubMed, EMBASE, Psychlit, and Science Citation Index Expanded using the search words: "randomi*ed controlled trial" AND "cognitive" AND "depression" OR "depressive"

The timeframe for the search will be all trials published before February 2010.

Selection of trials

Two of the review authors will independently select relevant trials, based on criteria described in the above. If a trial only has been identified by one of the two, it will be discussed whether the trial should be included. If the two review authors disagree, a third review author will decide if the trial should be included. Excluded trials are entered on a list, stating the reason for exclusion.

Data extraction

The following data will be extracted from the included trials:

1. Date published.
2. Time frame of the trial period.
3. Inclusion- and exclusion criteria.
4. Whether a calculation of sample size has been published.
5. Number of research participants.
6. Number of included research participants.
7. Whether personality was assessed or not and the assessment method used.
8. Proportion of participants with or without comorbid personality disorder.
9. Proportion of participants with or without borderline personality disorder.
10. Distribution of age and sex.
11. The extent of the cognitive treatment (individual or group; number of therapy-sessions).
12. Experience and education of the therapists (classified in 3 groups: low, intermediate or high).
13. Assess whether the trial- intervention should be classified under 'Interpersonal psychotherapy', or 'Interpersonal psychotherapy, not adequately defined' (see above).
14. Choice of outcome measures.
15. Outcome measures.
16. Assessment of whether the relevant assessment methods include documentation of reliability.
17. Whether a protocol has been published before launch of randomization.
18. The choice of method and an evaluation of the quality of this choice of method (see below).

Methods

We will use the instructions in the Cochrane Handbook for Systematic Reviews of Interventions²⁸ in our evaluation of the methodology and hence bias risk of the included trials. Again, two review authors will assess the included trials independent of each other. We will evaluate the methodology in respect of: allocation sequence, allocation concealment, blinding, intention-to-treat analysis, drop-outs, reporting of outcome measures, economic bias, and academic bias. These components enable classification of the included trials into trials with 'low risk of bias' or with 'high risk of bias'. The trials will overall be classified as 'high risk of bias' if one or more of these components are 'unclear' or 'inadequate'.²⁹⁻³³ This classification is important because trials with 'high risk of bias' may overestimate positive intervention effects and underestimate negative effects,^{29-31 33} and we want to relate the validity of our results to the risk of bias in the included trials.

We will classify the trials according to the components below:

Method for generating allocation sequence

Adequate: If randomizing is performed by computer or a "random number table". If the randomizing is a random process, e.g., "heads or tails" or a throw of a dice; and the person performing the procedure in no other way is involved in the trial.

Uncertain: If the procedure in respect of randomizing is not sufficiently described.

Inadequate: If the trial uses, e.g., date of admission or alternation for allocating the participants. Such trials will be included only in the assessment of harms.

Method of allocation concealment

Adequate: If the allocation sequence is concealed from the investigators, treatment providers and participants, for example by central randomization. And this procedure is described and documented.

Uncertain: If the procedure to conceal allocation is not sufficiently described.

Inadequate: If the treatment providers/clinical principal investigators/study participants are able to predict the allocation sequence. Such trials will be included only in the assessment of harms.

Blinding

Because the intervention is interpersonal psychotherapy, it is not possible to blind the treatment providers or trial participants. We therefore expect to find no trials comparing interpersonal psychotherapy with placebo or sham. If an observer-dependent assessment method (e.g., Hamilton Rating Scale of Depression) is used, it is possible to blind this observer. Personnel who supply or assess the observer-dependent questionnaires may also be blinded.

Adequate: If the personnel who instruct or supply or assess the observer-dependent questionnaire are blinded and this is described. Thus, personnel performing these procedures must not be otherwise involved in the trial

Uncertain: If the procedure of blinding is insufficiently described

Inadequate: If blinding is not performed or if the procedure cannot be classified as 'adequate' or 'uncertain'.

Drop-outs

Adequate: If drop-outs following randomizing can be described as being the same in the two intervention groups.

Uncertain: If drop-outs are not stated, or if the reasons why the participants dropped out are unclear.

Inadequate: If the pattern of drop-outs can be described as being different in the two intervention groups.

Reporting of outcome measures

Adequate: If all outcome measures are stated in the results. And the hierarchy of the efficacy variables are documented in a protocol before launch of randomization.

Uncertain: If the method of choosing outcome measures is inadequately described.

Inadequate: If there is incongruence between the original protocol and the outcome measures used in the results, or if not all of the outcome measures are stated.

Economic bias

Adequate: If the trial is not financed by an authority that might have an interest in a given result.

Uncertain: If there is no description of how the trial is financed.

Inadequate: If the trial is financed by an authority which could have an interest in a specific result from the trial.

Academic bias sources

Adequate: If the trialists do not have an academic/personal interest in a given result from the trial.

Uncertain: If there is no description of any academic interests that trialists might have.

Inadequate: If the trialists have a direct interest in a given result from the trial.

Intention to treat

Adequate: If intention to treat (ITT) analysis is performed or allowed. We will note which ITT method is used (e.g., imputation, last observation carried forward)

Uncertain: If it is unclear whether ITT is performed or allowed.

Inadequate: If ITT analysis is not performed or allowed.

Statistical methods

We will undertake this meta-analysis according to the recommendations stated in The Cochrane Handbook for Systematic Reviews of Interventions.²⁹ In analyzing continuous outcomes we will use the mean difference (MD) with a 95% confidence interval. We will use the odds ratio (OR) with a 95% confidence interval to estimate intervention effects on dichotomous outcomes.

In order to compare if the effect of interpersonal psychotherapy differed between the participants with or without comorbid personality disorder, we will perform 'test of interaction'²⁷ on both primary and secondary outcomes.

We plan to undertake two sub-group analyses:

- We will investigate whether the participants with borderline personality disorder respond differently to interpersonal psychotherapy compared with the participants without personality disorder.
- We will investigate whether the participants with borderline personality disorder respond differently to interpersonal psychotherapy compared with the participants with a personality disorder other than borderline.

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