Psychological treatments for people with epilepsy (Review)

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[Intervention Review]

Psychological treatments for people with epilepsy

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ABSTRACT

Background

Given the significant impact epilepsy can have on the health-related quality of life (HRQoL) of individuals with epilepsy and their families, there is great clinical interest in evidence-based psychological treatments, aimed at enhancing psychological well-being in people with epilepsy. A review of the current evidence was needed to assess the effects of psychological treatments for people with epilepsy on HRQoL outcomes, in order to inform future therapeutic recommendations and research designs.

Objectives

To assess the effects of psychological treatments for people with epilepsy on HRQoL outcomes.

Search methods

We searched the following databases on 20 September 2016, without language restrictions: Cochrane Epilepsy Group Specialized Register, CENTRAL, MEDLINE, PSYCHINFO, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform (ICTRP). We screened the references from included studies and relevant reviews, and contacted researchers in the field for unpublished studies.

Selection criteria

We considered randomized controlled trials (RCTs) and quasi-RCTs for this review. HRQoL was the main outcome measure. For the operational definition of ‘psychological treatments’, we included a broad range of treatments that used psychological or behavioral techniques designed to improve HRQoL, seizure frequency and severity, and psychiatric comorbidities for adults and children with epilepsy, compared to treatment as usual (TAU) or an active control group.

Data collection and analysis

We used standard methodological procedures expected by the Cochrane Collaboration.
Main results

We included 24 completed RCTs, with a total of 2439 participants. Eleven studies investigated psychological interventions, such as cognitive, behavioral, and mindfulness-based interventions. The remaining studies were classified as educational interventions (N = 7), self-management interventions (N = 3), adherence interventions (N = 1), and mixed interventions (N = 2). Two studies investigated interventions for children and adolescents, and five studies investigated interventions for adolescents and adults. Based on satisfactory clinical and methodological homogeneity, we pooled data from six adult studies, two studies on adolescents and adults, and one on adolescents and young adults (468 participants) for HRQoL, measured with the Quality of Life in Epilepsy-31 (QOLIE-31). We found significant mean changes for the QOLIE-31 total score and six subscales (emotional well-being, energy and fatigue, overall QoL, seizure worry, medication effects, and cognitive functioning). The mean changes of the QOLIE-31 total score (mean improvement of 5.68 points (95% CI 3.11 to 8.24; P < 0.0001), and three subscales, emotional well-being (mean improvement of 7.03 points (95% CI 2.51 to 11.54; P = 0.002); energy and Fatigue (mean improvement of 6.90 points (95% CI 3.49 to 10.31; P < 0.0001); and overall QoL (mean improvement of 6.47 points (95% CI 2.68 to 10.25; P = 0.0008)) exceeded the threshold of minimally important change (MIC), indicating a clinically meaningful post-intervention improvement of QoL. We downgraded the quality of the evidence provided by the meta-analysis because of serious risk of bias in some of the included studies. Consequently, these results provided evidence of moderate quality that psychological treatments for adults with epilepsy may enhance overall QoL in people with epilepsy.

Authors’ conclusions

Implications for practice: Psychological interventions and self-management interventions improved QoL, and emotional well-being, and reduced fatigue in adults and adolescents with epilepsy. Adjunctive use of psychological treatments for adults and adolescents with epilepsy may provide additional benefits to QoL in those who incorporate patient-centered management.

Implications for research: Authors should strictly adhere to the CONSORT guidelines to improve the quality of reporting on their interventions. A thorough description of the intervention protocol is necessary to ensure reproducibility.

When researching psychological treatments for people with epilepsy, the use of Quality of Life in Epilepsy Inventories (QOLIE-31, QOLIE-31-P, and QOLIE-89) would increase comparability. There is a critical gap in pediatric RCTs for psychological treatments, particularly those that use an epilepsy-specific measure of HRQoL.

Finally, in order to increase the overall quality of study designs, adequate randomization with allocation concealment and blinded outcome assessment should be pursued when conducting RCTs. As attrition is often high in research that requires active participant participation, an intention-to-treat analysis should be carried out.

Plain Language Summary

Psychological Treatments for People with Epilepsy

Background

Epilepsy is defined as the chronic predisposition of the brain to have recurrent seizures. It has been recognised that individuals with epilepsy, especially those who continue to have seizures despite adequate medication (drug-resistant epilepsy), are at increased risk of psychiatric disorders and psychological difficulties. Individuals with epilepsy often have lower quality of life (QoL) compared to those with other chronic diseases. Factors that have been shown to contribute to poor health-related quality of life (HRQoL) include medical parameters (such as seizure frequency and severity and antiepileptic drug side effects) and complex psychological parameters (including depression and anxiety, fear of losing control, worries about seizure occurrence, and negative coping). While medical providers focus on minimizing seizures and side effects, a primary role that mental and behavioral health providers (i.e. psychologists, psychiatrists, and social workers) can have with individuals with epilepsy is to optimize HRQoL by providing evidence-based psychological treatments.

Research Question

This review aimed to assess the effects of psychological treatments on HRQoL for people with epilepsy.

Characteristics of the Studies

We included 24 studies that met the inclusion criteria (2439 participants). The majority of trials investigated psychological interventions, such as cognitive, behavioral and mindfulness-based interventions. The remaining studies focused on education, self-management,
and drug adherence. Two studies investigated interventions for children and adolescents, and five studies investigated interventions for adolescents and adults. The evidence presented in this review is up to date to September 2016.

Quality of the Studies

We assessed variable quality in the design and reporting across studies. However, there were some quality issues with the majority of studies.

Results

Based on satisfactory comparability, we combined data from nine adult studies (468 participants) providing HRQoL outcomes in a meta-analysis. These results provided moderate-quality evidence that psychological treatments may enhance overall QoL and emotional well-being, and reduce fatigue in adults and adolescents with epilepsy.

Conclusions

We found moderate-quality evidence that psychological and self-management interventions were beneficial for adults and adolescents with epilepsy, by improving overall quality of life and emotional well-being and reducing fatigue. Adjunctive use of psychological treatments may provide additional benefits to QoL in adults with epilepsy who incorporate patient-centered management. The uniform use of Quality of Life in Epilepsy Inventories when researching psychological treatments for people with epilepsy, would increase comparability.
# Summary of Findings for the Main Comparison

**Psychological treatments compared with usual or supportive care**

**Patient or population:** people with epilepsy  
**Setting:** clinical setting  
**Intervention:** psychological treatments  
**Comparison:** usual care (UC) or supportive care (SC)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Comparative effect sizes* (95% CI)</th>
<th>Number of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOLIE-31 total score</td>
<td>The range of mean change in the control groups was -1.9 to 3.97 points</td>
<td>The mean change from baseline in the intervention groups was on average 5.68 higher (95% CI 3.11 to 8.24). The range of mean change was 3.27 to 17.2 points</td>
<td>468 (9 RCTs)</td>
<td>⊗⊗⊗ ⊗ MODERATE1</td>
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<tr>
<td>QOLIE-31 emotional well-being subscale</td>
<td>The range of mean change in the control groups was -6.23 to 20 points</td>
<td>The mean change from baseline in the intervention groups was on average 7.03 higher (95% CI 2.51 to 11.54). The range of mean change was 0.91 to 20.57 points</td>
<td>440 (8 RCTs)</td>
<td>⊗⊗⊗ ⊗ MODERATE1</td>
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<tr>
<td>QOLIE-31 energy or fatigue subscale</td>
<td>The range of mean change in the control groups was -5.3 to 8.13 points</td>
<td>The mean change from baseline in the intervention groups was on average 6.90 higher (95% CI 3.49 to 10.31). The range of mean change was 0.44 to 20.0 points</td>
<td>440 (8 RCTs)</td>
<td>⊗⊗⊗ ⊗ MODERATE1</td>
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<tr>
<td>QOLIE-31 subscale</td>
<td>Mean change from baseline in the intervention groups was on average 6.47 higher (95% CI 2.68 to 10.25). The range of mean change was 0.13 to 19.64 points.</td>
<td>440 (8 RCTs)</td>
<td>⭐⭐⭐⭐ ⭐⭐⭐⭐ MODERATE(^1)</td>
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<tr>
<td>QOLIE-31 overall QoL subscale</td>
<td>The range of mean change in the control groups was -2.63 to 4.09 points</td>
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<td>QOLIE-31 seizure worry subscale</td>
<td>The range of mean change in the control groups was -5.18 to 5.96 points</td>
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<tr>
<td>QOLIE-31 cognitive functioning subscale</td>
<td>The range of mean change in the control groups was -2.71 to 8.9 points</td>
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<tr>
<td>QOLIE-31 medication effects subscale</td>
<td>The range of mean change in the control groups was -8.11 to 12.04 points</td>
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<tr>
<td>QOLIE-31 social functioning subscale</td>
<td>The range of mean change in the control groups was -4.28 to 7.35 points</td>
<td>438 (8 RCTs)</td>
<td>⭐⭐⭐⭐ ⭐⭐⭐⭐ MODERATE(^1)</td>
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</table>

* Comparative effect sizes were calculated from the mean changes between baseline and post-intervention in the intervention and control groups

CI: Confidence interval; RCT: randomized controlled trial

\(^1\) Moderate risk of bias.
### GRADE Working Group grades of evidence

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate quality:** 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 quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

**Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

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1 - Serious risk of bias
BACKGROUND

Description of the condition

Epilepsy is defined as the chronic predisposition of the brain to have recurrent unprovoked seizures. According to the most recent update of the clinically-oriented definition of epilepsy, the diagnosis can be made after an individual suffers only one reflex or unprovoked seizure, if further diagnostic test results indicate the likelihood of an organic predisposition to recurring seizures (Fisher 2014). It is estimated that from 0.6% (pediatric) to 1% (adult) of the world population has epilepsy, which makes it one of the most common neurological conditions (CDC 2012; Russ 2012; WHO 2017).

To date, about one third to one half of individuals with epilepsy have drug-resistant seizures (Kwan 2000); even the new generation of anticonvulsive drugs has failed to significantly change this situation. Some individuals with drug-resistant seizures are eligible for epilepsy surgery (Téllez-Zenteno 2005). However, the risks of permanent, significant neurological injury and seizure recurrence need to be considered when the irreversible surgical treatment option is recommended to the individual patient (Tanriverdi 2009; Téllez-Zenteno 2010; Wellmer 2012). Likewise, surgical resection and neuromodulation (e.g. vagus nerve stimulation, responsive neurostimulation, and deep brain stimulation) have seizure-free rates of 10% to 40% (Jehi 2014).

Individuals with epilepsy, especially those whose epilepsy is treatment-resistant, are at increased risk of psychiatric comorbidities or psychological difficulties (Selassie 2014; Wagner 2015). For example, children and adolescents with epilepsy are at a three- to six-fold increased risk (21% to 60%) of psychosocial comorbidities (e.g. attention deficit hyperactivity disorder (ADHD) and depression (Ort 2000; Ort 2003)) compared to the general population and youth with non-neurological (Davies 2003; Ekinci 2009; Rutter 1970), and neurological medical conditions (Wagner 2015). Individuals with epilepsy often have lower health-related quality of life (HRQoL) compared to those with other chronic diseases (Wang 2012). Even a single seizure is associated with poor HRQoL (Modi 2011). Factors contributing to poor HRQoL include medical parameters, such as seizure frequency and severity (Camfield 2001; Conner 1992; Devinsky 1999; Williams 2003), antiepileptic drug (AED) side effects (Benevente 2004; Gilliam 2004; Loisele 2016), and medication adherence (Wu 2014), as well as socioeconomic status (Loisele 2016; Loisele 2016), and psychological comorbidities (Loisele 2016; Lefee 2016). Notably, psychological distress and loneliness show the closest correlation with HRQoL, while seizure-related factors are much more important (Suurmeijer 2001). When investigating the association between medical parameters and HRQoL, side effects (Loisele 2016; Modi 2011; Ramsey 2016; Wu 2014), and the number of prescribed AEDs have emerged as stronger predictors of HRQoL than seizure control (Ferro 2013; Ramsey 2016).

Epilepsy and psychiatric disorders share a bi-directional relationship, which has been supported by both population-based and experimental studies in human and animal models (Chang 2011; Hesdorffer 2006; Jones 2013; Kanner 2006; Kanner 2009). Individuals with a previous history of psychiatric disorder are four to seven times more likely to develop an unprovoked seizure or chronic epilepsy, compared to individuals without this history (Hesdorffer 2000; Hesdorffer 2000). In a review of seizure incidence in psychopharmacological clinical trials (N = 75,873), the incidence of seizures was significantly lower among participants who received antidepressants compared to placebo. The study concluded that second-generation antidepressants, other than bupropion, could have an apparent antiepileptic effect. In addition, depression, psychotic disorders, and obsessive compulsive disorder have been found to be associated with a reduced seizure threshold (Alper 2007). These findings have prompted further research on the role of psychosocial states on the development and manifestation of seizures, as well as the potential effects of psychological therapy on individuals with epilepsy (Kanner 2006; Tang 2014). The association between epilepsy and psychiatric comorbidities is high (Gainoyle 2015; Gülpek 2011; Wagner 2012). The increase in depression and anxiety one year after diagnosis of epilepsy is correlated with the degree to which an individual senses loss of self-control, rather than the actual number of seizures (Velissaris 2012). Moreover, QoL is correlated with depression symptoms in epilepsy (Gilliam 2002). Concerns over recurring seizures may diminish QoL, even in individuals with well-controlled epilepsy (Snyder 1990). This may hamper psychosocial functioning and the achievement or maintenance of higher education and employment, despite seizure freedom (Gilbert 2012). By permeating the individual's sense of self-efficacy, and consequently decreasing self-confidence, the worries about seizure recurrence that stem from the assumed unpredictability of the course of epilepsy, to subjective helplessness, can be far more disabling than the seizures themselves (Stevanovic 2007). Greater depressive symptoms were also associated with negative coping, which suggests that interventions targeting negative coping may improve depressive symptoms in youth with epilepsy (Wagner 2010). Daily routines and activities of daily living are often affected, including sleep, work productivity, school, and recreational and sports activities. This may incur significant indirect costs for the wider economy (Larson 2012; Painter 2014). Notably, the healthcare costs for children with epilepsy in the first year of diagnosis are approximately USD 20,000. Seizure side effects, and HRQoL are strong drivers of healthcare charges (Ryan 2015; Ryan 2016). Self- or family-management has been identified as a key health variable, and is broadly defined to encompass the personal resources needed to manage a chronic condition in the context of everyday life. Self-management of adult epilepsy has been defined as “activities that an individual can perform alone that are known to either control frequency of seizures or promote well-being of the person with seizures” (Dilorio 1992). In pediatric chronic illness,
self-management behaviors are modifiable behaviors linked to influences (e.g. coping responses) through processes (e.g. allocation of treatment responsibility) operating within individual, family, community, and healthcare system domains (Dilorio 1992; Modi 2012; Schilling 2002). Comprehensive evidence in the Institute of Medicine’s Report on Epilepsy supports the relevance of self-management domains, regardless of the age at onset, or of the epilepsy type (Institute of Medicine 2012). An adult self-management instrument has been developed and published to measure behaviors, and psychometrics show high internal consistency factor reliability (Escoffery 2015a; Escoffery 2015b).

Description of the intervention

While medical providers can minimise seizures and side effects, a primary role that mental health professionals (including psychologists, psychiatrists, and social workers) can have for individuals with epilepsy is optimising HRQoL. Given the high level of psychiatric comorbidity in the epilepsy population, and the significant impact epilepsy and its treatments can have on the HRQoL of individuals with epilepsy and their families, psychological interventions that target people with epilepsy could be an adjuncive treatment option. In addition, self-management and adherence can play a pivotal role in outcomes for these individuals, and should be proactively addressed.

Our operational definition of ‘psychological therapy’ included a broad range of interventions that used psychological techniques for children and adults with epilepsy. These interventions may be given singly or in combination, either alone or in addition to AEDs, and can be grouped into different themes:

1. Psychological interventions - these interventions are defined as interventions that are developed based on a theory of psychotherapy. Examples include cognitive behavioral or behaviorally-based interventions, and mindfulness-based interventions (such as acceptance and commitment therapy). Common therapeutic strategies include counselling, cognitive strategies, such as thought restructuring or acceptance, conditioning, behavioral activation, systematic desensitization, and behavioral countermeasures (such as breathing and visualization techniques) at aura onset, applied by the patient. Other therapeutic approaches may include family systems therapy, mindfulness interventions, motivational interviewing, and acceptance and commitment therapy.

2. Self- or family-management - defined as activities or steps that an individual or family can perform that are known to either control the frequency of seizures, or promote the well-being of the person with seizures. Activities or steps can lie within the individual, family, community, or healthcare system domains. Examples include relaxation, physical exercise, coping skills, etc. (Dilorio 1992; Modi 2012).

3. Adherence interventions - defined as efforts to assist individuals adhere to the advice of healthcare providers, including taking prescribed self-administered medications, following a ketogenic diet, and avoiding seizure triggers. Taking medication can be broken down into several components, including optimal dose timing, and adequate frequency of dosing.

4. Educational interventions - defined as interventions that aim to increase knowledge of epilepsy, its comorbidities, and its treatments, or the working of the brain (including psychoeducation).

How the intervention might work

The high level of psychiatric comorbidities in people with epilepsy has yielded interventional efforts for both children and adults. Several promising studies have been conducted with the objective of decreasing psychological co-morbidities in adults with epilepsy (e.g. Project UPLIFT, PEARLS (Ciechanowski 2010; Thompson 2010)). In one study, over 12 months, the proportion of participants with suicidal ideation differed significantly between groups, increasing 12% in the control group and decreasing 24% in the mindfulness-based therapy group (Ciechanowski 2010). Compared with participants in the control group, participants assigned to the intervention groups had less severe depression. Martinović delivered a cognitive behavioral psychological therapy intervention to prevent depressive symptoms in youth with epilepsy who were at risk of depression (Martinović 2006). Based on the bi-directional model of epilepsy and psychological states, psychological therapy for people with epilepsy can also emphasize the individuals’ role and participation in the management of their own condition. Well-being in individuals with epilepsy may be enhanced by general stress reduction or tolerance techniques, which may be effective in reducing psychological stress and its physiological correlates (Novakova 2013). For example, Tang and colleagues developed a mindfulness-based therapy for participants with drug-resistant epilepsy. Significantly more participants in the mindfulness-based therapy group had a clinically important improvement in the Quality of Life in Epilepsy Inventory (QOLIE-31 (11.8 or above)) compared to those in the attention-placebo intervention control group (Tang 2015). Reiter and Andrews developed a multi-modal therapy for people with epilepsy that included biofeedback, relaxation, aura identification, and behavioral modification (Reiter 2009). Aura interruption techniques may also be part of psychological therapy, and allow individuals to learn new sets of reactions to preictal and early ictal phenomena, which may decrease fear of recurring seizures and provide a subjective sense of control (Elsas 2011; Fried 1990; Michaelis 2012). Wagner and colleagues developed an intervention for youth with epilepsy to promote coping and self-management of their epilepsy (Wagner 2010). Similarly, Dilorio and colleagues developed an online self-management program for adults (WebEase (Dilorio 2011)). Adherence-promotion interventions that used intention as a strategy (Brown 2009), or fam-
ily-based problem-solving about adherence barriers (Modi 2013; Modi 2016b), appeared to be promising.

**Why it is important to do this review**

Psychological treatments have been developed that aim to enhance psychological well-being and seizure control, and reduce psychiatric comorbidities in people with epilepsy. Establishing evidence of the effects of such interventions is methodologically challenging. A review of the current evidence is needed to inform future therapeutic recommendations and research designs.

**OBJECTIVES**

To assess the effects of psychological treatments for people with epilepsy on HRQoL outcomes.

**METHODS**

Criteria for considering studies for this review

**Types of studies**

Randomized controlled trials (RCTs), quasi-RCTs (e.g. studies in which the randomization is according to the day of the week or date of birth).

**Types of participants**

Men, women, and children of any age, with any type of epilepsy, treatment-responsive or treatment-resistant, with or without learning disabilities or intellectual disabilities, whether or not they were taking antiepileptic drugs (AEDs).

**Types of interventions**

For the operational definition of 'psychological treatments', we included a broad range of treatments that were designed to improve health-related quality of life (HRQoL), seizure frequency and severity, and reduce psychological and psychiatric comorbidities. We explained these different streams of psychological treatments in detail in the Description of the intervention:

1. Psychological interventions
2. Self-management
3. Adherence interventions
4. Educational interventions
5. A combination of the above

We included studies that included a comparison of two or more of the above treatments, and comparisons to 'wait-list control' and 'treatment as usual'.

**Types of outcome measures**

**Main outcome measures**

We included all studies that reported changes from baseline in validated HRQoL measures. If those studies also reported other quality of life-related parameters, symptoms of psychiatric comorbidities, or seizure-related outcome measures, we extracted data from these parameters too. We excluded studies without a HRQoL measure.

**Primary outcomes**

1. Mean of change from baseline, or comparisons of post-intervention scores from validated HRQoL measures.

**Secondary outcomes**

1. Comparisons of post-intervention scores from validated measures of psychiatric comorbidities, such as depressive and anxiety symptoms.
2. Comparisons of post-intervention data from validated seizure-related outcome measures.

**Search methods for identification of studies**

**Electronic searches**

We searched the following databases. There were no language restrictions.

- Cochrane Epilepsy Group Specialized Register (searched 20 September 2016); search strategy shown in Appendix 1.
- Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 9) in the Cochrane Library, via Cochrane Register of Studies Online (searched 20 September 2016); search strategy shown in Appendix 2.
- MEDLINE Ovid (1946 to 20 September 2016); search strategy shown in Appendix 3.
- PsycINFO EBSCO host (1887 to 20 September 2016); search strategy shown in Appendix 4.
- ClinicalTrials.gov (20 September 2016) using the search terms: (psychological OR psychotherapy) AND epilepsy.
- WHO International Clinical Trials Registry Platform (ICTRP; 20 September 2016) using the search terms: psychological AND epilepsy OR psychotherapy AND epilepsy.
Searching other resources

References from published studies and relevant systematic reviews
We reviewed the reference lists of retrieved studies and relevant reviews to search for additional reports of relevant studies.

Other sources
We contacted colleagues to ask if they were aware of any studies or unpublished data that we had missed.

Data collection and analysis
Two review authors (Rosa Michaelis and Venus Tang) independently assessed trials for inclusion, resolving disagreements through discussion.

Selection of studies
Two review authors (Rosa Michaelis and Venus Tang) independently assessed trial abstracts for inclusion, resolving disagreements through discussion.

Data extraction and management
The same two review authors independently extracted the following data, using an electronic Cochrane data collection form that we had adapted to fit the scope of this review:

- Type of intervention used
- Design
- Duration of study
- Sequence generation and allocation concealment
- Blinding method
- Controlled confounding variables
- Other 'Risk of bias' concerns

Participants
- Total sample size and total number of participants allocated to each group
- Age, sex, and gender distribution
- Seizure type and epilepsy syndrome
- Duration of epilepsy
- Etiology of epilepsy
- Seizure frequency and severity
- Presence or absence of learning disability or intellectual disability
- Presence or absence of psychiatric comorbidity or other medical diagnoses
- Anticonvulsant medication and co-medication
- Setting of the study
- Inclusion and exclusion criteria
- Country of study

Outcome data
- Name and definition of outcome
- Units of measurement

Results
- Study attrition
- Sample size for each outcome
- Missing data
- Summary data for intervention and control groups (for example, means and standard deviations for all outcomes)

The authors tested the applicability of the data collection form by piloting the form. Again, they resolved any differences of opinion through discussion.

Assessment of risk of bias in included studies
The same two review authors independently assessed risk of bias for each randomized trial using Cochrane's recommended domain-based evaluation tool for randomized trials, in which critical assessments were made separately for different domains, including selection bias (random sequence generation, allocation concealment), performance bias (blinding of personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other sources of bias (Higgins 2011). We examined all outcomes reported in papers for selective outcome reporting. Any differences of opinion were resolved by mutual discussion.

Measures of treatment effect
We expressed the treatment effect for each continuous outcome measuring HRQoL as a mean difference (MD) with 95% confidence intervals (CI). For studies that did not provide mean changes and standard deviation (SD), we used correlation values from other studies of comparable intervention method, treatment setting (group versus individual), and total treatment time. We only performed meta-analyses for HRQoL data. Since HRQoL constituted the main outcome measure of this review, and we only included studies that investigated HRQoL, we excluded some studies that included other outcome measures, e.g. psychiatric symptoms. From this perspective, a meta-analysis of any outcome other than HRQoL would imply a serious selection bias.
Unit of analysis issues
When assessing randomized trials, we took the level at which randomization occurred into account.
In trials with cluster-randomization, we considered the biases particular to a cluster-randomized trial, such as recruitment bias, baseline imbalance, loss of clusters, incorrect analysis, and comparability with individually-randomized trials, and chose the appropriate measure of analysis.
Considering the lasting nature of the intervention in question, a cross-over trial design would not have been appropriate, because of the likelihood of serious carry-over. Hence, we would only have included data from the first period.
When assessing multi-intervention studies, we listed all intervention groups in the ‘Characteristics of included studies’ tables. We only used the intervention groups relevant to the review in analyses. We would have included studies that included three or more of the interventions listed in Types of interventions as separate comparisons in the analysis.

Dealing with missing data
Whenever possible, we contacted the original investigators to request missing data and clarification of methodology. If we assumed that the data were missing for reasons unrelated to the intervention, we said the data were ‘missing at random’ and we based the analyses on the available data. We discussed the potential reasons for the missing data and addressed the potential impact of missing data on the findings in the discussion section of the review.

Assessment of heterogeneity
We assessed clinical heterogeneity by examining the distribution of important prognostic variables between studies. To assess the statistical heterogeneity of observed differences of study results, we used the Chi² test, forest plots, and the I² statistic. We judged that an I² > 70% and a Chi² result of P < 0.01 indicated statistical heterogeneity of concern.

Assessment of reporting biases
The reported outcomes were compared with the outcome measures and points of measurement stated in the study methods to assess reporting bias within the publication. The authors assessed reporting bias by comparing the reported outcomes with the original study protocol. To assess reporting biases and to collect missing information, if needed, the authors contacted all study investigators for their original protocols or comparable documents.

Data synthesis
To assess whether meta-analysis was appropriate, we compared the types of interventions and types of outcome measures or scales used in the studies, by tabulating the study characteristics. After we completed this, a group of studies appeared to be sufficiently homogeneous for meta-analysis. We meta-analyzed the results of clinically and statistically homogeneous studies using Review Manager 5 software (RevMan 2014). We used the inverse variance method for continuous outcomes and a random-effects model. We conducted a narrative synthesis for any outcomes for which the included studies were not sufficiently homogeneous, or for which insufficient data were found for meta-analysis.

Subgroup analysis and investigation of heterogeneity
Due to the scope of the review, there were several different interventions of interest and the included studies were diverse. If possible, we would have investigated the following subgroups as a means of investigating heterogeneous results:
• Children versus adults;
• Individuals with treatment-resistant epilepsy versus individuals with treatment-responsive epilepsy;
• Individuals with primary generalized epilepsy versus individuals with focal epilepsy versus unclassified epilepsy syndromes;
• Individuals with versus those without intellectual disability (IQ below 70 versus IQ of 70 and above);
• Individuals with nocturnal seizures versus individuals with diurnal seizures (seizure-related outcomes only);
• Individuals with seizure warning (aura) versus individuals without seizure warning (seizure-related outcomes only).
We assessed methodological heterogeneity by examining the study design.

Sensitivity analysis
If reasonable, we would have conducted a sensitivity analysis by comparing the results of a second meta-analysis, including only studies at low risk of bias, to those of the overall meta-analysis.

Summarising and interpreting results
We used the GRADE approach to interpret findings (Schünemann 2011), and GRADEpro GDT software (which imports data from Review Manager 5 software (GRADEPro 2015)), to create a ‘Summary of findings’ table for the primary outcome of HRQoL.

RESULTS

Description of studies
We restricted the search to randomized controlled trials (RCT) and quasi-RCTs that investigated psychological treatments for epilepsy (as described in our operational definition of psychological treatments for epilepsy). Only those that measured health-related quality of life (HRQoL) outcome parameters as primary or secondary outcomes, using validated HRQoL outcome measures, were included in the meta-analysis.

**Results of the search**

The electronic search yielded 1155 titles from the databases outlined, and three titles were found through handsearching. Following the removal of duplicates, 877 titles remained. We excluded 608 titles due to irrelevance (i.e. these titles clearly indicated that the studies were related to the investigation of psychological interventions for people with epilepsy). We screened the abstracts of the remaining 269 titles for eligibility, and obtained the full texts of 52 reports to assess for eligibility. We excluded 18 full text reports (17 studies, see Figure 1 and Characteristics of excluded studies). The main reason for exclusion was lack of HRQoL outcome measures (N = 18). One study with three publications was still ongoing (see Characteristics of ongoing studies).
Figure 1. Study flow diagram.

1,155 titles identified through database searching

3 additional titles identified through other sources

877 titles after duplicates removed

808 titles excluded due to irrelevance

289 abstracts of remaining titles screened

217 abstracts excluded due to irrelevance

52 full-text articles of remaining abstracts assessed for eligibility

18 full-text articles excluded, with reasons:

Wrong outcomes (no HROOL outcome measures)

N = 18

24 studies included in qualitative synthesis (31 publications)
Ongoing studies
N = 1 with 3 publications

9 studies included in quantitative synthesis (meta-analysis)
Included studies
We included 24 completed RCTs (2439 participants) in 31 publications in this review. Table 1 and the 'Characteristics of included studies' tables outline the details of the studies and the components of the interventions. Six studies were conducted in the USA (Caller 2016; Ciechanowski 2010; Diliorio 2011; Fraser 2015; Pramuka 2007; Thompson 2010), five in Germany (Jantzen 2009; May 2002; Pfafflin 2016; Rau 2006; Schröder 2014), three in Iran (Hosseini 2016; Pakpour 2015; Yadegary 2015), two in Hong Kong (Au 2003; Tang 2015), and two in Sweden (Lundgren 2006; Lundgren 2008). The remaining studies were conducted in Australia (Gandy 2014), Italy (Beretta 2014), Malaysia (Luo 2013), Norway (Helde 2005), Serbia (Martinovic 2006), and Mexico (Orjuela-Rojas 2015).

Interventions
The authors grouped the investigated psychological treatments according to the above mentioned operational definition of 'psychological treatments' for adults and children with epilepsy (see also Table 1). Because most interventions encompassed a broad spectrum of treatment techniques and treatment goals, the grouping of treatment methods and techniques may overlap.

1. Psychological interventions (11 studies, 470 participants)
Six psychological interventions were cognitive or behavior-based interventions, or both, with the primary goal of treating depressive symptoms in adolescents or adults with epilepsy and varying levels of depression severity (Ciechanowski 2010; Gandy 2014; Martinovic 2006; Orjuela-Rojas 2015; Schröder 2014; Thompson 2010). The most common treatment strategies were cognitive restructuring to address depressive thoughts, and behavioral and social activation (see Characteristics of included studies for additional strategies in each study). Three of the interventions used a group format (Martinovic 2006; Orjuela-Rojas 2015; Thompson 2010), while the other three used individual treatment (Ciechanowski 2010; Gandy 2014; Schröder 2014). Three of the interventions were conducted in a clinical setting (Gandy 2014; Martinovic 2006; Orjuela-Rojas 2015), one was home-based (Ciechanowski 2010), one was Internet-based with complementing telephone calls (Thompson 2010), and one intervention was solely Internet-based (Schröder 2014). Two of these interventions included mindfulness techniques (Schröder 2014; Thompson 2010). Only one study targeted seizure frequency as a primary treatment goal imparting - among other things - general and epilepsy-specific (i.e. identifying and addressing seizure provoking situations) stress management strategies (Au 2003).

Four studies focused on the primary treatment goal of improving HRQoL. Three of them used mindfulness interventions and evaluated mindfulness techniques in combination with seizure management techniques, by introducing acceptance and coping related to seizure disturbances (Lundgren 2006; Lundgren 2008; Tang 2015). Lundgren 2006 and Lundgren 2008 included management of seizure triggers and development of aura interruption techniques. Hosseini 2016 investigated motivational interviewing, which focused on enhancement of internal motivation for coping with epilepsy.

2. Self-management interventions (3 studies, 261 participants)
One internet-based self-management program (WebEase) focused on the primary treatment goals of improving adherence and perceived stress levels, by targeting medication adherence, stress and self-management (Diliorio 2011). One consumer-driven psychoeducation intervention focused on the primary treatment goal of self-management behaviors, by discussing medical and psychosocial aspects of epilepsy self-management and epilepsy-related communication in a face-to-face group setting (Fraser 2015). Another self-management intervention applied similar techniques, but evaluated the impact of the intervention on HRQoL outcomes (Yadegary 2015).

3. Adherence interventions (1 study, 275 participants)
We found one study investigating an adherence intervention using motivational interviewing in an individual setting (Pakpour 2015). In this study, a program was designed to enhance medication adherence behavior and clinical outcomes in people with epilepsy, as measured by drug adherence, drug-taking behaviors, seizure severity, and HRQoL.

4. Educational interventions (7 studies, 883 participants)
All epilepsy educational interventions focused on epilepsy knowledge, advocacy topics, daily self-management behaviors, and psychosocial aspects in order to enhance quality of life (four trials (Jantzen 2009; Luo 2013; May 2002; Pramuka 2007)), increase knowledge and coping (Rau 2006), or satisfaction of participants with information and support (Pfafflin 2016), or reduce drug-related problems (Beretta 2014). Three intervention programs were designed to be delivered in a group setting during a two-day weekend course (Flip&Flap (Jantzen 2009); MOSES (May 2002); FAMOSES (Rau 2006)). Two of these interventions were geared towards the education of children, adolescents, and their parents (Jantzen 2009; Rau 2006). One intervention investigated...
the MOSES material using a short message service (SMS)-based system to deliver the general content of the educational intervention, complemented by information tailored to the individual (Lua 2013). One intervention provided participant-tailored medication education in individual sessions in order to reduce drug-related problems (Beretta 2014).

5. Combined interventions (2 studies, 160 participants)

One intervention combined one epilepsy education group session, covering epilepsy knowledge (including the topic of drug adherence) and nurse-led personalized counselling, with the primary treatment goal of enhancing quality of life (Helde 2005). One home- and telephone-based intervention combined self-management and cognitive training (Home-Based Self-management and Cognitive Training Changes lives (HOBSCOTCH)) in order to increase quality of life, mood, and objective and subjective neurocognitive functions (Caller 2016).

Intervention delivery

A specialized team, usually consisting of medical (doctors, nurses) and mental health specialists (e.g. psychologist, psychiatric nurses, social workers) delivered most of the education interventions, psychologists with different levels of clinical experience and training delivered most of the psychological and self-management interventions. Two interventions included a peer coach with epilepsy (Fraser 2015; Thompson 2010). One pragmatic design left the delivery of the educational intervention to the treating physician (Beretta 2014).

Control groups

Almost half of all study designs (11 trials) included a wait-list control group (Au 2003; DiIorio 2011; Fraser 2015; Gandy 2014; Hosseini 2016; Jantzen 2009; May 2002; Pfafflin 2016; Rau 2006; Schröder 2014; Thompson 2010). Six studies included an immediate active control group (paper-based education intervention (Lua 2013); cognitive therapy (Lundgren 2006); yoga (Lundgren 2008); counselling as usual (Martinović 2006); pharmacotherapy with a selective serotonin reuptake inhibitor (Orjuela-Rojas 2015); social support (Tang 2015). The remaining seven studies used usual care or treatment as usual as the control group (Beretta 2014; Caller 2016; Ciechanowski 2010; Helde 2005; Pakpour 2015; Pramuka 2007; Yadegary 2015). The use of a usual care or treatment as usual design, instead of a wait-list control group was especially comprehensible in long-term interventions (six months or longer (Ciechanowski 2010; Helde 2005)).

Outcome measures

We organized the outcome measures according to the types of outcome defined in the protocol (Types of outcome measures). The characteristics of included studies’ tables outlined the outcome measures in each study. Altogether, the 24 included studies used more than 40 different outcome measures.

Health-related quality of life

‘Quality of Life in Epilepsy inventories (QOLIE)

Among the 24 studies, 21 used the QOLIE-31; (Au 2003; Beretta 2014; Caller 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Lua 2006; Martinović 2006; Orjuela-Rojas 2015; Pakpour 2015; Schröder 2014), two studies used the patient-weighted Quality of Life in Epilepsy-31 (QOLIE-31-P; (Tang 2015; Yadegary 2015), three studies used the Quality of Life in Epilepsy-89 (QOLIE-89; (Helde 2005; Hosseini 2016; Pramuka 2007)), and one study used a subscale item of the QOLIE-31 to inquire about overall QoL (Pfafflin 2016). The QOLIE-31-P is a modification of the QOLIE-31, with an additional question about an individual's subjective level of distress in each of the six subscales, which allows for an individually weighted calculation of scores with regard to the individual's subjective evaluation (Cramer 2003). All studies using QOLIE-31, QOLIE-31-P, and QOLIE-89 questionnaires reported pre- and post-intervention mean scores (± standard deviation (SD)). Three studies included the mean difference between pre- and post-intervention scores (± SD; (Fraser 2015; Helde 2005; Tang 2015)). Only Tang 2015 reported the percentage of participants achieving a minimum clinically important change.

Of the 15 studies that included the most commonly used epilepsy specific HRQoL questionnaires to measure outcomes (QOLIE-31, QOLIE-31-P, and QOLIE-31/89), we considered 12 studies that were clinically and methodologically homogeneous, for meta-analyses (Au 2003; Caller 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Helde 2005; Hosseini 2016; Martinović 2006; Orjuela-Rojas 2015; Pramuka 2007; Tang 2015; Yadegary 2015). Due to substantial baseline differences between intervention and control groups, we used the mean change from baseline (± SD) for the meta-analysis, rather than post-intervention scores (± SD). We sought required data from all authors. Five study authors provided unpublished data we could include in the meta-analysis: Orjuela-Rojas 2015 provided raw data to calculate the mean change from baseline (± SD); Fraser 2015 provided the mean change from baseline (± SD) for the control group; Helde 2005 provided raw data so we could convert the results from QOLIE-89 to QOLIE-31; Tang 2015 provided all converted scores from QOLIE-31-P to QOLIE-31, and the mean change from baseline (± SD); Caller 2016 provided the unadjusted mean change from baseline (± SD). Three studies did not provide the mean change from baseline (± SD; (Au 2003; Ciechanowski 2010; Martinović 2006)). We calculated the mean change from baseline as a difference between pre- and post-intervention means. In order to
calculate an adjusted SD, we grouped these three studies with studies investigating interventions that were comparable in intervention method, treatment setting (group versus individual), and total treatment time: Au 2003 with Tang 2015; Ciechanowski 2010 with Gandy 2014, and Martinović 2006 with Orjuela-Rojas 2015. This allowed us to calculate the adjusted SD of the mean change from baseline, based on the correlation between pre- and post-intervention means (± SD) of the studies with which they were grouped. Unfortunately, Martinović 2006 could not provide QOLIE-31 subscale outcomes, therefore, we only included the total score from his study. We presented the results of the studies that did not provide the raw QOLIE-89 data (Hosseini 2016; Pramuka 2007), or raw QOLIE-31-P data (Yadegary 2015) that would allow us to convert the results into QOLIE-31 scores, in narrative form. As a result, the meta-analysis finally comprised data from nine studies (Au 2003; Caller 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Helde 2005; Martinović 2006; Orjuela-Rojas 2015; Tang 2015).

We did not include five studies using QOLIE-31 outcome measures in the meta-analysis due to meaningful clinical heterogeneity. In two, the intervention delivery was not face-to-face; it was either web-based (Schröder 2014), or SMS-based (Lua 2013). In three others, the intervention goals were narrowly defined: increasing drug-related problems (Beretta 2014); increasing drug-adherence (Pakpour 2015); and increasing satisfaction with treatment and support (Pfäfflin 2016). We presented their results in narrative form. Two authors provided raw data that allowed us to calculate and present unpublished QOLIE-31 scores (Beretta 2014; Schröder 2014).

Other HRQoL outcome measures

Three studies used the World Health Organization Quality of Life instrument, short version (WHOQOL-BREF; (Lundgren 2006; Lundgren 2008; Schröder 2014)). We assumed satisfactory clinical homogeneity, so we considered data from Lundgren 2006 and Lundgren 2008 for meta-analysis. We did not include data from Schröder 2014 in the meta-analysis because they used a different intervention delivery, but they did provide unpublished data so that we could present WHOQOL-BREF results in narrative form. Three studies used the Satisfaction with Life Scale (SWLS; (Lundgren 2006; Lundgren 2008; Thompson 2010)). Thompson 2010 did not provide unpublished data (SD of post-intervention data), but we considered the data from Lundgren 2006 and Lundgren 2008 for meta-analysis because we assumed satisfactory clinical homogeneity.

We excluded seven studies from the meta-analyses because their HRQoL outcome measures were not comparable (DiIorio 2011; Jantzen 2009; Lundgren 2006; Lundgren 2008; May 2002; Rau 2006; Thompson 2010). We presented all of these outcomes in narrative form.

Psychiatric comorbidities: depression and anxiety

Several included studies also assessed psychiatric comorbidities. Even though some of them used the same outcome measure, we grouped individual results by outcome measures in narrative form rather than a meta-analysis. Since HRQoL constituted the main outcome measure of this review, we only included studies that investigated HRQoL, which led to the exclusion of some studies that included psychiatric symptoms as outcome measure, but not HRQoL. From this perspective, a meta-analysis of any outcome other than HRQoL would imply a serious selection bias.

Depression

Among the 24 included studies, ten studies examined the changes in level of depression (Caller 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Martinović 2006; May 2002; Orjuela-Rojas 2015; Schröder 2014; Tang 2015; Thompson 2010). Five studies used the Beck Depression Inventory or Beck Depression Inventory-II (Martinović 2006; Orjuela-Rojas 2015; Schröder 2014; Tang 2015; Thompson 2010); three studies used the Patient Health Questionnaire (Caller 2016; Fraser 2015; Thompson 2010). Two studies used the Hospital Anxiety and Depression Scale (Gandy 2014; Orjuela-Rojas 2015), and the other two studies used the Neurological Disorders Depression Inventory-Epilepsy Scale (Caller 2016; Gandy 2014). Two studies assessed suicidal ideation (Ciechanowski 2010; Orjuela-Rojas 2015). The ten studies used a total of six different outcome measures for depression.

Anxiety

Among the 24 included studies, four studies examined the changes in level of anxiety. Two studies used the Hospital Anxiety and Depression Scale for assessing anxiety (Gandy 2014; Orjuela-Rojas 2015). One study used the Generalized Anxiety Disorder-7 (Fraser 2015)), and one study used the Beck Anxiety Inventory (Tang 2015).

Seizure-related Outcomes

Eight studies measured seizure frequency (Au 2003; Ciechanowski 2010; Jantzen 2009; Lundgren 2006; Lundgren 2008; May 2002; Rau 2006; Tang 2015). Two studies used seizure severity measures: the Seizure Severity Index (Tang 2015) and the Liverpool Seizure Severity Scale (Pakpour 2015).

Participants

The majority of studies evaluated the benefit of interventions for adults with epilepsy; only two studies investigated educational interventions for children and adolescents with epilepsy (Jantzen...
(Rau 2006), one study investigated a psychological intervention for adolescents and young adults with epilepsy (Martinović 2006), two studies investigated mixed interventions for adolescents and adults (Caller 2016; Helde 2005), and two studies investigated educational interventions for adolescents and adults (May 2002; Pfafflin 2016).

Several studies used the participant's psychological functioning (e.g., depressive symptoms) as one of the inclusion criterion. Four studies included only adolescents with epilepsy and depressive symptoms (Ciechanowski 2010; Orjuela-Rojas 2015; Schröder 2014; Thompson 2010), one study included adolescents and young adults with epilepsy and subthreshold depressive symptoms (Martinović 2006), and one study included adults with epilepsy and self-reported psychological distress (Au 2003). Two studies included only adults with significant depression as assessed by the Patient Health Questionnaire (PHQ-9 score ≥ 10; (Ciechanowski 2010)), or major depression according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV (Orjuela-Rojas 2015). Another study included adults with self-reported depressive symptoms (Schröder 2014), but not severe depression, as indicated by a score of < 38 on the Center for Epidemiological Studies Depression scale (Thompson 2010). One study included only adults with epilepsy and other chronic comorbidities, because the intervention targeted adverse effects stemming from drug interactions (Beretta 2014). Another study included adolescents and adults with subjective memory complaints, since the intervention included special cognitive and memory training (Caller 2016).

Only six studies used inclusion criterion related to seizure frequency, epilepsy type, or drug-responsiveness: Au 2003 only included participants with at least two seizures per month; Lundgren 2006 and Lundgren 2008 only included participants with at least four seizures over three months; Tang 2015 only included participants with drug-resistant epilepsy; Hosseini 2016 only included participants with primary generalized tonic-clonic epilepsy and uncontrolled seizures; and Yadegary 2015 only included participants with at least one seizure during the past year. Altogether, the number of individuals with drug-responsive epilepsy and primary generalized epilepsy was comparably small in the study populations of all included studies.

Most studies excluded individuals with intellectual disability, and none of the studies reported whether individuals experienced nocturnal or diurnal seizures, or if individuals experienced seizure warnings.

We included more details on study participants in Table 1 and the 'Characteristics of included studies' tables. Since the subgroups outlined in the review protocol were either comparatively small or the information was unavailable, we did not undertake any subgroup analysis.

We found one study that was still ongoing. See Characteristics of ongoing studies for details.

Excluded studies

We excluded 17 RCTs, since they did not examine HRQoL outcomes.

Risk of bias in included studies

We included details of our judgements and the rationale in the 'Characteristics of included studies' tables, and displayed summaries in Figure 2 and Figure 3. We shared the details of our judgements with all study authors prior to the publication of this review for further clarification.

Figure 2. 'Risk of bias' graph: review authors' judgements about each 'risk of bias' domain presented as percentages across all included studies.
Figure 3. 'Risk of bias' summary: review authors' judgements about each 'risk of bias' domain for each included study

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Allocation

The majority of studies (N = 17) reported an adequate method of random sequence generation (Beretta 2014; Caller 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Helde 2005; Lua 2013; Lundgren 2006; Lundgren 2008; Martinovic 2006; May 2002; Pakpour 2015; Pfafflin 2016; Pramuka 2007; Schröder 2014; Tang 2015; Yadegary 2015). Two studies did not provide a sufficient description of the randomization process, hence they were classified as unclear (Hosseini 2016; Thompson 2010). Reasons for a high risk of bias rating included quasi-randomized trial designs, such as a matched design (Au 2003), alternating assignment (DiLorio 2011), and allocation based on participants’ application to one of two available courses and the availability of spaces, in a wait-list control design (Jantzen 2009; Rau 2006). One study was rated with very serious risk of bias, since the allocation depended on the participants’ ability to attend the meetings (Orjuela-Rojas 2015). One author provided further information to clarify the randomization procedure that had not been sufficiently described in the publication (Rau 2006).

The majority of the studies (N = 13) reported proper procedures for allocation concealment (Beretta 2014; Ciechanowski 2010; DiLorio 2011; Fraser 2015; Gandy 2014; Helde 2005; Lundgren 2006; Lundgren 2008; Martinovic 2006; Pfafflin 2016; Schröder 2014; Tang 2015; Hosseini 2016). Allocation concealment can be considered inherent in study designs investigating a web-based intervention with a web-based registration and allocation procedure, hence a study with a low-quality randomization procedure could indeed feature a high-quality allocation concealment (DiLorio 2011). Seven studies reported an incorrect allocation procedure (Au 2003; Caller 2016; Jantzen 2009; May 2002; Rau 2006; Thompson 2010; Orjuela-Rojas 2015), and four studies provided insufficient descriptions (Luo 2013; Pakpour 2015; Pramuka 2007; Yadegary 2015). Seven authors provided further information to clarify the allocation concealment procedure that had not been sufficiently described in the publication (Au 2003; Beretta 2014; Fraser 2015; Lundgren 2006; Lundgren 2008; May 2002; Tang 2015).

Blinding

Blinding of participants and personnel is almost impossible to achieve when studying psychological treatments, hence the majority of studies had a high risk of bias (N = 22, Au 2003; Beretta 2014; Caller 2016; Ciechanowski 2010; DiLorio 2011; Fraser 2015; Gandy 2014; Helde 2005; Hosseini 2016; Jantzen 2009; Lundgren 2006; Lundgren 2008; May 2002; Orjuela-Rojas 2015; Pakpour 2015; Pfafflin 2016; Pramuka 2007; Rau 2006; Schröder 2014; Tang 2015; Thompson 2010; Yadegary 2015). Four studies managed to blind the participants in both the treatment and the active control group, by telling them that they would participate in an intervention to improve coping with epilepsy (Lua 2013; Lundgren 2006; Lundgren 2008; Tang 2015). This was, of course, only possible if the study designs used an immediate and active control arm (social support group in two trials, Lundgren 2006; Tang 2015; yoga in one trial; Lundgren 2008; and paper-based education material in one trial, Lua 2013). There were no randomized personnel in two studies investigating a web-based intervention (Lua 2013; Schröder 2014). One study was classified as overall low risk, as the therapists who delivered the treatment (Cognitive Behavioral Intervention (CBI) and counselling as usual) were blinded to the participants’ group status: the researchers only told the therapists that they would deliver psychological means to improve coping with epilepsy (Martinovic 2006).

In one study, the blinding status of the personnel delivering an SMS-based intervention remained unclear (Lua 2013). The risk of non-blinding of any type of control group that did not receive an immediate control intervention was considered to be especially problematic, since it might lead to baseline imbalances of participant-reported outcome parameters, due to disappointment, i.e. the impression of having been denied an opportunity. Thus, the risk was considered to be lower in studies that obtained baseline measures prior to randomization. Seven studies achieved this (DiLorio 2011; Fraser 2015; Gandy 2014; Helde 2005; Hosseini 2016; Lua 2013; Pfafflin 2016).

Blinding of the assessment of participant-reported outcome data was adequate in the majority of studies (N = 15, Au 2003; Beretta 2014; Caller 2016; Ciechanowski 2010; Fraser 2015; Helde 2005; Hosseini 2016; Jantzen 2009; Martinovic 2006; May 2002; Orjuela-Rojas 2015; Pfafflin 2016; Rau 2006; Schröder 2014; Tang 2015). Four studies provided insufficient information (Lua 2013; Pakpour 2015; Thompson 2010; Yadegary 2015). Five studies had a high detection bias, because personnel conducting the outcome assessment were aware of the treatment status (DiLorio 2011; Gandy 2014; Lundgren 2006; Lundgren 2008; Pramuka 2007), although additional information was provided by Lundgren 2006 and Lundgren 2008 that outcome assessment was blinded only on seizure-related data. Ten authors provided further information on 11 studies to clarify the blinding of outcome assessment that had been insufficiently described in the publication (Au 2003; Beretta 2014; DiLorio 2011; Fraser 2015; Gandy 2014; Jantzen 2009; Lundgren 2006; Lundgren 2008; Martinovic 2006; May 2002; Orjuela-Rojas 2015).

Incomplete outcome data

Psychological treatments for people with epilepsy (Review)
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We rated three studies at low risk of attrition bias because all randomized participants completed the study (Au 2003; Lundgren 2006; Lundgren 2008). We rated eight studies at low risk, as there were only a small amount of missing data, which was balanced across the groups, with justifiable reasons (Beretta 2014; Ciechanowski 2010; Helde 2005; Jantzen 2009; Lua 2013; Martinovic 2006; Pakpour 2015; Tang 2015). We rated 10 studies at high risk of bias, because of larger amounts of missing data (we applied a cut-off of 15% for short term interventions (shorter than six months), and 20% for long-term interventions (at least six months)). Losses were balanced in one study (Fraser 2015), and unbalanced in seven studies (Caller 2016; DiIorio 2011; Gandy 2014; Hosseini 2016; Orjuela-Rojas 2015; Pfafflin 2016; Praamuka 2007). One study excluded participants who had missed more than one intervention session, which indicated that no intention-to-treat (ITT) analysis had been undertaken (Hosseini 2016). Three studies with overall high attrition only provided the total number of participants lost to follow-up, without reporting whether they belonged to the intervention or the control group (May 2002; Rau 2006; Thompson 2010). We assigned an unclear risk to one study that did not provide data on their attrition rate (Yadegary 2015). The risk of attrition is usually quite high in experimental studies that require regular, active, and personal involvement of study participants, as is the case with psychological treatments. There were two studies that reimbursed their participants for participation in the study, but had a high attrition rate nonetheless (DiIorio 2011; Praamuka 2007).

### Selective reporting

Sixteen studies were rated low risk of bias, as there was no evidence of selective outcome reporting within the publications, when examining all outcomes reported in the papers (Au 2003; Beretta 2014; Caller 2016; Fraser 2015; Gandy 2014; Helde 2005; Hosseini 2016; Jantzen 2009; Lua 2013; Lundgren 2006; Lundgren 2008; May 2002; Orjuela-Rojas 2015; Pakpour 2015; Pfafflin 2016; Rau 2006; Tang 2015; Yadegary 2015). We had initially rated six studies at a high risk of bias, as there was evidence of selective outcome reporting within the publications (Ciechanowski 2010; DiIorio 2011; Martinovic 2006; Praamuka 2007; Schröder 2014; Thompson 2010). Two authors provided additional data (DiIorio 2011; Schröder 2014). Therefore, we only assessing four studies at high risk of bias due to evidence of selective outcome reporting within the publications (Ciechanowski 2010; Martinovic 2006; Praamuka 2007; Thompson 2010).

We requested study protocols. We received nine responses with complete registered protocols or documentation of the included outcome measures, and assessed the risk against these documents (Beretta 2014; Caller 2016; DiIorio 2011; Fraser 2015; Helde 2005; May 2002; Rau 2006; Schröder 2014; Tang 2015). We confirmed a rating of low risk of bias in five of these studies as there was no evidence of selective outcome reporting following review of the documents (Beretta 2014; Caller 2016; Fraser 2015; Rau 2006; Tang 2015). For one study, additional outcome measures that would have been part of the scope of this review had originally been planned but not obtained, due to a change of protocol (Schröder 2014). For three studies, it appeared that additional outcome measures had been obtained during the course of the study, but was not mentioned in the final publication (DiIorio 2011, Helde 2005; May 2002). However, these data were not part of the scope of this study. Nonetheless, we sought and obtained these data in two cases (DiIorio 2011; May 2002). In one case, the omitted outcome data that had aimed at capturing the development of the health-economic variables (such as frequency of hospital admissions, missed school or work days, etc.) had been collected but had never been analyzed (Helde 2005).

### Other potential sources of bias

We considered other potential sources of bias, such as language bias, selective recruitment, and fidelity to the intervention protocol. Language bias remained unclear. We included one non-English publication, which was published in German (Rau 2006). However, we did not search non-English databases. In general, we did not have enough evidence to judge risks of bias in selective recruitment and fidelity to the intervention protocol. As a result, we judged the risk of bias as unclear in most cases. Three studies provided details on their attempts to ensure fidelity to the intervention protocol. Ciechanowski 2010 and Gandy 2014 used standard training protocols and supervision; Thompson 2010 included additional adherence checklists. We assessed that the risk of infidelity to the intervention protocol could be considered to be relatively low in the five studies in which the intervention was delivered by one therapist (Fraser 2015; Helde 2005; Hosseini 2016; Lundgren 2006; Lundgren 2008), or two therapists who had developed the intervention (Tang 2015; Pakpour 2015), and very low in the two studies in which the delivery of the intervention was Internet based (DiIorio 2011; Schröder 2014).

### Effects of interventions

See: Summary of findings for the main comparison

Psychological treatments compared with usual or supportive care

We have listed our outcomes, categorized according to our operational definition of psychological treatment types, in Table 2.

### Health-related quality of life

#### Quality of Life in Epilepsy Inventory (QOLIE-31, QOLIE-31-B QOLIE-89)

Nine studies (468 participants) investigated comparable psychological interventions and used the most common quality-of-life...
tool (QOLIE-31) as their outcome measure (also see Summary of findings for the main comparison). Two studies on adolescents and adults (Caller 2016; Helde 2005), one on adolescents and young adults (Martinovic 2006), and six on adults contributed data to the meta-analysis (Au 2003; Ciechanowski 2010; Fraser 2015; Gandy 2014; Orjuela-Rojas 2015; Tang 2015). We found statistically significant mean changes in the total score and each sub-scale measure, except social functioning. A positive mean change indicated a post-intervention improvement.

- Total score (nine RCTs, 468 participants): significant mean change of 5.68 points (95% CI 3.11 to 8.24; P < 0.0001; Chi² P = 0.08; I² = 43%); Analysis 1.1; Figure 4

**Figure 4. Forest plot of comparison: 1 QOLIE-31- Comparison of mean change from baseline, outcome: 1.1 QOLIE-31- total score.**

- Emotional well-being (eight RCTs, 440 participants): significant mean change of 7.03 points (95% CI 2.51 to 11.54; P = 0.002; Chi² P = 0.02; I² = 59%); Analysis 1.2; Figure 5

**Figure 5. Forest plot of comparison: 1 QOLIE-31- Comparison of mean change from baseline, outcome: 1.2 QOLIE-31 - emotional well-being subscale.**

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• Energy and fatigue (eight RCTs, 440 participants): significant mean change of 6.90 points (95% CI 3.49 to 10.31; P < 0.0001; Chi² P = 0.24; I² = 24%); Analysis 1.3; Figure 6.

Figure 6. Forest plot of comparison: I QOLIE-31 - Comparison of mean change from baseline, outcome: 1.3 QOLIE-31 - energy and fatigue subscale.

- Overall QoL (eight RCTs, 440 participants): significant mean change of 6.47 points (95% CI 2.68 to 10.25; P = 0.0008; Chi² P = 0.06; I² = 49%); Analysis 1.4; Figure 7.

Figure 7. Forest plot of comparison: I QOLIE-31 - Comparison of mean change from baseline, outcome: 1.4 QOLIE-31 - overall QoL subscale.

• Seizure worry (eight RCTs, 440 participants): significant mean change of 5.96 points (95% CI 2.50 to 9.42; P = 0.0007; Chi² P = 0.86; I² = 0%); Analysis 1.5.

• Cognitive functioning (eight RCTs, 440 participants): significant mean change of 3.00 points (95% CI 0.21 to 5.78; P = 0.04; Chi² P = 0.93; I² = 0%); Analysis 1.6.

• Medication effects (eight RCTs, 440 participants): significant mean change of 3.84 points (95% CI 0.28 to 7.41; P
We reported the results of the seven studies, which could not be included in the meta-analysis, in narrative form. They were excluded because of the uniqueness of the intervention protocol (four studies, Beretta 2014; Lua 2013; Pakpour 2015; Schröder 2014), or inadequate data (use of QOLIE-89; two studies, Hosseini 2016; Pramuka 2007); use of QOLIE-31-P (Yadegary 2015). Four studies reported significant improvements in the treatment group when comparing the mean post-intervention outcomes: Lua 2013 (intervention mean 69.2 (SD 17.4) versus control mean 58.4 (SD 13.6); P = 0.007); Pakpour 2015 (intervention mean 62.14 (SD 13.21) versus control mean 56.01 (SD 12.12); P < 0.001 (adjusted for variables such as age and gender); Yadegary 2015 (intervention mean 72.18 (SD 11.34) versus control mean 53.49 (SD 15.97); P < 0.001)). Hosseini 2016 reported a significant mean increase in the total score for the intervention group (mean change 35.95 (SD 8.74); P < 0.001) and a significant mean decrease for the control group (mean change -8.07 (SD 8.91); P < 0.001). The remaining four studies did not report a significant mean post-intervention difference in total scores between the treatment and control groups: Beretta 2014 (intervention mean 63.75 (SD 15.48) versus control mean 65.04 (SD 14.38); P value was reported to be non-significant, without precise value); Pfafflin 2016 (intervention mean 68 (SD 21) versus control mean 66 (SD 20), P value was reported to be non-significant, without precise value); Pramuka 2007 (intervention mean 67.3 (SD 2.6) versus control mean 65.0 (SD 2.8); P value was reported to be non-significant, without precise value); Schröder 2014 (intervention mean 31.72 (SD 13.37) versus control mean 32.73 (SD 13.37); P = 0.755). The potential impact of the three studies that did not contribute data to the meta-analysis was probably small (Hosseini 2016 (28 participants); Yadegary 2015 (30 participants); Pramuka 2007 (31 participants), especially since two studies also reported significantly higher post-intervention QoL in the treatment over the control groups (Hosseini 2016; Yadegary 2015).

Since the majority of included studies had at least some bias issues, we did not perform a sensitivity analysis to compare studies with low risk of bias with studies with high risk of bias.

Other HRQoL outcome measures

Eight studies used other HRQoL outcome measures (Diliorio 2011; Jantzen 2009; Lundgren 2006; Lundgren 2008; May 2002; Rau 2006; Schröder 2014; Thompson 2010). A positive mean change indicated a post-intervention improvement. Pooled post-intervention results from two studies, using the World Health Organization Quality of Life instrument, short version (WHOQOL-BREF), showed a non-significant mean difference of 0.57 points (95% CI -4.19 to 5.34; 45 participants; P = 0.09; I² = 33%; Analysis 2.1 (Lundgren 2006; Lundgren 2008)). Schröder 2014 also reported a non-significant mean difference between groups with the WHOQOL-BREF (intervention mean 75.9 (SD 15.04) versus control mean 78.62 (SD 17.39); P value was non-significant, without precise value).

Pooled post-intervention results from two studies, using the Satisfaction with Life Scale (SWLS), reported a non-significant mean difference of 5.46 points between groups (95% CI -2.97 to 13.89; 45 participants; P = 0.20; I² = 11%; Analysis 3.1 (Lundgren 2006; Lundgren 2008)). However, these results showed levels of statistical heterogeneity of concern, which might have been due to clinical heterogeneity, since different control groups were used in the studies (Lundgren 2006 used supportive therapy, while Lundgren 2008 used yoga). Using the SWLS, Thompson 2010 reported a non-significant difference between groups (21 (treatment mean) versus 18 (wait-list control mean); P = 0.090; SD was not reported).

Four studies could not be combined with other data because they used different HRQoL outcome measures. Jantzen 2009 reported that children and adolescents in the treatment group showed a significant increase in the social exclusion subscale in DISABKIDS, indicating better quality of life, based on post-intervention scores (P value was not provided; d = 0.3 (Cohen) Cohen 1988). The three remaining studies did not report a significant post-intervention difference in mean QoL scores between groups. Diliorio 2011 used the Quality of Life in Epilepsy-10 (intervention mean 33.77 (SD 7.96) versus wait-list control mean 33.27 (SD 7.52); P = 0.731); May 2002 used the Short-Form 36 mental component (intervention mean 43.69 (SD 11.51) versus wait-list control mean 42.46 (SD 11.75), and the physical component (intervention mean 50.39 (SD 9.37) versus wait-list control mean 52.00 (SD 8.7); P = 0.075); Rau 2006 used the self-reported German questionnaire, Gesundheitsbezogene Lebensqualität und psychosoziale Auswirkungen der Epilepsie, (HRQoL and psychosocial consequences of epilepsy (intervention mean 70.62 (SD 13.29) versus wait-list control mean 77.25 (SD 15.0); P = 0.075).

Psychiatric comorbidities outcome measures

Depression

A total of eleven studies included the level of depression as an outcome measure; all of them indicated that there were no statistical differences between the treatment and control group at baseline. We used post-intervention means to compare the differences between the two groups. Seven studies reported a significant post-intervention difference between the intervention and control groups (Ciechanowski 2010; Fraser 2015; Gandy 2014; Martinovic 2006; Schröder 2014; Tang 2015; Thompson 2010). Five studies used more than one outcome measure (Caller 2016; Ciechanowski...
One study, which used two outcome measures reported both significant and non-significant results (Ciechanowski 2010). Four studies reported only non-significant results ( Caller 2016; May 2002; Orjuela-Rojas 2015; Pfäfflin 2016). A lower mean score indicated less depressive complaints.

Beck Depression Inventory and Beck Depression Inventory-II (BDI and BDI-II)
In the five studies that used the BDI or BDI-II, four of them reported significantly better post-intervention mean depressive symptoms in the treatment groups: Martinović 2006 (intervention mean 5.4 (SD 2.97) versus control mean 7.8 (SD 2.66); P < 0.05); Schröder 2014 (intervention mean 15.84 (SD 13.00) versus control mean 18.37 (SD 10.23); P = 0.01); Tang 2015 (intervention mean 6.90 (95% CI 4.49 to 9.31) versus control mean 9.47 (95% CI 6.26 to 12.67); P = 0.045); Thompson 2010 (intervention mean 5.5 versus control mean 10.6; P value < 0.01). Orjuela-Rojas 2015 reported a non-significant difference (intervention mean 17.2 versus control mean 14.6; P = 0.58; SD was not reported).

Hospital Anxiety and Depression Scale (HADS) for assessing depression (HADS-D)
Three studies used the HADS to assess depressive symptoms (Gandy 2014; Pfäfflin 2016; Orjuela-Rojas 2015). Gandy 2014 reported significantly better post-intervention depressive symptoms in the treatment group (intervention mean 4.5 (SD 3.59) versus control mean 5.50 (SD 5.26); P = 0.048), while Orjuela-Rojas 2015 (intervention mean 5.4 versus control mean 8.1; P = 0.93; SD was not reported), and Pfäfflin 2016 (intervention mean 9.0% ≥11 and control mean 5.5% ≥11; P value was non-significant, without precise value) reported a non-significant difference.

Patient Health Questionnaire-9 for assessing depression (PHQ-9)
Three studies used the PHQ-9 to assess depressive symptoms (Caller 2016; Fraser 2015; Thompson 2010). Caller 2016 reported a non-significant difference in post-intervention changes (intervention mean change 0.7 (SD 1) versus control mean change 1.2 (SD 2)). Fraser 2015 reported significantly lower depression scores in the treatment group (intervention mean 6.3 (SD 5.5) versus control mean 8.6 (SD 6); P = 0.02). Thompson 2010 used the PHQ-9 to identify individuals with a major depressive disorder at baseline, however, did not provide post-intervention data.

Other depression outcome measures
Two studies that used other measures found significantly reduced post-intervention depressive symptoms in the treatment group. Martinović 2006 used the Center for Epidemiological Study on Depression scale (intervention mean 9.8 (SD 4.2) versus control mean 13.6 (SD 4.64); P < 0.05) and the Hamilton Depression Scale (intervention mean 3.3 (SD 1.29) versus control mean 5.8 (SD 1.98); P < 0.05). Gandy 2014 used the Neurological Depressive Disorders Inventory for Epilepsy (NDDI-E; intervention mean 14.3 (SD 3.4) versus waiting-list control mean 16.48 (SD 3.81); P = 0.045).

Three studies that used other measures found non-significant differences in depressive symptoms between groups. Caller 2016 used the NDDI-E (treatment mean change from baseline -0.4 (SD 0.6) versus control mean change from baseline 0.7 (SD 0.8); P = 0.30). Ciechanowski 2010 used the Hopkins Symptom Checklist-20 (treatment mean change from baseline -0.18 (SD 0.7) versus control mean change from baseline -0.48 (SD 0.7); P = 0.09). May 2002 used the Depressive Mood Scale (intervention mean 13.63 (SD 8.99) versus waiting-list control mean 12.22 (SD 8.80); the P value was non-significant, without precise value).

Suicidal ideation
While Ciechanowski 2010 reported a significantly smaller proportion of participants with suicidal ideation at follow-up (decreasing 24% in the intervention group and increasing 12% in the usual care group; P = 0.025; post-treatment outcomes were not reported), Orjuela-Rojas 2015 did not find a significant difference in suicide risk between groups, using the Mini International Neuropsychiatric Interview (intervention mean 1.1 versus control mean 0.6; P = 0.42; SD was not reported).

Anxiety
A total of five studies included anxiety level as an outcome measure (Fraser 2015; Gandy 2014; Orjuela-Rojas 2015; Pfäfflin 2016; Tang 2015). One study reported significant baseline differences between the intervention (11.2) and control (8.3); P = 0.04 (Orjuela-Rojas 2015). We used post-intervention means to compare the difference between the two groups. A lower mean score indicated fewer anxiety complaints.

Beck Anxiety Inventory (BAI)
Among the five studies that examined anxiety symptoms, only one study, using the BAI, reported significantly fewer post-intervention anxiety symptoms between groups (intervention mean 9.73 (95% CI 6.35 to 13.22) versus control mean 10.70 (95% CI 7.24 to 14.16); P = 0.008 (Tang 2015)). None of the remaining studies, assessing anxiety with validated outcome measures, reported a significant difference.
Hospital Anxiety and Depression Scale (HADS-A) for assessing anxiety (HADS-A)

Gandy 2014 reported a non-significant post-intervention difference between groups (intervention mean 6.11 (SD 2.96) versus control mean 7.45 (SD 3.78); P = 0.089). Similar findings were also reported by Pfafflin 2016 (20.9% with HADS-A ≥ 11 in the intervention group and 17.8% with HADS-A ≥ 11 in the control group; P value was non-significant, without precise value) and Orjuela-Rojas 2015 (intervention mean 9.7 versus control mean 9.2; P = 0.8). It was worth noting that in this study, the treatment group had a significantly higher anxiety score at baseline compared to control (11.2 versus 8.3; P value = 0.04).

Generalized Anxiety Disorder-7 (GAD-7)

Fraser 2015 did not find a significant difference between groups in symptoms of anxiety, using the Generalized Anxiety Disorder-7 (intervention mean 5.4 (SD 6.6) versus control mean 6.1 (SD 5.1); P = 0.282).

Seizure-related outcomes

A total of nine studies included seizure-related variables as outcome measures (Au 2003; Ciechanowski 2010; Jantzen 2009; Lundgren 2006; Lundgren 2008; May 2002; Pakpour 2015; Rau 2006; Tang 2015). All of them reported no evidence of baseline imbalance between groups except in Lundgren 2008, in which no statistics were provided, and baseline imbalance was indicated from the raw data (treatment group n = 10, seizure frequency = 414; active control group n = 8, seizure frequency = 33). However, this study reported that 50% of participants in both the intervention and the active control groups where seizure free at post-intervention. Three studies reported a significant post-intervention reduction in seizure frequency between groups: Tang 2015 (seizures in six weeks: intervention mean 5.9 (95% CI 2.88 to 8.92) versus control mean 7.33 (95% CI 3.46 to 11.21); P = 0.018); May 2002 (seizures per month in six months: intervention mean 2.77 (SD 1.64) versus control mean 2.74 (SD 1.62); P < 0.041); Lundgren 2006 (seizures in one month: intervention mean 0.71 (SD 0.91) versus control mean 0.70 (SD 3.51); P < 0.001). Five studies reported non-significant post-intervention differences in seizure frequency between groups (Au 2003; Ciechanowski 2010; Jantzen 2009; Lundgren 2008; Rau 2006). Pakpour 2015 reported a significant post-intervention reduction in seizure severity using the Liverpool Seizure Severity Scale (intervention mean 47.24 (SD 17.41) versus control mean 58.09 (SD 21.75); P < 0.05), while Tang 2015 found no significant post-intervention changes using the Seizure Severity Index (intervention mean 2.55 (95% CI 2.06 to 3.03) versus control mean 2.91 (95% CI 2.44 to 3.38); P > 0.05).

Lundgren 2006 and Lundgren 2008 measured seizure index (seizure frequency x seizure duration in seconds), which was not a validated outcome measure. With a comparable baseline seizure index, Lundgren 2006 reported significant post-intervention reduction. Lundgren 2008 reported a significant difference in change scores between the two groups.

DISCUSSION

Despite our broad operational definition, psychological treatments for people with epilepsy have been investigated in a relatively small number of randomized controlled trials. We found 24 RCTs that fit our operational definition and investigated HRQoL as a primary or secondary outcome parameter.

Summary of main results

Primary outcome measure

The Quality of Life in Epilepsy Inventory (QOLIE-31, QOLIE-31x, QOLIE-89) was the most commonly used outcome measure for HRQoL. It was used in 17 studies. Results from the meta-analysis (nine studies) found significant post-intervention improvement for the total score and six out of seven QOLIE-31 subscales (emotional well-being, energy and fatigue, overall QoL, seizure worry, cognitive functioning, medication effects; Au 2003; Callen 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Helde 2005; Martinovic 2006; Orjuela-Rojas 2015; Tang 2015). The mean improvement of the total score and three subscales (emotional well-being, energy and fatigue, and overall QoL) exceeded the minimally important change threshold established by Borchs 2012, for a small effect size [d = 0.3 (Cohen)], indicating a clinically meaningful post-intervention improvement of QoL. Four of the remaining eight studies, which were not included in the meta-analysis, reported significant differences between the treatment and control groups at post-treatment measures (Hosseini 2016; Lara 2013; Pakpour 2015; Yadegary 2015). For the eight studies that used six HRQoL outcome measures other than QOLIE inventories, only two studies found a significant difference between the mean post-intervention scores in the treatment and control groups, indicating significantly better QoL in the treatment groups (Jantzen 2009; Lundgren 2006).

Secondary outcome measures

The majority of studies (7/11) examining depressive symptoms reported a decrease in symptoms for those receiving the treatment intervention. In contrast, only one study out of five examining anxiety levels found a significant post-intervention reduction in the treatment groups. Slightly less than half of the studies (3/7) investigating seizure frequency reported a significant reduction at
post-intervention in the treatment groups. Only two studies investig-
tated seizure severity; one reported a significant reduction in the
treatment group. Two studies by the same lead author examined
seizure index (seizure frequency x seizure duration in seconds), a
non-validated measure, and reported significant post-treatment
reduction in the treatment groups.

Overall completeness and applicability of evidence

The studies in the current review evaluated complex psychological
treatments, typically applied in tertiary care settings, and in-
volved participant groups with comparable underlying epilepsy
diagnoses, but differing severities of psychiatric and somatic co-
morbidities, and diverse cultural, ethnic, and socioeconomic back-
grounds. There were differences between the included studies in
their stated treatment methods, goals, strategies, and theoretical
underpinnings. Psychologists with varying levels of experience de-
ivered most of the treatments; team efforts including a wider
range of specialists (doctors, nurses, social workers, etc.) were in-
volved in some educational interventions. In some cases, the work
of these therapists was carefully structured and supervised, while
some studies presumably relied on shorter training courses.

Nine different outcome measures were used to investigate our pri-
mary outcome measure. Hence, the efforts to pool data were com-
tered, to some extent, by the wide diversity of outcome measure
and interventions used in these trials. These circumstances were
addressed by focusing on our meta-analyses on psychological and self-
management interventions, while making an effort to include as
many QOLIE inventories as possible, in a meaningful way, by
converting QOLIE-31-P and QOLIE-89 to QOLIE-31, if the
necessary raw data were provided, and analyzing the mean change
from baseline. We have no reason to think that the results from
this meta-analysis should not be applicable in similar settings and
patient groups.

Quality of the evidence

We only pooled results from studies measuring the same construct
(QOLIE-31, QOLIE-31-P, QOLIE-89) and limited meta-an-
alysis to fairly similar interventions to avoid clinical heterogene-
ity. Overall, the quality of evidence of the meta-analysis was lim-
ited by a serious risk of bias in some of the included studies (e.g.
Orjuela-Rojas 2015 with four high risk and one unclear rating out
of seven ‘risk of bias’ parameters). Since the majority of included
studies had at least some bias issues, we did not perform a sensi-
tivity analysis comparing studies with low risk of bias with studies
with high risk of bias. Given that the evidence directly answered
our healthcare question, the results were precise enough, and fairly
consistent across studies, and we found no evidence of publication
bias or a dose-response gradient in the included studies, we as-
essed there was no reason to further downgrade the quality of ev-
dence. As the effect was not large, there was no reason to upgrade
the quality of evidence either. Consequentially, interpreting these
findings with the GRADE approach, we are moderately confident
in the effect estimate that psychological interventions and self-
management interventions may enhance overall quality of life in
people with epilepsy and in subdomains of epilepsy-related QOL,
namely energy and fatigue, overall QoL, and emotional well-be-
ing.

Potential biases in the review process

Identifying relevant studies that fit our broad operational defini-
tion of psychological treatments was challenging. As outlined in
the review protocol, we searched a wide variety of databases, in-
cluding trial registers, and scanned reference lists of relevant sys-
tematic reviews. Two review authors independently evaluated all
studies and referred to the wider group of authors or the Epilepsy
Review Group with any unresolved questions. Although this whole
process was carried out carefully, we cannot discount the possi-
bility that we may have missed a relevant study, or misjudged an
included study or study outcome. Since this review will be peri-
odically updated, we will include any missed relevant studies, and
correct misjudgements of included studies or study outcomes that
come to our attention, in future updates. Even though many of
the included studies were published despite finding non-signifi-
cant results, we cannot discount the potential risk of publication
bias. However, the research community did not make us aware
of trials that had been stopped or not published because of non-
significant findings.

Two authors of our author team had also authored three of the
included studies (Lundgren 2006; Lundgren 2008; Tang 2015). 
Following the strict standards of the Cochrane review process, we
had the impression that this contributed a necessary critical ex-
pertise with the implementation of RCTs in this area of research,
rather than an increased risk of bias. Lundgren had not been in-
volved in the review process. Since Tang had been involved in the
review process, eligibility and risk of bias of her study was assessed
by a second author with no conflict of interest (MR).

Agreements and disagreements with other studies or reviews

The results of this review reinforced the conclusions of a recent
systematic review of psychological treatments for epilepsy, which
suggested that cognitive behavioral therapy and mindfulness-based
interventions had consistently demonstrated significant improve-
ments in HRQoL in prospective uncontrolled, as well as in con-
trolled study designs (Tang 2014).

This review was in keeping with a systematic review of cognitive
behavioral therapy for depression in people with epilepsy, which
suggested that interventions tailored toward improving depression were possibly efficacious (Gandy 2013). Our results were also in line with the previous Cochrane review focusing on seizure frequency as a primary outcome parameter, in that no reliable conclusions could be drawn regarding the efficacy of psychological treatments in controlling seizures (Ramaratnam 2008).

When conducting a review of randomized controlled trials investigating psychological treatments, which categorizes the interventions according to main treatment methods, goals, and strategies, we need to include two fundamental aspects of criticism: The feasibility of using randomized trial designs to study psychological interventions has been repeatedly challenged, mainly because the possibility of realistically balancing prognostic factors, on average, across intervention groups, is questioned. The psychological (and psychopathological) make-up of most participants is regarded as being too multi-faceted for this endeavour to be successful (Tschuschke 2005).

Furthermore, it has been suggested that only a small percentage of the therapeutic effect in psychological treatment can be attributed to treatment methods and treatment strategies, whereas the biggest effect of psychological treatment is attributed to the therapeutic relationship between client and therapist (Baldwin 2013). This would be difficult to quantify, and as far as we know, no RCTs investigating psychological treatment for epilepsy included this as a variable.

**AUTHORS’ CONCLUSIONS**

**Implications for practice**

We found moderate-quality evidence that psychological interventions and self-management interventions benefited adults with epilepsy in terms of quality of life, emotional well-being, and reduced fatigue. The effect was significantly better than usual care, social support, counselling as usual, or selective serotonin reuptake inhibitors. Unfortunately, we found few interventions focused on quality of life in children and adolescents.

**Implications for research**

**Increasing overall quality of reporting**

In many cases, the quality of the study design and its implementation appeared to be better than the actual publication suggested. There are mechanisms available to raise the quality of reporting (e.g. submitting manuscripts of RCTs with a CONSORT check list (Schulz 2010)). Adherence to the CONSORT guidelines and use of the CONSORT check list may not only increase the effort by authors and reviewers, but it may also raise the quality of reporting in this resource intense field of research. The quality of reporting may be improved with small changes, such as including the descriptor ‘assessor blinded’ in the title, since depending on the study design, this may be the only type of blinding that is feasible in this area of research. Adhering to CONSORT guidelines may be made difficult by a journal’s word limitations policies. If that is the case, pertinent details regarding the study design should be submitted as supplementary materials published online. Publication of research designs prior to conducting a study is now required by many journals, which increases transparency. The CONSORT group has developed an extension for trials assessing nonpharmacological treatments, to acknowledge and help navigate the specific challenges that are not addressed in the original CONSORT guidelines (Boutron 2008).

In addition, specific information about participant screening and selection will allow clinicians to assess the applicability of an intervention to their clinical setting or to modify an intervention for their patient population. We encourage the reporting of non-significant study results, since they also make important contributions to the concerns of the whole scientific community.

**Increasing comparability by using common and meaningful HRQoL outcome measures**

Researchers need to make sure that their outcome measures match the treatment goal of the investigated intervention (e.g. self-management, coping, etc.), and HRQoL may only constitute a secondary outcome measure. Despite diverse treatment goals and outcomes, the broad use of QOLIE inventories would increase comparability of studies investigating psychological treatments for children and adults with epilepsy.

Since many psychological treatments involve patient-oriented goal setting, it would be interesting to explore if the extended Quality of Life in Epilepsy-31-P would provide a more accurate reflection of the treatment effects, due to the individually weighted calculation of scores with regard to the individual’s subjective evaluation. This exploration would require the correlation of this extended version with quantitative and qualitative clinical data in trials investigating psychological treatments. No pediatric RCTs were included in the meta-analysis due to lack of epilepsy specific HRQoL outcomes. Future studies should incorporate HRQoL measures that qualify as common data elements.

To help with the interpretation and evaluation of clinical rather than statistical relevance of outcomes, we recommend that all studies using HRQoL outcome measures for which a minimum clinically important change has been determined, include the percentage of participants whose results reached a minimum clinically important change, with confidence intervals.

If a minimum clinically important change has not been established, providing effect sizes would help readers to assess the clinical meaning of statistical results.
Increasing overall quality of study designs

In order to increase the overall quality of study designs, adequate randomization and allocation concealment, and blinded outcome assessment should be pursued when conducting RCTs investigating psychological treatments for people with epilepsy. As attrition is often high in this type of research, which requires active participant participation, an intention-to-treat analysis (or other appropriate statistical analysis accounting for follow-up data) should be carried out. In regard to active and immediate control groups, supportive therapy, social support, or regular counselling can be used as a control group for the effects of attention, which allows blinding of the participants to their treatment arm (Lundgren 2006; Martinovi 2006; Tang 2015). To facilitate the attribution of treatment effects, the use of antiepileptic drugs and the resulting changes should be recorded. There are measures available (fMRI), etc. However, the validity of a number of fMRI studies has recently been questioned, which may have a large impact on the interpretation of weakly significant neuroimaging results (Eklund 2016).

ACKNOWLEDGEMENTS

We thank Sridharan Ramaratnam, Gus A Baker, and Laura H Goldstein for their work on the original review (Ramaratnam 2008).

We thank the editorial team at Cochrane Epilepsy for their support with this protocol, especially Graham Chan for supporting us with the literature search and all related questions, Sarah Nevitt for supporting us during the statistical analysis process and all related questions, and Rachael Kelly for overall support.

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REFERENCES

References to studies included in this review

Au 2003 [published data only]

Beretta 2014 [published and unpublished data]

Caller 2016 [published data only]


Ciechanowski 2010 [published and unpublished data]

Dilorio 2011 [published and unpublished data]


Fraser 2015 [published data only]
Psychological treatments for people with epilepsy (Review)

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Gandy 2014 [published and unpublished data]

Heide 2005 [published and unpublished data]

Hosseini 2016 [published data only (unpublished sought but not used)]

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Lua 2013 [published data only (unpublished sought but not used)]

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Lundgren 2008 [published data only]

Martinovi 2006 [published data only]

May 2002 [published data only]

Pfäfflin 2016 [published data only]

Pramuka 2007 [published data only]

Rau 2006 [published data only]

Schröder 2014 [published and unpublished data]

Tang 2015 [published data only]
References to studies excluded from this review


References to studies excluded from this review

Aliasgharpour 2013 [published data only]

Dah 1985 [published data only]

Dahl 1992 [published data only]

Dash 2015 [published data only]

Davis 1984 [published data only]

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Helgeson 1990 [published data only]

Li 2016 [published data only]

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Oluwole 2001 [published data only]

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Tajrishi MP, Abbasi S, Fard TN, Yousefi S, Abadi AMM, Kazmaei HD. Efficacy of attribution retraining on mental health of epileptic children. Iranian Red Crescent Medical
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Cramer 2003

Cull 1997

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Devinsky 1999
Dilorio 1992

Ekinci 2009

Eklund 2016

Elsas 2011

Escoffery 2015a

Escoffery 2015b

Ferro 2013

Fisher 2014

Fried 1990

Gandy 2017

Gilbert 2012

Gilhull 2004

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Hesdorffer 2000

Hesdorffer 2006

Higgins 2011

Institute of Medicine 2012

Jehi 2014

Jones 2013

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Kanner 2009

Kwan 2000

Larson 2012

Lefebvre 2011

Loiselle 2016

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Modi 2012

Modi 2013

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Téllez-Zenteno 2010

Velissaris 2012

Wagner 2010

Wagner 2012

Wagner 2014

Wang 2012

Wellmer 2012

WHO 2017

Williams 2003

Wu 2014

References to other published versions of this review
Michaelis 2016
* Indicates the major publication for the study
### Characteristics of included studies [ordered by study ID]

#### Au 2003

<table>
<thead>
<tr>
<th>Methods</th>
<th>Prospective, randomized, assessor-blinded, controlled study comparing group cognitive behavioral therapy (CBT) to wait-list control (WLC) on QOL, seizure frequency and self-efficacy. Outcome measures were obtained at baseline (3-month prior to intervention) and post-intervention (3-month after intervention).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Inclusion criteria: at least 2 seizures per month, with subjectively reported psychological distress. Exclusion criteria: active serious medical disorders, psychotic features, severe mental deficiency and a history of neurosurgery within the last year. 17 adults were enrolled; 8/9 were allocated to CBT/WLC. The mean ages were 38.3 (SD 7.0) years in CBT and 41.4 (SD 7.7) years in WLC. The durations of epilepsy in years were 20.3 (SD 13.6) in CBT and 26.7 (SD 13.6) in WLC. 8/5 participants in CBT had complex partial seizure/secondary generalization. 1/8/4 participants in WLC had simple partial seizure/complex partial seizure/secondary generalization. The mean weekly seizure frequency at baseline was 3.71 (SD 1.82) in CBT and 3.48 (SD 2.23) in WLC. The study was conducted in the Neurology Clinic of the Queen Elizabeth Hospital, Hong Kong.</td>
</tr>
<tr>
<td>Interventions</td>
<td>The intervention group received a total of eight 2-hour sessions of group CBT, conducted weekly for 8 weeks. Following a structured format, the intervention was provided by two trained clinical psychologists, with the following components: understanding stress and its relationship to seizures, relaxation training, cognitive restructuring, identification of seizure-provoking situations, systematic desensitization, stress management, and communication skills. Participants were also asked to complete homework assignments between the sessions on relaxation, recording of negative thoughts, and coping methods.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Outcomes: QoL, self-efficacy, and seizure frequency, measured with the Quality of Life Inventory in Epilepsy-31 (QOLIE-31), the epilepsy self-efficacy scale (ESES), seizure frequency (average over 3 months of weekly self-report). Time points measured: 1) Baseline (3 months before treatment) 2) Post-intervention (3 months after the last treatment session).</td>
</tr>
<tr>
<td>Risk of bias</td>
<td></td>
</tr>
<tr>
<td>Bias</td>
<td>Authors' judgement</td>
</tr>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
</tr>
</tbody>
</table>
### Allocation concealment (selection bias)

- **High risk**
- Allocation was not concealed, based on information provided by study authors.

### Blinding of participants and personnel (performance bias)

- **Unclear risk**
- Insufficient information.

### Blinding of outcome assessment (detection bias)

- **Low risk**
- Assessors were blinded, based on information provided by study authors.

### Incomplete outcome data (attrition bias)

- **Low risk**
- There was no attrition.

### Selective reporting (reporting bias)

- **Low risk**
- No evidence to suggest selective reporting.

### Other bias

- **Unclear risk**
- Not enough information to evaluate fidelity to intervention protocol and selective recruitment bias.

### Beretta 2014

#### Methods

Unblinded, randomized, controlled study comparing a participant-tailored educational plan (Treatment) in adults with epilepsy and chronic comorbidity to usual care (UC) on drug-related problems and quality of life. Outcome measures were obtained at baseline, 1-month, and 6-month post baseline.

#### Participants

- **Inclusion criteria:** adults with epilepsy and the following criteria: the presence of at least one chronic clinical condition requiring medical treatment; clinically relevant adverse events (AE) attributable to the present treatment, clinically relevant drug interactions, or both; possible modification of the treatment schedule to eliminate AEs or risky drug interactions.
- **Exclusion criteria:** adults with a non-modifiable treatment schedule, who were unable to understand or comply with an educational plan, unable or unwilling to release a written informed consent.
- 174 adults randomized. 91/83 participants were allocated to Treatment/UC. The age ranged from 18 to 70+ in both groups. 65/17 participants in Treatment and 69/9 participants in UC had focal epilepsy/generalized epilepsy; the remaining were unclassifiable. The seizure frequency per month in the preceding 6 months ranged from 0 to 5+ in both groups. 60/51 participants had ≤ 2 comorbidities, and 27/29 participants had ≥ 3 comorbidities in Treatment/UC; the remaining were not specified.
- The study was carried out in San Gerardo University Hospital. Consecutive participants were randomized from December 2009 to December 2011. All follow-up were completed in June 2012.

#### Interventions

The treatment consisted of an educational plan (1 hour counselling), delivered by treating physician to the participant on an individual basis. The plan comprised the following components: The cause and nature of any AEs or drug interactions; the tolerability...
profile of each drug present in the schedule, illustrated as a simple list, including the commonest AEs, presented in decreasing order of frequency; the clinical manifestations (if any) associated with the current drug interactions; any contraindication to the use of over-the-counter drugs that may potentially interfere with the current treatment schedule; the reasons for, and the potential benefits of the suggested treatment change; an encouragement to withdraw any drug that may potentially interfere or be contraindicated. The educational plan was administered at admission and in the same form after 1 month, as a reminder.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Drug-related problems (particularly drug interactions), QoL, measured with the Quality of Life Inventory in Epilepsy inventory 31 (QOLIE-31)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time points measured: 1) Baseline 2) 1-month after baseline 3) 6-month after baseline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Risk of bias</th>
<th></th>
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<tbody>
<tr>
<td>Bias</td>
<td>Authors’ judgement</td>
</tr>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Low risk</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
</tr>
</tbody>
</table>
### Caller 2016

#### Methods

Assessor-blinded, randomized, controlled trial comparing a group receiving HOBSCOTCH (H: Home-Based Self-management and Cognitive Training Changes lives), HOBSCOTCH plus memory training (H+) and care as usual (Control) on quality of life, mood, objective and subjective neurocognitive functions. Outcome measures were obtained at baseline and post-intervention follow-up (8-week).

#### Participants

Inclusion criteria: epilepsy, with or without uncontrolled seizures, with subjective memory complaints (QOLIE-31 cognition subset questions ≤ 7) who provided informed consent

Exclusion criteria: severe mental disability, estimated IQ < 70, visual impairment precluding reading and writing, and those without a reliable phone access

66 participants (age 16 to 65 years). 22 were randomized to each of H, H+, and Control. A total of 17 participants withdrew. H/H+ were combined in the analysis (N = 29) compared with Control (N = 20). The mean age in H/H+ was 49.3 (± 9.2) and 41.4 (± 11.2) in Control. There were 19 women in H/H+ and 13 women in Control. 17 participants in H/H+ and 13 participants in Control had received epilepsy surgery.

The study was conducted at Dartmouth-Hitchcock Epilepsy Center between January 2013 and June 2014.

#### Interventions

A specialized ARNP or RN trained as 'memory coaches’, delivered the intervention. The intervention program was structured into eight weekly 45- to 60-minute sessions, with the first session in a group format and the subsequent 6 sessions conducted over the telephone, followed by a final in-person review session with outcome assessment. Participants randomized into H/H+ groups were offered an intervention based on self-efficacy principles, including organizational skills, seizure management, and social skills. It also comprised problem solving therapy and behavior modification strategies, focused on cognitive symptoms. Participants in the H+ group were also required to participate in cognitive training, using a Nintendo handheld console and the Brain Age program, with tasks consisting of multiple working memory exercises. The total time of training was equal to 20 to 40 minutes of daily training. Participants in the control group received usual care.

#### Outcome

Primary outcome measure was change in quality of life (QOLIE-31). Secondary outcome measures were mood (PHQ-9), neuropsychological status (RBANS), self-report cognitive function (FACT-Cog), self-perceived executive function (BRIEF-A), and patient satisfaction (a satisfaction survey)

Time points measured:
1) Baseline (after randomization)
2) 8 weeks after baseline
### Call 2016 (Continued)

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Randomization was ensured by using a computer-generated random assignment</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Allocation concealment was not performed.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Participants were not blinded to the treatment they received</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Outcome measures were collected by a research co-ordinator blinded to treatment arms</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>A total of 17/55 (25.8%) drop-outs. Treatment group H (7/22; 31.8%), Treatment group H+ (8/22; 36.4%), Control (2/22; 9.1%)</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence of selective reporting within publication.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Low risk for infidelity to intervention protocol. Not enough information to evaluate selective recruitment bias</td>
</tr>
</tbody>
</table>

**Ciechanowski 2010**

**Methods**

Assessor-blinded, randomized controlled trial evaluating the long-term effect on improving depressive symptoms between a home-based collaborative care intervention for adults with epilepsy and depression (PEARLS) and treatment as usual (TAU) control group. Outcome measures were obtained at baseline through 12-month follow-up.

**Participants**

Inclusion criteria: ICD-9 epilepsy diagnosis and significant depression based on PHQ-9 score ≥10

Exclusion criteria: pregnant women, bipolar or psychotic disorder, active psychiatric treatment, substance abuse history based on questionnaire, cognitive impairment based on screening test

80 adults were recruited; 40 were randomized to PEARLS and 40 to TAU, stratified by whether or not seizures were reported in the preceding 6 months.

The mean ages were 43.3 years (SD 11.0) in PEARLS, and 44.4 (SD 11.1) TAU. 23/29 were women in PEARLS/TAU. In the past 6 months prior to recruitment, 29/30 participants had at least 1 seizure in PEARLS/TAU. In the month prior to recruitment, 11/12 participants had seizures with loss of consciousness (LOC) and 14/18 participants...
Interventions

PEARLS is a home-based, multimodal depression intervention. Participants received problem solving treatment (PST) by masters-level trained social workers who participated in PEARLS training (pearlsprogram.org). PST is a skill-enhancing behavioral depression treatment addressing problems that cause and maintain depression symptoms. PST was modified in this study to emphasize social and physical activation. Participants were scheduled for 8 (50 minutes each) in-home sessions in week 1 to 3, 5, 7, 11, 15, and 19. From week 19 until study end (12 months), participants received monthly 5- to 10-minute telephone calls from the therapist for PHQ-9 administration, and assessment of their use of PST. Therapists reported to the study psychiatrist regularly; psychiatrist would call participants to clarify clinical issues (e.g. suicidal ideation). The TAU group received no active treatment, but physicians of participants assigned to the TAU arm received a letter reporting the depression diagnosis and encouraging depression treatment as clinically appropriate.

Outcomes

Hopkins Symptom Checklist-20 (HSCL-20), suicidal ideation, Quality of Life Inventory in Epilepsy-31 (QOLIE-31), seizure frequency, medication use, satisfaction with epilepsy health care.

Time points measured:
1) Baseline
2) 6-month (by phone)
3) 12-month (by phone)
4) 18-month follow-up (by phone)

Notes

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Computer-generated random assignment and block randomizations were used. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Concealment was ensured.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Participants were not blinded to the treatment they received</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Assessors were blinded.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Ciechanowski 2010

**Incomplete outcome data (attrition bias)**

All outcomes | Low risk | 8/5 and 7/11 were missed in the 6-month/12-month follow-up in PEARL and TAU, respectively. The attrition rates (20%/12.5% for 6-month follow-up and 15%/27.5% for 12-month follow-up for PEARL and TAU, respectively) were higher than the authors’ expectation (i.e. 10%) but lower than our cut-off for long-term studies (i.e. 20%).

10 (25%) and 12 (30%) were lost at the 18-month follow-up in PEARL and TAU, respectively. Although the attrition rates were comparable for the two groups, they were higher than the authors’ expectation, and higher than our cut-off for long-term studies. Therefore, the risk of bias was high for 18-month follow-up.

### Selective reporting (reporting bias)

High risk | Unpublished data were sought and provided. Post-intervention suicidal ideation was missing. Evidence to suggest reporting bias.

### Other bias

Low risk | Low risk for infidelity to intervention protocol since therapists reported to study psychiatrist regularly.

Not enough information to evaluate selective recruitment bias.

### DiIorio 2011

**Methods**

Unblinded, quasi-randomized, controlled trial comparing a 6-week online epilepsy self-management program (WebEase) to wait-list control (WLC) in adults with epilepsy, on medication adherence, perceived and sleep quality. Outcome measures were obtained at baseline, 6-week and 12-week after randomizations.

**Participants**

Inclusion criteria: adults aged 18 or older, with a diagnosis of epilepsy, had been on antiepileptie medication for at least 3 months, had access to Internet, willing to participate and had not participated in WebEase before, spoke and read English. Participants for this study were recruited through epilepsy-based websites and forums, online clinical research matching services, and referrals from healthcare professionals. 194 adults were recruited, 96 were allocated to each group. A secondary review of eligibility yielded 148 participants who were retained for analysis (70 in WebEase; 78 in WLC). The mean age was 41.8 years in WebEase and 40.0 in WLC. 48/61 were women in WebEase/WLC. 42/52 participants had seizures in the past 30 days in WebEase/WLC. The mean number of seizures in 30 days prior to recruitment was 10.8 (SD 32.9) in WebEase and 9.3 (SD 25.9) in WLC. The number of participants who reported tonic-clonic/complex partial/simple partial/absence of seizures were 25/22/8/4 in WebEase.
Interventions

WebEase is a theory-based, interactive, Internet-based self-management program for people with epilepsy. WebEase incorporates concepts and principles of social cognitive theory, the transtheoretical model of behavior change, and motivational interviewing. The WebEase program lasted for 6 weeks. Participants spent 2 weeks in each of the 3 modules (medication, stress, sleep) that constitute the core of WebEase. The program was designed to correspond with a person’s stage of change. Regular weekly reminders were sent to participants until the end of 6 weeks. Participants received an Amazon gift card at the end of their participation in the study.

Outcomes

Medication Adherence Scale (MAS), Perceived Stress Scale (PSS), Revised Epilepsy Stressor Inventory (ESI-R), Pittsburgh Sleep Quality Index (PSQI), Epilepsy Self-Management Scale (ESMS), Epilepsy Knowledge Profile, Quality of Life Inventory in Epilepsy-10 (QOLIE-10)

Time points measured:
1) Baseline prior to randomizations
2) 6-week after randomizations
3) 12-week after randomizations

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Author's judgment</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Quasi-randomization by assigning participants alternatively.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Concealment was ensured.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Participants were not blinded to their treatment; personnel were blinded since this was a web-based intervention</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>High risk</td>
<td>The assessors were not blinded at any assessment, based on information provided by study authors</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>High risk</td>
<td>22/70 and 12/78 missed the second assessment in WebEase and WLC, respectively. 18/70 and 33/78 missed the third assessment in WebEase and WLC. The attrition rate was considered high</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Unpublished data (QOLIE-10 outcomes) were sought and provided. No evidence to suggest reporting bias</td>
</tr>
</tbody>
</table>
### Other bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Low risk</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low risk for infidelity to intervention protocol, since the intervention was delivered via a web-based program. Not enough information to evaluate selective recruitment bias.</td>
<td></td>
</tr>
</tbody>
</table>

### Fraser 2015

#### Methods

Unblinded, randomized, controlled trial comparing group intervention (PACES) and wait-list control (WLC) in people with epilepsy. (on self-management and quality of life. Outcome measures were obtained at baseline (after randomizations), post-intervention (8 weeks) and 6 months follow-up.

#### Participants

Inclusion criteria: adults, age 18 and above, with an established diagnosis of epilepsy for at least 6 months, able to speak, read, and write English, and reasonably cognitively intact (Montreal Cognitive Assessment (MoCA) ≥ 21) Exclusion criteria: severe mental illness or psychosis, or known cognitive impairment (IQ < 70) 83 participants randomized. 46 were allocated to each group; 41/38/37 and 42/40/39 were analyzed in PACES and WLC, respectively, at baseline/post-intervention (8 weeks), and 6-months follow-up. The mean age in years was 44.9 (SD 12.5) and 45.4 (SD 12.6) in PACES and WLC, respectively. There were 23 women in each group. 8/7 had simple partial seizures; 20/23 had complex partial; 9/7 had secondarily generalized seizures; 14/20 had tonic-clonic seizures; 2/3 had myoclonic seizures; 6/4 had absence seizures; 2/2 had other seizures, in PACES and WLC, respectively.

All participants were recruited through the UW Regional Epilepsy Center and Swedish Epilepsy Center, both in Seattle. Recruitment took place from 2010 to 2013.

#### Interventions

PACES was a group-based, psychoeducational intervention, based specifically on initial consumer survey findings. The intervention was conducted in an 8-week group setting of 6 to 8 adults, co-led by a psychologist and trained peer with epilepsy, which met one evening per week, at a hospital, for 75 minutes. Topics included medical, psychosocial, cognitive, and self-management aspects of epilepsy, in addition to community integration and optimising epilepsy-related communication.

#### Outcomes

Epilepsy Self-Management Scale (ESMS), Epilepsy Self-Efficacy Scale (ESES), Quality of Life Inventory in Epilepsy (QOLIE-31), Patient Health Questionnaire-9 (PHQ-9), and the Generalized Anxiety Disorder-7 (GAD-7).

Time points measured:
1) Baseline (after randomizations)
2) Post-intervention (8 weeks)
3) 6-months follow-up

#### Notes

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>

Psychological treatments for people with epilepsy (Review)

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### Fraser 2015 (Continued)

<table>
<thead>
<tr>
<th>Random sequence generation (selection bias)</th>
<th>Low risk</th>
<th>A random number generator was used for randomized assignment. No evidence to suggest selection bias.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Information was sought and provided; allocation was concealed.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Participants and personnel were not blinded to the treatment they received or provided.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Information was sought and provided. According to authors, outcome assessment was blinded.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>The drop-out rate was 16/92 (17.4%) overall; 9/46 (19.6%) in the Intervention and 7/46 (15.2%) in the WLC group, respectively. The attrition rate was considered high.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence of selective reporting bias within the study or after review of documentation of outcome measures used in the study.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Relatively low risk of infidelity to intervention protocol, since the intervention was delivered by one therapist only. Not enough information to evaluate selective recruitment bias.</td>
</tr>
</tbody>
</table>

### Gandy 2014

| Methods | Unblinded, randomized, controlled trial comparing individual cognitive behavioral therapy (CBT) to wait-list control (WLC) in people with epilepsy on mood-related symptoms. Outcome measures were obtained at baseline, post-treatment and 3-month follow up. |
| Participants | Randomized 59 adults between the ages of 18 and 65, had a formal diagnosis of epilepsy according to the ILAE criteria, had an IQ of $\geq 80$ (at least low average) according to the National Adult Reading Test, who were fluent in English and provided written informed consent. Exclusion criteria: psychotic disorder, suicidal, severe personality disorder, about to undergo epilepsy surgery, primary health concern and reason for seeking psychological support related to chronic illness other than epilepsy (e.g. MS). 31 and 28 participants were randomly enrolled to CBT and WLC. The mean age in years was 41 (SD 12; range 19 to 66) in CBT, and 38 (SD 13; range 20 to 63) in WLC. 9/13 participants had refractory epilepsy in CBT/WLC. The mean duration of epilepsy... |
The mean number of AEDs was 2 (SD 0.8; range 0 to 4) in CBT, and 2 (SD 1; range 1 to 4) in WLC. 14/21 participants had focal epilepsy; 6/4 participants had generalized epilepsy in CBT/WLC. 13/10 participants had a history of previous illness in CBT/WLC. The estimated IQ was 104 (SD 10; range 84 to 118) in CBT, and 106 (SD 10; range 81 to 122) in WLC.

Participants were recruited from the Comprehensive Epilepsy Service at the Royal Prince Alfred Hospital, in Sydney, Australia. A minority (N = 7) were recruited through advertisements about the study by Epilepsy Action Australia. Recruitment took place between January 2011 and December 2011.

### Interventions
The CBT program included 9 individual sessions: one 1 to 2-hour assessment session for formulation of treatment goals, and 8 weekly, individualized 1-hour therapist-client sessions, with elements including home-based practical tasks, behavioral activation, CBT model, anxiety management, and communication skills about their illness. The intervention was delivered by postgraduate doctorate level intern psychologists under the supervision of senior clinical psychologists (> 10 years of experience). All therapists and supervisors attended a one-day workshop; a strict adherence checklist was completed by all therapists, who attended weekly supervision with senior clinical psychologists.

### Outcomes
The Neurological Depressive Disorders Inventory-Epilepsy (NDDI-E), the Hospital Anxiety Depression Scale (HADS), Quality of Life Inventory in Epilepsy-31 (QOLIE-31)

Time points measured:
1. Baseline (before randomizations)
2. Post-treatment
3. 3-month follow-up

### Notes

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>A list of random numbers, using the Bernoulli function, was generated and used consecutively for randomization. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Concealment was ensured.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Participants were not blinded to their treatment.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td>Outcome assessment was not blinded, based on information provided by study authors</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Gandy 2014  (Continued)

Incomplete outcome data (attrition bias)
All outcomes  High risk
12/31 (39%) and 5/28 (18%) withdrew from the study at 3-month follow-up. Attrition rate was considered high.

Selective reporting (reporting bias)
Low risk
Unpublished data were sought and provided. No evidence to suggest selective reporting.

Other bias
Low risk
Low risk for infidelity to intervention protocol, since all therapists had received training, followed a standard protocol, delivered the intervention under the weekly supervision of senior clinical psychologists (>10 years of experiences), and completed a strict adherence checklist. There was insufficient information to evaluate selective recruitment bias.

Helde 2005

Methods
Assessor-blinded, randomized controlled trial comparing a nurse-led intervention (Intervention) for adult people with epilepsy to a usual care (UC) control arm, on epilepsy-related quality of life. Outcome measures were obtained before randomizations and after 2 years.

Participants
 Randomized 114 participants with a definite diagnosis of epilepsy and antiepileptic medication for more than 1 year, ≥1 seizure during the previous year, the ability to cooperate, and understand written and oral information, and who provided written informed consent. 58/57 and 56/54 participants were randomized/analyzed in Intervention and UC, respectively. The mean age was 35.3 years (range 16 to 69) in Intervention, and 39.5 (range 16 to 67) in UC. There were 32 women in each group. 18/32/34/3/4/13/0 participants in Intervention, and 18/34/30/5/3/13/1 participants in UC, had simple partial/complex partial/secondarily generalized tonic-clonic/absence/myoclonic/predominantly generalized tonic-clonic/unclassified seizures. 8/2 participants had major seizures (convulsive seizure with reduced consciousness) more frequently than once a month in Intervention/UC; 14/12 had minor seizure more frequently than once a week. The mean duration of epilepsy was 19 years in both groups. 20/28/9 participants in Intervention, and 12/38/4 participants in UC had one/two/three or more AEDs. All participants were outpatients in the Neurological Clinic in Trondheim, Norway. Recruitment took place from February 2001 to March 2002.

Interventions
Intervention comprised a 1-day group education program (5 to 11 participants/group). General information about different aspects of living with epilepsy was provided by a multidisciplinary team consisting of the nurse, a neurologist, a social worker, and a clinical neurophysiologist. Extended nurse follow-up and counselling was provided after the group session for continuity of care (nurse’s presence in neurologist consultations; the nurse called the participants every 3 months to ensure consultation and to address individual needs; the importance of compliance with medical regimen was emphasized).
The UC group was offered conventional treatment according to individual needs.

### Outcomes

The Quality of Life Inventory in Epilepsy inventory-89 (QOLIE-89)
- Time points measured:
  1. Baseline (before randomization)
  2. 2 years after randomization
- 100-mm VAS scale (general satisfaction with the follow-up by the Neurological Clinic during the last 2 years)
- Time points measured:
  1. 3 months after the final interview (2 years after randomization)

### Notes

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Computer-generated block randomization was used. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Allocation concealment was ensured.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Neither participants nor service providers were blinded, based on information provided by study authors</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Low risk</td>
<td>The assessors were blinded.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>1/58 and 2/56 withdrew from the study. No evidence to suggest attrition bias</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Unpublished data (QOLIE-89 raw data) were sought and provided. No evidence to suggest selective reporting</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Relatively low risk of infidelity to intervention protocol, since the intervention was delivered by one therapist only. Not enough information to evaluate selective recruitment bias</td>
</tr>
</tbody>
</table>
### Methods

Assessor-blinded, quasi-randomized, controlled trial comparing individual CBT and wait-list control (WLC) in people with epilepsy on quality of life. Outcome measures were obtained at baseline and 2 months follow up.

### Participants

Randomized 56 participants (age 18 and above) with willingness to participate, epilepsy diagnosis for at least 1 year, with primary generalized tonic epilepsy and uncontrolled seizures that were diagnosed by a neurologist, no other chronic illness, and not enrolled in any other research. 28/23 and 28/24 were randomized/analyzed in Intervention and WLC, respectively. The mean age was 29.08 (SD 8.06) and 32.75 (SD 10.89) in Intervention and WLC. There were 10 women in Intervention and 12 women in WLC, respectively. The mean duration of epilepsy in years (was 18.17 (SD 12.74) in Intervention, and 15.2 (SD 8.89) in WLC, respectively. All participants were diagnosed with epilepsy at the Nour and Kashani Hospitals in Isfahan, Iran.

### Exclusion criteria:
- Immigrants
- Missing more than one intervention session
- Recent tragic life events (such as loss of life, divorce, etc.)

### Interventions

Intervention comprised 5 group sessions, each separated by 4 days. The structure of the motivational interviewing sessions was extracted from the book *Motivational Interviewing Group Intervention* for each session. Motivational interviewing is a strategy for fortification and enhancement of internal motivation, for changing thought exploration, identification, and overcoming doubts and dualism. Aspects of the group intervention included being hopeful to overcome issues, decreasing social isolation, helping others to solve their problems, and learning that others may have to grapple with the same issues.

The WLC was offered conventional treatment, according to individual needs.

### Outcomes

The Quality of Life Inventory in Epilepsy inventory-89 (QOLIE-89)

Time points measured:
1) Baseline (before randomization)
2) 2 months after the intervention and randomization

### Notes

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>The described procedure remained unclear, but suggested quasi-randomization by assigning participants alternatively</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Unclear if allocation was concealed.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Participants and personnel were not blinded to the treatment they received and provided</td>
</tr>
</tbody>
</table>
**Hosseini 2016 (Continued)**

<table>
<thead>
<tr>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Low risk</th>
<th>Outcome assessment was blinded.</th>
</tr>
</thead>
<tbody>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
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</tbody>
</table>

| Incomplete outcome data (attrition bias)     | High risk| The drop-out rate in the treatment group was 7/28 (17.9%). Attrition was considered high. Furthermore, the reason for exclusion (missing > 1 treatment session) indicated that the model of analysis was not ITT. |
| All outcomes                                  |          |                               |

<table>
<thead>
<tr>
<th>Selective reporting (reporting bias)</th>
<th>Low risk</th>
<th>No evidence to suggest selective reporting.</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Other bias</th>
<th>Low risk</th>
<th>Relatively low risk of infidelity to intervention protocol, since the intervention was delivered by one therapist only. Not enough information to evaluate selective recruitment bias</th>
</tr>
</thead>
</table>

**Jantzen 2009**

**Methods**

Unblinded, quasi-randomized controlled trial comparing the FLIP&FLAP epilepsy intervention group (IG) for children and adolescents with epilepsy to a wait-list control (WLC) on health-related quality of life (HRQOL) and the child's ability to explain epilepsy to others. Outcome measures were obtained at baseline and 6-month after treatment.

**Participants**

Inclusion criteria: diagnosis of epilepsy, taking antiepileptic drugs, sufficient German literacy, willingness of the child and at least one career to participate in the education programme.

A total of 192 families enrolled; 105 were enrolled to IG, and 87 were enrolled to WLC. At baseline, the final sample include 67 in IG, and 74 in WLC. Written consent was obtained from parents; children gave oral consent to participate.

Mean ages in years were 11.6 (SD 3.0; range 6 to 17) in IG, and 11.7 (SD 2.5; range 6 to 16) in WLC. Mean duration of seizures in years were 4.7 (SD 4.0) in IG, and 5.6 (SD 3.7) in WLC. 19/15/4/13/11 participants in IG and 22/15/7/3/10 participants in WLC had tonic-clonic/complex partial/simple partial/absence/myoclonic /unclassified seizures. 42 (IG) and 48 (WLC) participants were seizure free for > 6 months. 29 in IG and 39 in WLC were receiving monotherapy.

The study took place in the University of Luebeck, Germany; participants were recruited from 10 specialized German epilepsy centers, between autumn 2003 and spring 2005.

**Interventions**

The intervention group could be held as a 2-day (14 hours per course) or a two and a half-day (16 hours per course) continuous session in group format (5 to 8/group). The intervention was delivered by healthcare professionals, such as nurses, social workers, doctors, or psychologists; two trainers were required per course. The following domains were included: disease knowledge, disease-related emotions, communication, self-responsibility, self-management, participation, and educational insecurity. One of the
main aims was to help children to conceptualize their seizures. By watching the film and receiving age-appropriate information, the participants were enabled to understand their seizures and to develop a more adequate self-concept.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>DISABKIDS modular HRQOL questionnaire, disclosure of epilepsy, seizure-free episode</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time points measured:</td>
<td>1) Baseline (immediately before intervention for IG and at recruitment for WLC)</td>
</tr>
<tr>
<td></td>
<td>2) Follow-up assessment (6 months after intervention)</td>
</tr>
</tbody>
</table>

### Notes

#### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Grouping was based on participant’s time of application - those who applied for the first course were assigned to IG, while those who applied for the second course were assigned to WLC</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Allocation was not concealed.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Participants and therapists were not blinded.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Outcome assessment was blinded.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>The attrition was less than 10% in all subgroups of the sample</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence for selective reporting within publication.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Not enough information to evaluate fidelity to intervention protocol and selective recruitment bias</td>
</tr>
</tbody>
</table>
### Methods

Randomized, controlled, open-label trial comparing an SMS-based epilepsy education program (IG) to a paper-based epilepsy education program as control (CG) in individuals with epilepsy on epilepsy-related quality of life. Outcome measures were obtained at baseline and after intervention (3-month after randomizations).

### Participants

Inclusion criteria: adults (aged 18 or above), epilepsy, on regular treatment, able to either write, read, or understand and communicate in Malay or English language, capable of completing questionnaires (either written or verbal), mobile phone owners, and active users, provided written consent. 144 randomized, 72 into each group; 71 in IG and 65 CG were included in the final analysis. The mean age of all participants was 30.5 (SD 11.8) years. There were 38 and 33 women in IG and CG, respectively. 13 participants in IG and 16 in CG had a duration of epilepsy between 6 and 12 months, 15/16 participants in IG/CG had duration of >120 months. 36/36 and 40/32 in IG/CG had generalized seizures/partial seizures. The study was conducted in the Neurology Clinics of 3 public hospitals in the states of Terengganu, Pahang, and Kelantan in Malaysia.

### Interventions

The intervention for both IG and CG included a printed epilepsy education module. It was based on the Modular Service Package Epilepsy (MOSES), and was modified to suit the sociodemographic backgrounds of patients in the East Coast Peninsular Malaysia (May 2002; Ried 2001). Eleven parts were included: 1) basic knowledge, 2) history and statistics, 3) living with epilepsy, 4) diagnosis, 5) treatment and therapy, 6) prognosis, 7) self-control, 8) myth and facts, 9) psychosocial aspects, 10) laws and acts, and 11) reference. All participants were instructed to read one part per week at home, based on the schedule provided in the user manual. IG received an add-on SMS-based mobile epilepsy education system (MEES) throughout the 3 months. Three parts were included: 1) epilepsy education module, 2) drug-taking reminder, and 3) clinic appointment reminder. During the period, 2 simple SMS messages, generated from each printed education module, were automatically delivered to participants every 4 days; they also received SMS reminders once a month for their medication and their appointment, based on individual schedules. MEES allowed participants to send queries and comments regarding their healthcare services or their illness via SMS to a specific number, to be addressed by researchers.

### Outcomes

Malay Quality of Life Inventory in Epilepsy-30 (MQOLIE-30)

Time points measured:
1) Baseline (at recruitment)
2) 3 months (after intervention)

### Notes

Data was sought but not provided.

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>An interactive voice response system was used for randomization. No evidence to suggest selection bias</td>
</tr>
</tbody>
</table>
### Lua 2013  (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Risk Level</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No information provided.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>No information provided regarding blinding of personnel delivering the intervention.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information provided.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>1/72 (1%) and 7/72 (10%) withdrew from the study (both &lt; 20%, which was our cut-off). No evidence to suggest attrition bias.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence to suggest selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Not enough information to evaluate fidelity to intervention protocol and selective recruitment bias</td>
</tr>
</tbody>
</table>

### Lundgren 2006

**Methods**

Unblinded, randomized, controlled trial comparing Acceptance and Commitment Therapy (ACT) to supportive therapy (ST) in adults with epilepsy on quality of life and seizure control. Outcome measures were obtained at baseline, post-intervention, 6-month and 2-month following the end of interventions.

**Participants**

27 participants (aged 27 to 55 years) with epilepsy, who were institutionalized or day workers in a centre of epilepsy in South Africa participated; all of them were able and willing to participate, had a minimum of 4 seizures during the past 3 months, and had a verified diagnosis of epilepsy using EEG.

14/13 participants were randomly allocated to ACT/ST, respectively; 7 women in each group, 4 and 5 participants in ACT and ST needed interpreter. 10/1/2/4 participants in ACT and 9/0/1/7 participants in ST had generalized tonic-clonic seizures/myoclonic jerks/complex partial seizures/absence seizures.

Exclusion criteria: signs of an ongoing progressive illness.

**Interventions**

The treatment included an ACT (ACT plus behavioral techniques for seizure management) and ST. The design involved 4 sessions, comprised 1 individual session (1.5 hours), 2 group sessions (3 hours each), followed by 1 individual session (1.5 hour). All participants were subsequently provided individual boosters, and followed up for an additional session at 6 and 12 months (1 hour each). The booster sessions were conducted after the follow-up measures were taken. Total therapy time over the 12-month study was 11 hours. The ACT protocol can be downloaded at [www.contextualpsychology.org](http://www.contextualpsychology.org) and [www.ACT-Forum.se](http://www.ACT-Forum.se).

Participants in the ACT learned to improve their valued living by building a broader behavioral repertoire in valued life directions. Therapeutic components included techniques to build psychological flexibility around the chain of seizure behaviors, self as...
context, defusion, acceptance, contact with present moment, committed action, and empowerment. The patterns of seizures were discussed, as they occurred as obstacles to valued living. Participants were required to make records of seizure patterns, in terms of antecedents, seizure responses, and consequences. Individualized seizure management techniques (e.g. counter-measures) were taught.

The ST goal was to provide an equal amount of professional attention in a supportive environment. The therapists were instructed to give no active advice. The intervention was delivered by two clinical psychologists from Uppsala University, Sweden (first and second authors) trained in ACT, and with experience in behavioral treatment of epilepsy; the study took place in Epilepsy, South Africa, and the Department of Neurology, University of Cape Town.

Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Satisfaction with Life Scale (SWLS), World Health Organization Quality of Life instrument, short version (WHOQOL-BREF), seizure frequency, seizure index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time points measured:</td>
<td>1) Baseline</td>
</tr>
<tr>
<td></td>
<td>2) Post-intervention</td>
</tr>
<tr>
<td></td>
<td>3) 6-month follow-up</td>
</tr>
<tr>
<td></td>
<td>4) 12-month follow-up</td>
</tr>
</tbody>
</table>

Notes

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Author's judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>A computerized randomization table was used. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Allocation concealment was ensured, according to information provided by study authors</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Participants and personnel were not blinded to the treatment they received or provided</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>High risk</td>
<td>Outcome assessors were not blinded.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>There were no drop-outs.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence to suggest selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Low risk of infidelity to intervention protocol, since the intervention was provided by the therapists who had developed the</td>
</tr>
</tbody>
</table>
### Lundgren 2006 (Continued)

<table>
<thead>
<tr>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not enough information to evaluate selective recruitment bias</td>
<td></td>
</tr>
</tbody>
</table>

### Lundgren 2008

<table>
<thead>
<tr>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unblinded, randomized controlled trial comparing Acceptance and Commitment Therapy (ACT) to yoga in adults with epilepsy on seizure control and quality of life. Outcome measures were obtained at baseline, post-intervention, 6 months and 12 months following the end of interventions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria: adult (18 years or older), ability and willingness to participate in the program, a minimum of 3 seizures during the past 3 months, and an EEG-verified diagnosis of epilepsy</td>
</tr>
<tr>
<td>Recruited 18 adults (aged 18 to 55) from an outpatient clinic in southwest India. 10 and 8 were allocated to ACT and yoga, respectively. The mean age was 21.9 years in ACT and 25.8 years in yoga; 3 women in each group. 6 and 5 participants required an interpreter for the treatment in ACT and yoga, respectively. 6 in each group had generalized tonic-clonic seizures; 2 and 1 had myoclonic jerks in ACT and yoga, 3 and 2 had complex partial seizures in ACT and yoga, 1 had absence seizures in yoga</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refer to Lundgren 2006 for the structure and intervention details of ACT</td>
</tr>
<tr>
<td>The yoga training for epilepsy had two main features: stimulating activity that the participants considered meaningful, and using yoga techniques to decrease the risk of epileptic seizures and promote well-being. The program focused on 3 different physical dimensions and 2 psychological dimensions to unite the mind, body, and soul. The yoga teacher and the participants discussed barriers to living a life they considered important. Accepting private events and living meaningful lives were essential parts of the treatment. The teacher used metaphors, direct instructions, and encouragement to help the participants to be active in areas considered important. Examples of such domains were: relationships, work, health, and leisure time</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Satisfaction with Life Scale (SWLS), World Health Organization Quality of Life instrument, short version (WHOQOL-BREF), seizure frequency, seizure index</td>
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<tr>
<td>Time points measured:</td>
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<td>1) Baseline</td>
</tr>
<tr>
<td>2) Post-intervention</td>
</tr>
<tr>
<td>3) 6-month follow-up</td>
</tr>
<tr>
<td>4) 12-month follow-up</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Risk of bias</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
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<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
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<td>A computerized randomization table was used. No evidence to suggest selection bias</td>
</tr>
</tbody>
</table>
Lundgren 2008  (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Risk</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low</td>
<td>Allocation concealment was ensured, according to information provided by study authors.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High</td>
<td>Participants and personnel were not blinded to the treatment they received and provided.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High</td>
<td>Outcome assessors were not blinded.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low</td>
<td>There were no drop-outs.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low</td>
<td>No evidence to suggest selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low</td>
<td>Low risk of infidelity to intervention protocol, since the intervention was provided by the therapists who had developed the intervention. Selective recruitment bias still needs to be assessed.</td>
</tr>
</tbody>
</table>

Martinović 2006

Methods

Blinded, randomized, controlled trial comparing cognitive behavioral intervention (CBI) to counselling as usual (TAU) in adolescents with epilepsy on depressive symptoms. Outcome measures were obtained at baseline, 6-month and 9-month follow-up.

Participants

Inclusion criteria: newly diagnosed epilepsy (either focal or generalized, at least 2 unprovoked seizures within a period of not longer than 12 months), subthreshold depression (as defined by Hamilton Depression Scale, scores 6 to 8), normal intelligence
Exclusion criteria: epilepsy caused by progressive cerebral lesion, mental retardation, a diagnosis of depression, psychotic symptoms, schizophrenia, bipolar disorder, social phobia, agoraphobia, or panic disorder according to DSM-IV

32 participants were included in the study. All participants attended either elementary or high school classes depended on age. 16 were randomized into BCI and TAU. The final sample analyzed was 30, as 1 participant in each group withdrew after randomization

The mean age was 17.2 (SD 2.5; range 13 to 19) years in the CBI and 17.6 (SD 2.2; range 13 to 19) in TAU. There were 9 females in each group. 6/5 (CBI) and 9/10 (TAU) participants had generalized seizures/partial seizures. 7/9 and 8/6 participants were receiving monotherapy/polytherapy in CBI/TAU. 5 in CBI and 7 in TAU were drug-resistant. The mean IQ was 104 (SD 14.6; range 87 to 130) in CBI and 102 (SD 15.8; range 85 to 132) in TAU

All subjects were recruited from general practices in Belgrade and its surrounding areas. These subjects were then referred to the Outpatient Department of Epilepsy, located at the Institute of Mental Health.
Interventions

Cognitive behavioral intervention (CBI) was applied as part of an individual treatment plan, aimed at analysing and modifying distorted automatic thoughts related to negative depressive thinking. It was delivered in group format with 7 to 8 participants/group, administered in 8 sessions during the first 2 months, and then in 1 session per month during the next 4 months. Participants in CBI learned to recognize and correct all main types of cognitive errors: catastrophic, over-generalization, personalization, and selective abstraction. Sessions consisted of activity plans, relaxation, identification and correction of thought distortions through cognitive restructuring, role playing, development of social skills, and problem solving. All participants randomized to CBI were instructed to note, in a treatment diary, the occurrence of negative thoughts and countermeasures taken (positive thoughts). Negative and positive thoughts were rated on a 4-point scale.

TAU was administered in the same number of sessions and formats. It consisted of therapeutic counselling without elements of CBI.

Outcomes

Beck Depression Inventory (BDI), Center for Epidemiological Study on Depression (CES-D) scale, Hamilton Depression Scale (HAMD), Quality of Life in Epilepsy Inventory Total Score (QOLIE-31), seizure control, the rating of positive and negative thoughts on a 4-point scale.

Time points measured:
1) Baseline
2) 6-month follow-up
3) 9-month follow-up

Notes

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Author’s judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>A computer-generated list of numbers were used for randomization. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Allocation concealment was ensured.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>Low risk</td>
<td>Both the participants and the therapists who delivered the treatment (CBI and TAU) were unaware of the study hypotheses. They were told that they will be provided with or deliver psychological means to improve coping with epilepsy. No evidence to suggest performance bias</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Low risk</td>
<td>Assessors were blinded, according to information provided by study authors</td>
</tr>
</tbody>
</table>
Incomplete outcome data (attrition bias) | Low risk | 1 drop-out in each group. No evidence to suggest attrition bias
---|---|---
Selective reporting (reporting bias) | High risk | Results of the following parameters were unavailable: 1) familial risk factors, 2) environmental risk factors, 3) the rating of positive and negative thoughts on a 4-point scale, 4) seizure control. Unpublished data were sought but not provided
Other bias | Unclear risk | Not enough information to evaluate fidelity to the intervention protocol and selective recruitment

May 2002

Methods
Assessor-blinded, randomized, controlled trial comparing the Educational Epilepsy Program MOSES (Modular Service Package Epilepsy) to a wait-list control (WLC) in adults with epilepsy of quality of life, self-esteem, depressive symptoms, epilepsy knowledge and coping, seizure frequency, as well as epilepsy-specific daily living restrictions, fears, mobility, and leisure. Outcome measures were obtained at baseline and 6 months after intervention.

Participants
Inclusion criteria: epilepsy, regardless of syndrome, duration, or severity
Exclusion criteria: mental retardation, acute psychiatric illness, non-epileptic seizures only
Enrolled 383 people. The final sample included 242 participants (aged 16-80), 113 received MOSES and 129 were allocated in WLC. The mean age was 37.5 (SD 13.7; range 16 to 77) years in MOSES, and 38.4 (SD 13.5; range 16 to 80) years in WLC. There were 65/73 women in MOSES/WLC. The duration of epilepsy ranged from 1 to 54 years in MOSES and 1 to 61 years in WLC. 23/71/3 participants MOSES and 20/81/0 participants in WLC had generalized epilepsy/focal epilepsy/focal and generalized signs. The remaining had an undetermined type of epilepsy, or no data were available. 45/46/58/3/1/5 participants in MOSES, and 57/56/59/11/0/3 participants in WLC had simple partial seizures/complex partial seizures/tonic-clonic seizures/absence seizures/myoclonic seizures/tonic seizures. The remaining were undetermined. 23/35 participants had no seizures in the past 6 months in the MOSES and WLC groups. 38/39 had 1 to 5 seizures in the past 6 months; 21/30 had >1 seizure per month; 17/22 had >1 seizure per week; 11/1 had >1 seizure per day. 110 participants in MOSES and 125 in WLC received treatment with antiepileptic drugs (AED)
Participants were drawn from 22 epilepsy centers in Germany, Austria, and Switzerland

Interventions
The aims of MOSES were to improve participants' knowledge about epilepsy, its consequences, diagnostic and therapeutic measures, and to improve participants' understanding of psychosocial and occupational problems. The participants were encouraged to cope actively with their disease, to live with as few limitations as possible, to participate in the treatment process, and to gain more self-esteem. The program focused on enhancing the self-help potentials of the participants, and on promoting the participants...
to become ‘experts’ in dealing with their epilepsy. As results, a reduction of psychosocial problems and an improvement of quality of life were expected. The program included 9 units: living with epilepsy, epidemiology, basic knowledge, diagnostics, therapy, self-control, prognosis, psychosocial aspects, and network. To cover the program, 14 lessons (60 minutes each) were necessary. In this study, MOSES was offered as a 2-day course (course details were not specified).

Outcomes

Short-Form 36 (SF-36), Rosenberg self-esteem scale, Depression Scale (D-S), Restrictions in Daily Living Due to Epilepsy, Epilepsy Knowledge Profile, Coping with Epilepsy and Adaptation, seizure frequency, and contentedness of drug therapy, evaluation of the MOSES program.

Time points measured:
1) Baseline
2) 6 month after completion of the course

Notes

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random sequence generation was ensured, according to information provided by study authors</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Allocation was not concealed, according to information provided by study authors</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Participants were not blinded, according to information provided by study authors</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Low risk</td>
<td>Outcome assessors were blinded, according to information provided by study authors</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>High risk</td>
<td>133/383 withdrew after randomization; of the remaining 250, 8 were excluded due to violation of study protocol. 242 were included in the final sample. Attrition rate was considered high</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence to suggest selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Not enough information to evaluate fidelity to the intervention protocol and selective recruitment</td>
</tr>
</tbody>
</table>
### Methods

Assessor-blinded, quasi-randomized, controlled trial comparing group cognitive behavioral therapy (CBT) with selective serotonin reuptake inhibitors (SSRIs) treatment of major depressive disorder (MDD) in adults with temporal lobe epilepsy (TLE) on mood and quality of life. Outcome measures were obtained at baseline, 6 weeks (during treatment), and 12 weeks (immediately after treatment).

### Participants

Inclusion criteria: adults (aged over 18), diagnosed with MDD according to the criteria of the DSM-IV, diagnosed with TLE according to the criteria of the ILAE, literate; individuals on antidepressant treatments were allowed to participate only if they had been on stable doses for more than 8 weeks and still showed signs of significant depression. Exclusion criteria: high risk of suicide that required hospitalizations, abused or dependent on drugs, history of head trauma within 6 months prior to the recruitment, any condition that would prevent understanding the study or the psychotherapeutic process, such as mental retardation, psychosis, delirium, or dementia, previous CBT. The 15 participants were assigned to CBT (N = 7) and SSRIs (N = 8) according to the participant's ability to attend the weekly session. There was 1 woman in the CBT and 4 in the SSRI group. The mean age was 33.8 years in CBT, and 43.1 years in SSRI. The duration of epilepsy/age at seizure onset was 12.4/21.4 years in CBT, and 22.3/20.7 years in SSRIs. The average number of seizures per month was 5.2 in CBT, and 4.6 in SSRIs. 3 participants in each group had a comorbid anxiety disorder.

The study was conducted at the National Institute of Neurology and Neurosurgery in Mexico City. Recruitment took place between January 2013 and December 2013.

### Interventions

The CBT sessions comprised one weekly 90-minute session for 12 consecutive weeks. The components and structure of CBT were based on Crail-Melendez 2013. Therapeutic elements included the basics and relationship of depression and epilepsy, identification of emotions, modification of activities to improve mood, identification and reviewing of thought records, automatic thoughts, introduction of thought distortions, learning alternative thoughts, introduction of the concept of core beliefs, down-arrow techniques, etc.

According to the study protocol, the SSRI group received treatment with a SSRI (sertraline or citalopram) for a total of 12 weeks, based on the protocol suggested by the American Psychiatric Association in their practice guidelines for depression, in which titration is done at week 6, after the second evaluation.

### Outcomes

Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale (HADS), Quality of Life Inventory in Epilepsy-31 (QOLIE-31), Mini International Neuropsychiatric Interview (MINI)

**Time-points measured**
1) Baseline
2) 6-week during treatment
3) 12-week (immediately after treatment)

### Notes

Original data were sought and provided by study authors.

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
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</table>

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**Psychological treatments for people with epilepsy (Review)**

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
<table>
<thead>
<tr>
<th>Orjuela-Rojas 2015 (Continued)</th>
</tr>
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<tbody>
<tr>
<td><strong>Random sequence generation (selection bias)</strong></td>
</tr>
<tr>
<td><strong>Allocation concealment (selection bias)</strong></td>
</tr>
<tr>
<td><strong>Blinding of participants and personnel (performance bias)</strong></td>
</tr>
<tr>
<td><strong>Blinding of outcome assessment (detection bias)</strong></td>
</tr>
<tr>
<td><strong>Incomplete outcome data (attrition bias)</strong></td>
</tr>
<tr>
<td><strong>Selective reporting (reporting bias)</strong></td>
</tr>
<tr>
<td><strong>Other bias</strong></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Pakpour 2015</th>
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</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
</tr>
</tbody>
</table>
Interventions

MI intervention was a multifaceted program, designed to enhance medication adherence behavior and clinical outcomes in participants with epilepsy. 3 weekly, individual face-to-face sessions, each lasting for 40 to 60 minutes, were provided. Participants were encouraged to express their experiences, values, readiness, and confidence for behavior change during the intervention. The MI techniques used to resolve barriers and encourage participants to take medications regularly used open-ended questions, affirmations, reflective statements, and summaries to elicit change talk. The participants also received a drug diary calendar to help them monitor their plan on medication adherence. All sessions were delivered on an individual-basis, by a male health psychologist with 10 years of experience working with medication adherence in patients with chronic diseases, who had received 60 hours of training of MI in Qazvin and Tehran. All participants, in both MI and UC, received standard care consistent with ‘treatment as usual’ for patients with epilepsy.

Outcomes

The Medication Adherence Report Scale (MARS), AED serum levels, Beliefs about Medications Questionnaire (BMQ), Perceived behavioral control (PBC), behavioral intention, self-monitoring, action planning, coping planning, Self-Report Behavioural Automticity Index (SRBAI), Liverpool Seizure Severity Scale (LSSS), and the Quality of Life Inventory in Epilepsy-31 (QOLIE-31)

Time points measured:
1) Baseline before randomizations
2) 3-month after intervention
3) 6-month after intervention

Notes

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>A computer-generated code based on random number sequence with stratification by the study sites was used. Randomization was performed by independent researcher who was not involved in the study. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information was provided.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information on the blinding of participants was provided</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Unclear - insufficient information was provided</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>4/275 drop-outs at follow-up. Attrition rate was considered low</td>
</tr>
</tbody>
</table>
Selective reporting (reporting bias) | Low risk | No evidence to suggest selective reporting.
---|---|---
Other bias | Low risk | Intervention was provided by one psychologist with ≥10 yrs of experience in MI and adherence interventions. Risk of bias for fidelity to intervention protocol low. Not enough information to evaluate selective recruitment.

**Pfäfflin 2016**

Methods
Assessor-blinded, randomized, controlled trial comparing a group receiving individual counselling provided by an epilepsy nurse (EN) and wait-list control (WLC) in people with epilepsy (PWE) on satisfaction with treatment. Outcome measures were obtained at baseline and 6-month follow-up.

Participants
Inclusion criteria: adults (age 16 and above) with epileptic seizures, who were referred to an epilepsy outpatient clinic, and who agreed in writing to participate in the study. Exclusion criteria: unable of responding to the questionnaire (language or learning difficulties), only non-epileptic seizures. 187 participants, 92 and 95 were randomized, 67 and 76 were analyzed in EN and WLC. The mean age was 42.6 (± 14.8), and 44.9 (± 15.0) in EN and WLC group. There were 34 women in EN and 45 women in WLC. The mean duration of epilepsy was 20.7 (± 16.8) in EN and 23.5 (± 17.1) in WLC.

Two outpatient clinics that specialized in epilepsy participated.

Interventions
The two certified epilepsy nurses (‘epilepsy specialist assistant’ or ‘epilepsy specialist counselor’) who provided the intervention had received a 1-year part-time training, with blended e-learning, attendance periods, homework, visits to specialized epilepsy institutions, and train-the-trainer training, in order to engage in patient-education programs. Participants of the EN group were offered time for counselling, and advice during their routine visit. The epilepsy nurse handed out a short questionnaire in order to assess participants’ major needs. The questionnaire covered the following topics: epilepsy, therapeutic issues, risks and adverse effects of medication and other therapies, pregnancy, problems in daily life with seizures, consequences of seizures for driving, employment, the job, school and families, and social issues, and an open-ended question for topics not listed. The nurses provided leaflets and other written information about driving regulations, pregnancy, social support, and self-support groups. Participants of the control group had routine care only.

Outcomes
Primary outcome measure was satisfaction of participants with information and support. Secondary outcome measures were satisfaction with patient-doctor relationship, organization of treatment, epilepsy knowledge, coping, and restrictions in daily life. Hospital Anxiety and Depression Scale and global Quality of Life (item from QOLIE-31).

Time points measured:
1) Baseline (before randomization)
2) 6 months after baseline
### Pfafflin 2016 (Continued)

<table>
<thead>
<tr>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk of bias</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Supporting judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random allocation by a computer-generated block randomization list</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Random allocation by a computer-generated block randomization list</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>WLC group design. The epilepsy nurse was a new service, added to the standard service of the outpatient clinics</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Questionnaires were returned anonymously to the Society for Epilepsy Research (GfE) for statistical analyses</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Drop-out rate in EN group: 27%; drop-out rate in WLC group: 20%</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>HADS scores were available as a supplementary table, online.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Low risk for infidelity to the intervention protocol, and not enough information to evaluate selective recruitment</td>
</tr>
</tbody>
</table>

### Pramuka 2007

<table>
<thead>
<tr>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unblinded, randomized, controlled trial comparing a psychoeducational program (Treatment) to treatment as usual (TAU) in participants with epilepsy on epilepsy-related quality of life, self-efficacy, locus of control, and personality. Outcome measures were obtained at baseline, and 1-month and 6-month follow-up</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria: adults (18 or above) with a diagnosis of epilepsy made by a neurologist, ability to understand and participant in the consent process</td>
</tr>
<tr>
<td>Exclusion criteria: not specified</td>
</tr>
<tr>
<td>55 adults were enrolled. 31 and 24 were allocated to Treatment and TAU, respectively. The mean ages were 48.89 years (SD 14.3) in Treatment, and 48.1 years (SD 14.3) in TAU. The mean ages at first seizure were 22.5 years (SD 16.7) in Treatment, and 20.32 years (SD 13.1) in TAU</td>
</tr>
<tr>
<td>Participants were recruited at a university hospital-based regional epilepsy centre (from August 2003 to April 2005), and the VA Pittsburgh Healthcare System Neurology Clinic (from May 2004 to May 2005)</td>
</tr>
</tbody>
</table>
Interventions
The treatment was delivered in group format (6 to 12 per group), with weekly 2 hour sessions, for 6 consecutive weeks. Participants were reimbursed USD 10 for each intervention they attended, and USD 20 for completion of baseline or follow-up questionnaires. The curriculum and materials were developed with a multidisciplinary team (epilepsy centre neuropsychologist, an epilepsy nurse, rehabilitation psychologist, an exercise physiologist, and a behavioral interventionist). The specific components included a mixture of psychoeducation, medical information, and advocacy topics, framed in the self-management activities of self-evaluation, self-monitoring, stimulus control, and self-reward, plus peer support. The topics for the 6 weekly treatment were 1) taking charge of your medical care, 2) taking charge of your self-advocacy, 3) taking charge of stress, 4) taking charge of your schedule and goals, 5) taking charge of your relationships, and 6) taking charge of your future. Group interventions were co-led by two licensed psychologists and a research associate, with a guest lecture on medical issues, by an epilepsy nurse clinician.
Those in the TAU maintained their regular schedule of follow-up appointments with their neurologists and the epilepsy nurse in the clinic.

Outcomes
Quality of Life Inventory in Epilepsy-89 (QOLIE-89), Epilepsy self-efficacy scale (ESES), Washington Psychosocial Seizure Inventory (WPSI), Locus of control scale (LOC), Millon Clinical Multiaxial Inventory-III (MCMI-III)
Time points measured:
1) Baseline
2) 1-month follow-up
3) 6-month follow-up

Notes
Data were sought but not provided.

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>A table of random number was used to generate a randomization sequence. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Participants and investigators who led the group were not blinded to group assignment</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>High risk</td>
<td>Outcome assessors were not blinded.</td>
</tr>
</tbody>
</table>
| Incomplete outcome data (attrition bias) All outcomes | High risk | 12/31 (38%) in the Treatment, and 5/24 (21%) in the TAU groups withdrew after randomization. Attrition rate was consid-
### Pramuka 2007  (Continued)

<table>
<thead>
<tr>
<th>Bias Type</th>
<th>Risk Level</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective reporting (bias)</td>
<td>High risk</td>
<td>Baseline scores for both groups, and data for 6-month follow-up after baseline assessment for the TAU group were unavailable. Data were sought but not provided</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Time point of measurement was not clearly described. While the psychoeducation group lasted for 6 weeks after baseline, the first post-measurement was set at '1-month after baseline'. Clarification was sought but not provided. Not enough information to evaluate fidelity to the intervention protocol and selective recruitment</td>
</tr>
</tbody>
</table>

### Rau 2006

**Methods**

Assessor-blinded, quasi-randomized, controlled multi-center trial comparing a group educational program for children and their parents (FAMOSES) and wait-list control (WLC) in children with epilepsy on knowledge, coping, and treatment outcome. Outcome measures were obtained at baseline and 3-month follow-up.

**Participants**

Inclusion criteria: children with epilepsy, able to read and write in German, parents of children with epilepsy, whether or not they could read and write German

Exclusion criteria: children with non-epileptic seizures only, and their families

70 children (8 to 13 years) and 159 parents were enrolled. 82/55 and 77/48 parent were allocated/analyzed in the FAMOSES and WLC groups, respectively. 38/31 and 32/19 children were allocated/analyzed the FAMOSES and WLC groups, respectively. The mean ages in years were 10.8 (SD 1.8) and 10.3 (SD 1.8) in FAMOSES and WLC. There were 18 girls in FAMOSES and 12 girls in WLC. The mean durations of epilepsy in years were 5.4 (SD 3.6) years in FAMOSES and 4.3 years (SD 3.1) in WLC. 15/12 had focal epilepsy; 6/3 had generalized epilepsy; 6/1 had epilepsy with focal and generalized features; 2/1 had non-classified epilepsy; 2/2 did not provide information about their epilepsy in FAMOSES/WLC. 15/11 had further illnesses in FAMOSES/WLC. 28/17 took at least one AED in FAMOSES/WLC.

The participating nine institutions in Germany were Epilepsy Center Bethel, Bielefeld, Epilepsy Center Berlin-Brandenburg, Epilepsy Center Kleinwachau, Epilepsy outreach clinic, Regensburg, paediatric practice Dr. Bettendorf, Epilepsy Center Vogtareuth, Epilepsy Center Raisdorf, and the paediatric clinic Links der Weser, Bremen. Recruitment took place January 2003 to January 2004.

**Interventions**

FAMOSES is an educational program developed by an interdisciplinary project group to improve knowledge, coping, and treatment outcome, emotional and practical adaptation to the condition. The educational program comprised 1 group session (14 hours) for children (4 to 6 children) and 1 separate group session for parents (6 to 10 adults) The WLC group was offered conventional treatment according to individual needs.
Outcomes

KINDL (Gesundheitsbezogene Lebensqualität und psychosoziale Auswirkungen der Epilepsie/Health-related Quality of Life and psychosocial consequences of epilepsy), epilepsy knowledge, seizure frequency, contentment with therapeutic regimen, missed school days, evaluation of FAMOSES by participants

Time points measured:
1) Baseline (before randomization)
2) 3 months after the intervention (FAMOSES/baseline (WLC))

Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Unclear in publication. According to information sought from authors, the allocation depended on the participants’ application to the 1st or 2nd available course and the availability of places in the chosen course</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Unclear in publication. According to information sought from authors, the allocation was not concealed</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Blinded to final assessor only. Neither participants nor service providers were blinded</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>The participating research institutes that assessed the data received an anonymous set of collected data</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>76.4% of all study participants returned the questionnaires (parents: 78.6%; children: 71.4%; FAMOSES (children): 18.4%; WLC (children): 40.6%)</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes were reported at all measured times.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Not enough information to evaluate fidelity to the intervention protocol and selective recruitment</td>
</tr>
</tbody>
</table>
Schröder 2014

Methods

Assessor-blinded, randomized, controlled trial comparing an online psychological intervention for depression (Deprexis) to a wait-list control (WLC) in adults with epilepsy. The study aimed to evaluate the feasibility and efficacy of the program on depressive symptoms and quality of life. Outcome measures were obtained at baseline and 9 weeks after baseline (after intervention).

Participants

Inclusion criteria: self-reported epilepsy diagnosis (externally validated based on an epilepsy-specific inventory, the Performance, Sociodemographic Aspects, Subjective Estimation (PESOS) questionnaire), self-reported depressive symptoms
Exclusion criteria: acute suicidal ideation, diagnosis of psychosis, bipolar disorder, or suicidality, insufficient time to take part in the online program for 9 weeks
78 adults were enrolled. 38 and 40 were randomized to Deprexis and WLC, respectively. The mean age was 35.03 years (SD 9.99; range 18 to 57) in Deprexis and 40.03 (SD 11.85; range 22 to 77) in WLC. 27 and 32 were women in Deprexis and WLC. AEDs were well tolerated/badly tolerated by 17/20 participants in Deprexis and 19/20 participants in WLC. One participant in each group was not taking any AEDs. 26/12 participants in Deprexis had ≤ 1 seizure per month, and 27/13 in WLC had >1 seizure per month. 15/18/5 participants in Deprexis and 22/14/4 participants in the WLC had 1/2/≥ 3 different seizure types.
Participants in WLC group were, on average, significantly older than participants in the intervention group (P = 0.048). To take this group difference into account, the variable “age” had been entered as a covariate in the statistical analyses. Participants were recruited via a patient database from the Epilepsy Center Alsterdorf and postings in moderated epilepsy-specific online forums. Recruitment took place between May 2012 and July 2013.

Interventions

This trial used the Internet-based program Deprexis, which is aimed at reducing symptoms of depression. It predominantly comprised elements of CBT, such as cognitive restructuring and behavioral activation, and complemented these with mindfulness and acceptance exercises, among others. Users interacted with the program via a simulated dialogue, in which they were continuously asked to select one of several response options, and were presented with subsequent content that aimed to match their expressed preferences and requirements. Depending on reading speed and each user's individual path through the program, each module lasted for approximately 10 to 60 min. The participants could log in for a duration of 9 weeks.

Outcomes

Beck Depression Inventory (BDI-I), The World Health Organization (WHO) Quality of Life questionnaire (WHOQOL-BREF), Quality of Life Inventory in Epilepsy (QOLIE-31)
Time points measured:
1) Baseline
2) 9 weeks after the baseline

Notes

Risk of bias

Bias | Authors' judgement | Support for judgement
---|---------------------|----------------------

Psychological treatments for people with epilepsy (Review)

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### Schröder 2014 (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Risk</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation</td>
<td>Low</td>
<td>Allocation was done in consecutive order, using a computer-generated randomized number table. No evidence to suggest selection bias.</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Low</td>
<td>Allocation concealment was ensured.</td>
</tr>
<tr>
<td>Blinding of participants and personnel</td>
<td>High</td>
<td>Since the intervention was delivered by an internet platform, the provision was considered blinded; this conclusion was discussed with and agreed by study authors. However, the participants could not be blinded to their group status.</td>
</tr>
<tr>
<td>Blinding of outcome assessment</td>
<td>Low</td>
<td>All assessments and outcome measures were obtained online.</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>High</td>
<td>14/38 (Deprexis) and 8/40 (WLC) withdrew from the study. The overall attrition rate was 28%, which was higher than the expected rate (25%), as stated in the study methodology. Attrition bias was considered high for this short-term intervention.</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>Low</td>
<td>Unreported data were sought and provided by study authors. Comparison with registered protocol showed that some outcome parameters had originally been planned, but due to a change of protocol, had not been collected during the course of the study.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low</td>
<td>Low risk of infidelity to intervention protocol, since the intervention was provided via a web-based program. Not enough information to evaluate selective recruitment.</td>
</tr>
</tbody>
</table>

### Tang 2015

**Methods**

Assessor-blinded, randomized, controlled trial comparing a mindfulness-based therapy (MT) to a placebo attention social support (SS) in adults with epilepsy on quality of life, mood and anxiety symptoms, and seizure control. Outcome measures were obtained at 6-week pre-intervention baseline and 6 weeks post-intervention.
## Participants

| Inclusion criteria: adults (18 or above) with drug-resistant epilepsy according to ILAE definition |
| Exclusion criteria: primary diagnosis of organic mental disorder, psychotic disorders, psychogenic nonepileptic seizures, learning disability, or mental retardation |

61 adults were enrolled, 30 and 31 were randomly allocated to MT and SS. The mean age was 34.77 years (SD 10.26) in MT and 35.47 (SD 11.22) in SS. There were 14 women in each group. The mean disease duration in years was 20.43 (SD 9.95) in MT and 18.93 (SD 11.08) in SS. 36.7%/23.3%/36.7%/3.3% of the participants in MT and 40%/40%/16.7%/3.3% of the participants in SS were under AED monotherapy/two drugs/three drugs/four or more drugs. The total number of seizure in 6 weeks pre-intervention was 9.83 (SD 9.78) in MT, and 9 (SD 11.79) in SS. 40%/40%/36.7% of participants in MT/SS had experienced seizures within the past week.

Participants were recruited from the Neurology Outpatient Clinic in the Prince of Wales Hospital, the teaching hospital of the Chinese University of Hong Kong. The study took place between September 2011 and January 2013.

## Interventions

| Intervention comprised an active treatment: MT, and a placebo attention control, SS. Intervention was delivered in group format (7 to 8/group) with four 2.5-hour biweekly sessions, conducted by the same clinical psychologist. All participants received an identical educational package with basic knowledge and management of epilepsy, including layman terms of the etiology and types of seizure, sleep hygiene, and the importance of drug adherence and regular exercise. The MT protocol was based on several guiding references on mindfulness for patients with chronic diseases. The concept of mind-body connection that is rooted in the Chinese culture was emphasized. Therapeutic components, such as mindfulness techniques (e.g. mindful eating, body scan), the concept of acceptance, and coping with seizure related disturbances (i.e. auras and postictal physical and psychological reactions) were included. Participants had experiential, progressive training on mindfulness techniques during sessions. No direct intervention was provided in the SS group. It was designed to create a supportive atmosphere for sharing of illness experiences and self-help strategies with the same contact hours (10 hours) and format as the MT group. |

## Outcomes

| Patient-weighted Quality of Life Inventory on Epilepsy-31 (QOLIE-31-P), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), seizure frequency, Seizure severity questionnaires (SSQ) |
| Time points measured: |
| 1) Baseline (6 weeks before intervention) |
| 2) Follow-up (6 weeks after the intervention) |

## Notes

| Risk of bias |

| Bias | Authors’ judgement | Support for judgement |
| Random sequence generation (selection bias) | Low risk | Block randomization was used. No evidence to suggest selection bias |
**Tang 2015 (Continued)**

<table>
<thead>
<tr>
<th>Bias Type</th>
<th>Risk</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low</td>
<td>Allocation concealment was ensured, based on information provided by study authors.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High</td>
<td>All participants were told that they were provided 'supportive treatment'; they were not aware of the experimental/control design of the study. Investigator who led the group was not blinded to group assignment.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low</td>
<td>All outcome assessors were blinded.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low</td>
<td>1 participant in the SS group withdrew. No evidence to suggest attrition bias.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low</td>
<td>No evidence to suggest selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low</td>
<td>Relatively low risk of infidelity to the intervention protocol, since the intervention was only delivered by one therapist. Not enough information to evaluate selective recruitment.</td>
</tr>
</tbody>
</table>

**Thompson 2010**

**Methods**

Unblinded, controlled trial comparing a home-based depression intervention (UPLIFT) to wait-list control (WLC) in adults with epilepsy and symptoms of depression. The study aimed to explore the efficacy of UPLIFT in reducing depression, increasing knowledge, skills, and self-efficacy, and improving quality of life. Outcome measures were obtained at baseline, interim (8 weeks after intervention, post-intervention time point for UPLIFT), and post-test (16 weeks after intervention, post-intervention time point for WLC; repeated measure for UPLIFT).

**Participants**

Inclusion criteria: adults diagnosed with epilepsy for >1 year, had depressive symptoms as indicated by a score of >13 on the Center for Epidemiological Studies Depression scale (CES-D), but not severe depression (<38 on CES-D), who were English speaking and willing to be audio-taped.

Exclusion criteria: active suicidal ideation and cognitive impairment (i.e. score lower or equal to 20 on the telephone MMSE).

53 adults were enrolled. 26 and 27 were allocated to the UPLIFT and WLC, respectively. The mean/median age was 36.4/34.0 years in UPLIFT and 35.4/31.0 in WLC. 20 (UPLIFT) and 23 (WLC) were women. 13 participants in UPLIFT and 19 in WLC had a seizure in the 4 weeks prior to enrolment. 10 participants in UPLIFT and 9 in TAU had a major depressive disorder with mean/median CES-D scores of 25.7/24.5 in UPLIFT and 27.33/30.0 in WLC. Recruitment and screening were coordinated by the physicians and nurses at the participating hospital-based epilepsy clinic from June 2007 to November 2008.
### Interventions

Intervention was delivered either via telephone or web in group conferencing format, with weekly 1-hour sessions for 8 consecutive weeks. The UPLIFT acronym refers to both mindfulness (using practice) and CBT (learning to increase favorable thoughts) which formed the basis of the intervention materials. The telephone and web intervention contained the same elements and structure. Each session included a check-in, instruction, skill building, and discussion, with homework between sessions that was reviewed in the next session. Therapeutic components included knowledge about depression, epilepsy, CBT, mindfulness, and skills related to CBT and mindfulness. Participation in the sessions involved skills practice, discussion, and group exercises based on session’s main topics. CBT-related topics included thought monitoring, identifying cognitive distortions, self-esteem, problem identification, goal setting, and identifying supports. Relaxation exercises, including a body scan and progressive muscle relaxation, were used for coping and to facilitate awareness of the body. Mindfulness activities consisted of attention to breath, sights, and sounds, and other meditations. All sessions were co-facilitated by a layperson with epilepsy and a student research assistant in the Master of Public Health program, supervised by a licensed clinical psychologist.

### Outcomes

- Modified Beck Depression Inventory (mBDI), Beck Depression Inventory (BDI), Patient Health Questionnaire (PHQ-9), knowledge and skills, Depression Coping Self-Efficacy Scale (DCSES), Satisfaction with life scale (SWLS), Behavioral Risk Factor Surveillance System (BRFSS), Self-compassion scale (SCS)

### Time points measured:

1. Baseline (0 week, baseline)
2. Interim (8 weeks post-intervention for the first telephone and web UPLIFT)
3. Post-test (16 weeks post-intervention for the first telephone and web UPLIFT and 8 weeks post-intervention for the WLC)

### Notes

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Detailed information on method of randomization was unavailable</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Allocation was not concealed.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Neither the participants nor the project staff were blinded to the group assignment</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No information was provided.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>13 persons lost from the study (3 attended one 1 session; 10 attended none). The authors did not provide details of the drop-</td>
</tr>
</tbody>
</table>
### Thompson 2010  *(Continued)*

<table>
<thead>
<tr>
<th>Selective reporting (reporting bias)</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome parameters were unavailable for the post-test time point, except BDI and mBDI. Results of PHQ-9 and self-compassion were unavailable for all time points. Evidence of selective reporting noted. Unpublished data were sought but not provided.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other bias</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk for infidelity to intervention protocol since all therapists were supervised by a licensed clinical psychologist. Not enough information to evaluate selective recruitment.</td>
<td></td>
</tr>
</tbody>
</table>

### Yadegary 2015

**Methods**

Randomized, controlled trial comparing a self-management training program (Intervention) with a usual care control group (UC) in adults with epilepsy on epilepsy-related quality of life. Outcome measures were obtained at baseline and 1 month after intervention.

**Participants**

- **Inclusion criteria:** adults with epilepsy for at least 1 year, using antiepileptic drugs, had at least 1 seizure in the past year, able to read and write, were willing to participate.
- **Exclusion criteria:** conditions in which intensive care was needed, enrolled in other research studies, were absent from each training session.

60 participants (aged between 18 and 65) were recruited. 30 were randomly assigned to each of intervention and UC. 9/12/7/2 participants in intervention and 12/8/5/5 participants in UC were aged 18 to 25/26 to 35/36 to 45/46 to 65, respectively. 14 (intervention) and 15 (UC) were women. 2/1 participants in intervention and 28/29 in UC had partial seizures/generalized seizures. 17 participants had a seizure in the last month in both groups. 20/10 participants in intervention and 23/7 participants in UC had monotherapy/polytherapy.

The study took place in a teaching hospital in Zanjan, Iran.

**Interventions**

The intervention was delivered in group format (5 to 6 participants per group) with four 2-hour sessions within one month. Participants were phoned before every session to encourage them to attend. The intervention materials consisted of 2 parts. The first part (1st session) included medical aspects of epilepsy, e.g. definition of epilepsy, description of seizures, types of seizures, observation and classification of its causes, and diagnosis of epilepsy. Participants also received instructional booklet with the content. The second part (2nd to 4th session) was designed to promote self-management; details included...
Continued

medication management, information management, safety management, lifestyle management, and seizure management. All materials were presented using PowerPoint presentations.

The UC control group received only the routine clinical care, and was contacted through two short phone calls during the month.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Quality of Life Inventory in Epilepsy-31-P (QOLIE-31-P). Time points measured 1) Baseline 2) 1-month after intervention</th>
</tr>
</thead>
</table>

**Notes**

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>A table of random numbers was used. No evidence to suggest selection bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information was provided.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information was provided.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information was provided.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>Insufficient information was provided.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>No evidence to suggest selective reporting.</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Participants who were absent from each training session were excluded. Not using intention-to-treat analysis suggested participant selection bias. Not enough information to evaluate fidelity to the intervention protocol or selective recruitment</td>
</tr>
</tbody>
</table>
### Characteristics of excluded studies  [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aliasgharpour 2013</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Dahl 1985</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Dahl 1992</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Dash 2015</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Davis 1984</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Dilorio 2009</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Helgeson 1990</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Li 2016</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>McLaughlin 2011</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Modi 2016a</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Olley 2001</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Peterson 1984</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Pfafflin 2012</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Ridsdale 2000</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Tajrishi 2015</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Tan 1986</td>
<td>No HRQOL outcome measures</td>
</tr>
<tr>
<td>Thompson 2015</td>
<td>No HRQOL outcome measures</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Kralj-Hans 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial name or title: Self-Management education for adults with poorly controlled epilepsy (SMILE (UK): a randomized controlled trial protocol)</td>
</tr>
</tbody>
</table>
Methods
Prospective multi-center, pragmatic, parallel group randomized controlled trial comparing the effects of a group education program to wait-list control (WLC) on QoL, seizure frequency, and psychological distress (anxiety and depression).

Participants
Four hundred and twenty eight adult participants (aged ≥ 16) who attended specialist epilepsy outpatient clinics at 15 NHS participating sites in the previous 12 months, and who are currently being prescribed AEDs, are able to provide informed consent, participate in the workshops, and complete the questionnaires in English, have ≥ 2 seizures in previous 12 months.
Exclusion criteria: actual or suspected psychogenic non-epileptic seizures only, acute symptomatic seizures related to acute neurological illness, substance misuse, severe psychiatric disorder (e.g. psychosis), or terminal medical condition, enrolled in other epilepsy-related non-pharmacological treatment studies.

Interventions
Two-day Self-Management education for epilepsy (SMILE) (UK), which was originally developed in Germany (MOSES)

Outcomes
QoL (QOLIE-31-P), seizure frequency, psychological distress (Hospital Anxiety and Depression scale), perceived impact of epilepsy (Impact of epilepsy scale), adherence to medication (Epilepsy Self-Management Scale), management of adverse effects from medication (QOLIE-31-P), perceived stigma (Stigma of Epilepsy Scale), mastery or control of epilepsy (Epilepsy-specific scale), health economics (Client Service Receipt Inventory and EQ-5D)

Starting date
March 2014

Contact information
Department of Clinical Neuroscience PO 43, Institute of Psychiatry, King’s College London, Denmark Hill Campus, London SE5 8AF, UK, leone.ridsdale@kcl.ac.uk

Notes
### Data and Analyses

#### Comparison 1. QOLIE-31: Comparison of mean change from baseline

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 QOLIE-31- total score</td>
<td>9</td>
<td>468</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>5.68 [3.11, 8.24]</td>
</tr>
<tr>
<td>2 QOLIE-31 - emotional well-being subscale</td>
<td>8</td>
<td>440</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>7.03 [2.51, 11.54]</td>
</tr>
<tr>
<td>3 QOLIE-31 - energy and fatigue subscale</td>
<td>8</td>
<td>440</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>6.90 [3.49, 10.31]</td>
</tr>
<tr>
<td>4 QOLIE-31 - overall QoL subscale</td>
<td>8</td>
<td>440</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>6.47 [2.68, 10.25]</td>
</tr>
<tr>
<td>5 QOLIE-31 - seizure worry subscale</td>
<td>8</td>
<td>440</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>5.96 [2.50, 9.42]</td>
</tr>
<tr>
<td>6 QOLIE-31 - cognitive functioning subscale</td>
<td>8</td>
<td>440</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>3.00 [0.21, 5.78]</td>
</tr>
<tr>
<td>7 QOLIE-31 - medication effects subscale</td>
<td>8</td>
<td>440</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>3.84 [0.28, 7.41]</td>
</tr>
<tr>
<td>8 QOLIE-31 - social function subscale</td>
<td>8</td>
<td>438</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>2.77 [-1.02, 6.57]</td>
</tr>
</tbody>
</table>

#### Comparison 2. WHQOL-BREF: Comparison of post-intervention outcomes

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 WHOQOL-BREF - score</td>
<td>2</td>
<td>45</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>0.39 [-5.49, 6.28]</td>
</tr>
</tbody>
</table>

#### Comparison 3. SWLS: Comparison of post-intervention outcomes

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 SWLS - score</td>
<td>2</td>
<td>45</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>5.46 [-2.97, 13.89]</td>
</tr>
</tbody>
</table>
### Analysis 1.1. Comparison of QOLIE-31 - Comparison of mean change from baseline, Outcome 1 QOLIE-31 - total score.

**Review:** Psychological treatments for people with epilepsy

**Comparison:** QOLIE-31 - Comparison of mean change from baseline

**Outcome:** QOLIE-31 - total score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Psychological tx</th>
<th>N</th>
<th>Mean (SD)</th>
<th>UC or SC</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV/Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td>8</td>
<td>10.42 (6.58)</td>
<td>9</td>
<td>-0.9 (8.18)</td>
<td>90 %</td>
<td>11.32 [ 4.30, 18.34 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caller 2016</td>
<td>29</td>
<td>4.7 (10.3)</td>
<td>20</td>
<td>-1.9 (12.7)</td>
<td>95 %</td>
<td>6.60 [ -0.11, 13.31 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciechanowski 2010</td>
<td>32</td>
<td>5.73 (14.36)</td>
<td>33</td>
<td>1.33 (10.64)</td>
<td>10.6 %</td>
<td>4.40 [-1.76, 10.56 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fraser 2015</td>
<td>38</td>
<td>5.82 (9.61)</td>
<td>40</td>
<td>-1.29 (9.02)</td>
<td>16.0 %</td>
<td>7.11 [ 2.97, 11.25 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gandy 2014</td>
<td>20</td>
<td>3.92 (11.3)</td>
<td>25</td>
<td>0.33 (8.58)</td>
<td>11.0 %</td>
<td>3.59 [-2.40, 9.58 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helde 2005</td>
<td>56</td>
<td>3.27 (11.53)</td>
<td>53</td>
<td>2.63 (12.06)</td>
<td>15.1 %</td>
<td>0.64 [-3.79, 5.07 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martinović 2006</td>
<td>15</td>
<td>15.83 (11.8)</td>
<td>15</td>
<td>2.87 (7.16)</td>
<td>8.9 %</td>
<td>12.96 [ 5.88, 20.04 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td>7</td>
<td>17.25 (20.58)</td>
<td>8</td>
<td>8.14 (11.34)</td>
<td>2.1 %</td>
<td>9.11 [-8.02, 26.24 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tang 2015</td>
<td>30</td>
<td>7.29 (7.06)</td>
<td>30</td>
<td>2.29 (7.33)</td>
<td>17.7 %</td>
<td>3.32 [-0.32, 6.96 ]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)**: 235 233

Heterogeneity: Tau² = 6.21; Chi² = 14.14, df = 8 (P = 0.08); I² = 43%

Test for overall effect: Z = 4.34 (P = 0.000014)

Test for subgroup differences: Not applicable
### Analysis 1.2. Comparison 1 QOLIE-31 - Comparison of mean change from baseline, Outcome 2 QOLIE-31 - emotional well-being subscale.

**Review:** Psychological treatments for people with epilepsy

**Comparison:** 1 QOLIE-31 - Comparison of mean change from baseline

**Outcome:** 2 QOLIE-31 - emotional well-being subscale

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>psychological tx</th>
<th>UC or SC</th>
<th>Mean (SD)</th>
<th>Mean Difference</th>
<th>N</th>
<th>Weight</th>
<th>IV,Random,95% CI</th>
<th>Mean Difference</th>
<th>N</th>
<th>Weight</th>
<th>IV,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td></td>
<td></td>
<td>11.5 (11.01)</td>
<td>-6.23 (9.58)</td>
<td>8</td>
<td>11.0 %</td>
<td>17.73 [7.86, 27.60]</td>
<td></td>
<td>9</td>
<td>-6.23 (9.58)</td>
<td>17.73 [7.86, 27.60]</td>
</tr>
<tr>
<td>Caller 2016</td>
<td></td>
<td></td>
<td>1.1 (15.7)</td>
<td>-9.8 (21.8)</td>
<td>29</td>
<td>9.6 %</td>
<td>10.90 [-0.23, 22.03]</td>
<td></td>
<td>20</td>
<td>-9.8 (21.8)</td>
<td>10.90 [-0.23, 22.03]</td>
</tr>
<tr>
<td>Fraser 2015</td>
<td></td>
<td></td>
<td>5.39 (11.97)</td>
<td>-3.28 (11.19)</td>
<td>38</td>
<td>17.7 %</td>
<td>8.67 [3.52, 13.82]</td>
<td></td>
<td>40</td>
<td>-3.28 (11.19)</td>
<td>8.67 [3.52, 13.82]</td>
</tr>
<tr>
<td>Gandy 2014</td>
<td></td>
<td></td>
<td>5.8 (16.49)</td>
<td>-2.24 (11.72)</td>
<td>20</td>
<td>12.6 %</td>
<td>8.04 [-0.52, 16.60]</td>
<td></td>
<td>25</td>
<td>-2.24 (11.72)</td>
<td>8.04 [-0.52, 16.60]</td>
</tr>
<tr>
<td>Helde 2005</td>
<td></td>
<td></td>
<td>0.91 (16.37)</td>
<td>0.59 (17.93)</td>
<td>57</td>
<td>15.7 %</td>
<td>0.32 [-6.08, 6.72]</td>
<td></td>
<td>54</td>
<td>0.59 (17.93)</td>
<td>0.32 [-6.08, 6.72]</td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td></td>
<td></td>
<td>20.57 (19.92)</td>
<td>20 (19.36)</td>
<td>7</td>
<td>4.2 %</td>
<td>0.57 [-19.37, 20.51]</td>
<td></td>
<td>8</td>
<td>20 (19.36)</td>
<td>0.57 [-19.37, 20.51]</td>
</tr>
<tr>
<td>Tang 2015</td>
<td></td>
<td></td>
<td>3.3 (11.79)</td>
<td>3.6 (13.70)</td>
<td>30</td>
<td>16.9 %</td>
<td>-0.30 [-5.94, 5.34]</td>
<td></td>
<td>30</td>
<td>3.6 (13.70)</td>
<td>-0.30 [-5.94, 5.34]</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

221 219 100.0 % 7.03 [2.51, 11.54]

Heterogeneity: \( \tau^2 = 23.06; \chi^2 = 17.27, \text{df} = 7 \ (P = 0.02); \ I^2 = 59% \)

Test for overall effect: \( Z = 3.05 \ (P = 0.0023) \)

Test for subgroup differences: Not applicable
### Analysis 1.3. Comparison 1 QOLIE-31- Comparison of mean change from baseline, Outcome 3 QOLIE-31- energy and fatigue subscale.

#### Review: Psychological treatments for people with epilepsy

#### Comparison: 1 QOLIE-31- Comparison of mean change from baseline

#### Outcome: 3 QOLIE-31- energy and fatigue subscale

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>psychological tx</th>
<th>UC or SC</th>
<th>Mean Difference</th>
<th>Wgt.</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td></td>
<td>8</td>
<td>18.75 (6.74)</td>
<td>9</td>
<td>7.78 (12.62)</td>
</tr>
<tr>
<td>Caller 2016</td>
<td></td>
<td>29</td>
<td>4.7 (15.8)</td>
<td>20</td>
<td>-5.3 (18.1)</td>
</tr>
<tr>
<td>Ciechanowski 2010</td>
<td></td>
<td>32</td>
<td>5.06 (21)</td>
<td>33</td>
<td>2.41 (13.47)</td>
</tr>
<tr>
<td>Fraser 2015</td>
<td></td>
<td>38</td>
<td>8.89 (17.6)</td>
<td>40</td>
<td>-4.35 (14.86)</td>
</tr>
<tr>
<td>Gandy 2014</td>
<td></td>
<td>20</td>
<td>3.75 (16.29)</td>
<td>25</td>
<td>-4.8 (12.54)</td>
</tr>
<tr>
<td>Helde 2005</td>
<td></td>
<td>57</td>
<td>0.44 (20.64)</td>
<td>54</td>
<td>0.37 (18.32)</td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td></td>
<td>7</td>
<td>20 (16.83)</td>
<td>8</td>
<td>8.13 (25.6)</td>
</tr>
<tr>
<td>Tang 2015</td>
<td></td>
<td>30</td>
<td>8.84 (9.16)</td>
<td>30</td>
<td>4 (12.3)</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

|                      | 221               | 219               | 100.0 % | 6.90 [ 3.49, 10.31 ] |

Heterogeneity: $I^2 = 5.73$; $Chi^2 = 9.23$, df = 7 ($P = 0.24$); $I^2 = 24$

Test for overall effect: $Z = 3.96$ ($P = 0.000074$)

Test for subgroup differences: Not applicable

---

Psychological treatments for people with epilepsy (Review)  
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### Analysis 1.4. Comparison of mean change from baseline, Outcome 4 QOLIE-31 - overall QoL subscale.

**Review:** Psychological treatments for people with epilepsy  
**Comparison:** 1 QOLIE-31 - Comparison of mean change from baseline  
**Outcome:** 4 QOLIE-31 - overall QoL subscale

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>psychological tx</th>
<th>UC or SC</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td>8</td>
<td>9</td>
<td>1.39 (9.75)</td>
<td>9.1 %</td>
<td>15.46 [ 5.15, 25.77 ]</td>
</tr>
<tr>
<td>Caller 2016</td>
<td>29</td>
<td>20</td>
<td>-6 (16.9)</td>
<td>11.4 %</td>
<td>8.20 [ -0.38, 16.78 ]</td>
</tr>
<tr>
<td>Ciechanowski 2010</td>
<td>32</td>
<td>33</td>
<td>-2.63 (13.64)</td>
<td>11.7 %</td>
<td>3.62 [ -4.80, 12.04 ]</td>
</tr>
<tr>
<td>Fraser 2015</td>
<td>38</td>
<td>40</td>
<td>-0.78 (11.3)</td>
<td>13.5 %</td>
<td>0.91 [-6.48, 8.30]</td>
</tr>
<tr>
<td>Gandy 2014</td>
<td>20</td>
<td>25</td>
<td>0.13 (13.49)</td>
<td>15.2 %</td>
<td>10.06 [ 3.55, 16.57 ]</td>
</tr>
<tr>
<td>Helde 2005</td>
<td>57</td>
<td>54</td>
<td>4.09 (16.34)</td>
<td>15.7 %</td>
<td>-0.80 [-7.07, 5.47]</td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td>7</td>
<td>8</td>
<td>2.82 (18)</td>
<td>4.0 %</td>
<td>16.82 [-0.76, 34.40]</td>
</tr>
<tr>
<td>Tang 2015</td>
<td>30</td>
<td>30</td>
<td>0.75 (8)</td>
<td>19.5 %</td>
<td>7.75 [ 3.11, 12.39]</td>
</tr>
</tbody>
</table>

**Total (95% CI):** 221  
219  

Heterogeneity: $\tau^2 = 13.54$; $\chi^2 = 13.61$, df = 7 ($P = 0.06$); $I^2 = 49\%$

Test for overall effect: $Z = 3.35$ ($P = 0.00082$)

Test for subgroup differences: Not applicable

---

**Psychological treatments for people with epilepsy (Review)**

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### Analysis 1.5. Comparison 1 QOLIE-31- Comparison of mean change from baseline, Outcome 5 QOLIE-31 - seizure worry subscale.

**Review:** Psychological treatments for people with epilepsy

**Comparison:** 1 QOLIE-31 - Comparison of mean change from baseline

**Outcome:** 5 QOLIE-31 - seizure worry subscale

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>psychological tx</th>
<th>UC or SC</th>
<th>Mean (SD)</th>
<th>N</th>
<th>Mean (SD)</th>
<th>N</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>IV Random,95% CI</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td></td>
<td>UC</td>
<td>6.33 (26.47)</td>
<td>8</td>
<td>-5.18 (16.68)</td>
<td>9</td>
<td>2.6%</td>
<td>11.51 [-9.83, 32.85]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caller 2016</td>
<td></td>
<td>SC</td>
<td>8.5 (15)</td>
<td>29</td>
<td>-1.2 (18.3)</td>
<td>20</td>
<td>12.7%</td>
<td>9.70 [0.00, 19.40]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciechanowski 2010</td>
<td></td>
<td>UC</td>
<td>6.42 (26.49)</td>
<td>32</td>
<td>0.78 (25.74)</td>
<td>33</td>
<td>7.4%</td>
<td>5.64 [-7.06, 18.34]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fraser 2015</td>
<td></td>
<td>SC</td>
<td>6.07 (13.41)</td>
<td>38</td>
<td>0.53 (13.64)</td>
<td>40</td>
<td>33.2%</td>
<td>5.54 [-0.46, 11.54]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gandy 2014</td>
<td></td>
<td>UC</td>
<td>2.74 (21.67)</td>
<td>20</td>
<td>-3.08 (20.31)</td>
<td>25</td>
<td>7.8%</td>
<td>5.82 [-6.57, 18.21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helde 2005</td>
<td></td>
<td>SC</td>
<td>5.57 (24.64)</td>
<td>57</td>
<td>3.89 (17.73)</td>
<td>54</td>
<td>18.9%</td>
<td>1.68 [-6.27, 9.63]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td></td>
<td>UC</td>
<td>28.56 (33.88)</td>
<td>7</td>
<td>5.96 (20.31)</td>
<td>8</td>
<td>1.4%</td>
<td>22.60 [-6.22, 51.42]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tang 2015</td>
<td></td>
<td>SC</td>
<td>10.55 (19.15)</td>
<td>30</td>
<td>3.83 (25.74)</td>
<td>30</td>
<td>15.9%</td>
<td>6.72 [-1.95, 15.39]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td>221</td>
<td></td>
<td>219</td>
<td>100.0%</td>
<td>5.96 [2.50, 9.42]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.0; Chi² = 3.27, df = 7 (P = 0.86); I² = 0.0%
Test for overall effect: Z = 3.38 (P = 0.00073)
Test for subgroup differences: Not applicable
### Analysis 1.6. Comparison 1 QOLIE-31- Comparison of mean change from baseline, Outcome 6 QOLIE-31 - cognitive functioning subscale.

Review: Psychological treatments for people with epilepsy

Comparison: 1 QOLIE-31- Comparison of mean change from baseline

Outcome: 6 QOLIE-31 - cognitive functioning subscale

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>psychological tx</th>
<th>UC or SC</th>
<th>N</th>
<th>Mean(SD)</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>IV-Random,95% CI</th>
<th>IV-Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td>8</td>
<td>9</td>
<td>7.81 (14.82)</td>
<td>2.71 (11.36)</td>
<td>4.8%</td>
<td>10.52</td>
<td>[-2.15, 23.19]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caller 2016</td>
<td>29</td>
<td>20</td>
<td>8.8 (16.4)</td>
<td>6 (14.1)</td>
<td>10.5%</td>
<td>2.80</td>
<td>[-5.79, 11.39]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciechanowski 2010</td>
<td>32</td>
<td>33</td>
<td>4.37 (21.05)</td>
<td>2.32 (13.1)</td>
<td>10.6%</td>
<td>2.05</td>
<td>[-5.79, 11.39]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fraser 2015</td>
<td>38</td>
<td>40</td>
<td>2.36 (12.09)</td>
<td>1.32 (14.18)</td>
<td>22.8%</td>
<td>3.68</td>
<td>[-2.16, 9.52]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gandy 2014</td>
<td>20</td>
<td>25</td>
<td>3.16 (16.97)</td>
<td>1.68 (13.43)</td>
<td>9.3%</td>
<td>1.48</td>
<td>[-7.63, 10.59]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helde 2005</td>
<td>57</td>
<td>54</td>
<td>2.28 (13.98)</td>
<td>1.26 (15.39)</td>
<td>25.8%</td>
<td>1.02</td>
<td>[-4.46, 6.50]</td>
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<td></td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td>7</td>
<td>8</td>
<td>16.07 (26.58)</td>
<td>6.9 (13.5)</td>
<td>1.6%</td>
<td>9.17</td>
<td>[-12.62, 30.96]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tang 2015</td>
<td>30</td>
<td>30</td>
<td>7.66 (15.76)</td>
<td>3.61 (13.40)</td>
<td>14.5%</td>
<td>4.05</td>
<td>[-3.27, 11.37]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI):** 221 219 100.0% 3.00 [0.21, 5.78]

Heterogeneity: Tau² = 0.0; Chi² = 2.45, df = 7 (P = 0.93); I² = 0.0%

Test for overall effect: Z = 2.11 (P = 0.035)

Test for subgroup differences: Not applicable
### Analysis 1.7: Comparison 1 QOLIE-31 - Comparison of mean change from baseline, Outcome 7 QOLIE-31 - medication effects subscale.

**Review:** Psychological treatments for people with epilepsy

**Comparison:** 1 QOLIE-31 - Comparison of mean change from baseline

**Outcome:** 7 QOLIE-31 - medication effects subscale

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Psychological tx</th>
<th>UO or SC</th>
<th>Mean Difference</th>
<th>Mean Difference 95% CI</th>
<th>Weight</th>
<th>Mean Difference 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td>8</td>
<td>9</td>
<td>-4.06 (15.87)</td>
<td>3.7% 9.62 [-8.86, 28.10 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caller 2016</td>
<td>29</td>
<td>20</td>
<td>-4.6 (24.4)</td>
<td>5.4% 11.00 [-4.31, 26.31 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciechanowski 2010</td>
<td>32</td>
<td>33</td>
<td>-3.68 (22.93)</td>
<td>9.4% 7.36 [-4.26, 18.98 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fraser 2015</td>
<td>38</td>
<td>40</td>
<td>-8.11 (20.83)</td>
<td>13.8% 9.04 [-0.54, 18.62 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gandy 2014</td>
<td>20</td>
<td>25</td>
<td>4.11 (16.98)</td>
<td>11.5% -2.58 [-13.11, 7.95 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helde 2005</td>
<td>57</td>
<td>54</td>
<td>2.57 (23.95)</td>
<td>18.4% 3.38 [-4.93, 11.69 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td>7</td>
<td>8</td>
<td>12.04 (14.85)</td>
<td>1.3% -7.29 [-38.30, 23.72 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tang 2015</td>
<td>30</td>
<td>30</td>
<td>0.74 (8.15)</td>
<td>36.4% 1.96 [-3.95, 7.87 ]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI):** 221 219 100.0% 3.84 [0.28, 7.41]

Heterogeneity: Tau² = 0.0; Chi² = 5.02, df = 7 (P = 0.66); I² =0.0%

Test for overall effect: Z = 2.11 (P = 0.035)

Test for subgroup differences: Not applicable
### Analysis 1.8. Comparison 1 QOLIE-31 - Comparison of mean change from baseline, Outcome 8 QOLIE-31 - social function subscale.

**Review:** Psychological treatments for people with epilepsy  
**Comparison:** QOLIE-31 - Comparison of mean change from baseline  
**Outcome:** 8 QOLIE-31 - social function subscale

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Psychological tx</th>
<th>UC or SC</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au 2003</td>
<td>8</td>
<td>5.48 (12.4)</td>
<td>9</td>
<td>-4.28 (21.85)</td>
<td>5.2 %</td>
<td>9.76 [-6.90, 26.42]</td>
<td></td>
</tr>
<tr>
<td>Caller 2016</td>
<td>29</td>
<td>2.3 (18.8)</td>
<td>20</td>
<td>-1.6 (20.1)</td>
<td>11.6 %</td>
<td>3.90 [-7.25, 15.05]</td>
<td></td>
</tr>
<tr>
<td>Ciechanowski 2010</td>
<td>32</td>
<td>4.77 (22.34)</td>
<td>33</td>
<td>2.1 (40.15)</td>
<td>5.8 %</td>
<td>2.67 [-13.06, 18.40]</td>
<td></td>
</tr>
<tr>
<td>Fraser 2015</td>
<td>38</td>
<td>8.12 (16.48)</td>
<td>40</td>
<td>3.18 (19.69)</td>
<td>22.3 %</td>
<td>4.94 [-3.10, 12.98]</td>
<td></td>
</tr>
<tr>
<td>Gandy 2014</td>
<td>20</td>
<td>7 (18.52)</td>
<td>25</td>
<td>4.84 (17.51)</td>
<td>12.8 %</td>
<td>2.16 [-8.47, 12.79]</td>
<td></td>
</tr>
<tr>
<td>Helde 2005</td>
<td>56</td>
<td>6.08 (21.01)</td>
<td>53</td>
<td>5.17 (22.82)</td>
<td>21.2 %</td>
<td>0.91 [-7.34, 9.16]</td>
<td></td>
</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td>7</td>
<td>10.49 (34.85)</td>
<td>8</td>
<td>4.69 (22.28)</td>
<td>1.6 %</td>
<td>5.80 [-24.30, 35.90]</td>
<td></td>
</tr>
<tr>
<td>Tang 2015</td>
<td>30</td>
<td>7.34 (16.19)</td>
<td>30</td>
<td>7.35 (16.19)</td>
<td>19.6 %</td>
<td>-0.01 [-8.58, 8.56]</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)** | 220 | 218 | 100.0 % | 2.77 [-1.02, 6.57] |

Heterogeneity: $\tau^2 = 0.0$, $\text{Chi}^2 = 1.65$, df = 7 ($p = 0.98$); $I^2 = 0.0$

*Test for overall effect: $Z = 1.43$ ($p = 0.15$)*
*Test for subgroup differences: Not applicable*
Analysis 2.1. Comparison 2 WHQOL-BREF - Comparison of post-intervention outcomes, Outcome 1 WHOQOL-BREF - score.

Review: Psychological treatments for people with epilepsy

Comparison: 2 WHQOL-BREF - Comparison of post-intervention outcomes

Outcome: 1 WHOQOL-BREF - score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>mindfulness therapy (MT)</th>
<th>supportive therapy (ST)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lundgren 2006</td>
<td>N = 14 , Mean(SD) 58.36 (9.66)</td>
<td>N = 13 , Mean(SD) 55.31 (6.59)</td>
<td>3.05 [ -3.15, 9.25 ]</td>
<td>56.0 %</td>
<td>3.05 [ -3.15, 9.25 ]</td>
</tr>
<tr>
<td>Lundgren 2008</td>
<td>N = 10 , Mean(SD) 57.2 (7.2)</td>
<td>N = 8 , Mean(SD) 60.2 (8.6)</td>
<td>-3.00 [ -10.45, 4.45 ]</td>
<td>44.0 %</td>
<td>-3.00 [ -10.45, 4.45 ]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>24</td>
<td>21</td>
<td>0.39 [-5.49, 6.28]</td>
<td>100.0 %</td>
<td>0.39 [-5.49, 6.28]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau^2 = 6.08; Chi^2 = 1.50, df = 1 (P = 0.22); I^2 = 33%
Test for overall effect: Z = 0.13 (P = 0.90)
Test for subgroup differences: Not applicable

Analysis 3.1. Comparison 3 SWLS - Comparison of post-intervention outcomes, Outcome 1 SWLS - score.

Review: Psychological treatments for people with epilepsy

Comparison: 3 SWLS - Comparison of post-intervention outcomes

Outcome: 1 SWLS - score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>mindfulness therapy (MT)</th>
<th>supportive therapy (ST)</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lundgren 2006</td>
<td>N = 14 , Mean(SD) 23.28 (4.58)</td>
<td>N = 13 , Mean(SD) 13.85 (5.98)</td>
<td>9.43 [ 5.39, 13.47 ]</td>
<td>54.0 %</td>
<td>9.43 [ 5.39, 13.47 ]</td>
</tr>
<tr>
<td>Lundgren 2008</td>
<td>N = 10 , Mean(SD) 21.8 (6.3)</td>
<td>N = 8 , Mean(SD) 21.0 (7.1)</td>
<td>0.80 [-5.48, 7.08 ]</td>
<td>46.0 %</td>
<td>0.80 [-5.48, 7.08 ]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>24</td>
<td>21</td>
<td>5.46 [-2.97, 13.89 ]</td>
<td>100.0 %</td>
<td>5.46 [-2.97, 13.89 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau^2 = 29.98; Chi^2 = 5.13, df = 1 (P = 0.02); I^2 = 81%
Test for overall effect: Z = 1.27 (P = 0.20)
Test for subgroup differences: Not applicable
### Table 1. Intervention methods, strategies, and treatment goals

<table>
<thead>
<tr>
<th>Study (intervention acronym)</th>
<th>Main treatment method</th>
<th>Primary treatment goal</th>
<th>Main treatment strategy</th>
<th>Setting</th>
<th>Delivery</th>
<th>Timing</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychological Interventions</strong></td>
<td>Au 2003</td>
<td>Cognitive behavioral therapy (CBT)</td>
<td>Seizure frequency</td>
<td>Clinic</td>
<td>Group</td>
<td>8 weekly 2-h sessions</td>
<td>N = 17 adults with at least 2 seizures per month, with subjectively reported psychological distress</td>
</tr>
<tr>
<td></td>
<td>Clechanowski 2010 (PEARLS)</td>
<td>Cognitive behavioral therapy (CBT)</td>
<td>Depressive symptom</td>
<td>Home-based + telephone calls</td>
<td>Individual</td>
<td>8 50-min in-home sessions in 5 months + 7 monthly 5- to 10-min telephone calls</td>
<td>N = 80 adults with epilepsy with significant depression</td>
</tr>
<tr>
<td></td>
<td>Gandy 2014</td>
<td>Cognitive behavioral therapy (CBT)</td>
<td>Depressive symptoms</td>
<td>Clinic</td>
<td>Individual</td>
<td>1 1 to 2 h assessment session + 8 weekly 1-h sessions</td>
<td>N = 59 adults with epilepsy</td>
</tr>
<tr>
<td></td>
<td>Martinović 2015</td>
<td>Cognitive behavioral therapy (CBT)</td>
<td>Depressive symptoms</td>
<td>Clinic</td>
<td>Group</td>
<td>8 weekly sessions + 4 monthly sessions</td>
<td>N = 32 adolescents with epilepsy and subthreshold depression</td>
</tr>
<tr>
<td>Study</td>
<td>Intervention Method/Type</td>
<td>Strategy/Treatment</td>
<td>Symptom(s)</td>
<td>Setting</td>
<td>Format</td>
<td>N</td>
<td>Notes</td>
</tr>
<tr>
<td>-------------------------------</td>
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</tr>
<tr>
<td>Orjuela-Rojas 2015</td>
<td>Cognitive-behavioral therapy (CBT)</td>
<td>Cognitive restructuring to address negative depressive thinking + behavioral activation</td>
<td>Depressive symptoms</td>
<td>Clinic</td>
<td>Group</td>
<td>12 weekly 90-min sessions</td>
<td>N = 15 adults with epilepsy and major depression</td>
</tr>
<tr>
<td>Schröder 2014 (Deprexis)</td>
<td>Cognitive-behavioral therapy (CBT)</td>
<td>Cognitive restructuring to address negative depressive thinking + behavioral activation</td>
<td>Depressive symptoms</td>
<td>Individual</td>
<td>9 weekly modules (10 to 60 min)</td>
<td>N = 78 adults with self-reported depressive symptoms</td>
<td></td>
</tr>
<tr>
<td>Thompson 2010 (UP-LIFT)</td>
<td>Cognitive-behavioral therapy (CBT)</td>
<td>Cognitive restructuring to address negative depressive thinking + behavioral activation</td>
<td>Depressive symptoms</td>
<td>Internet-based + telephone calls</td>
<td>Group</td>
<td>8 weekly 1-h sessions</td>
<td>N = 53 adults with epilepsy and depression (but not severe depression)</td>
</tr>
<tr>
<td>Hosseini 2016</td>
<td>Motivational interviewing (MI)</td>
<td>Enhancement of internal motivation for change, by overcoming dualism</td>
<td>Quality of life</td>
<td>Clinic</td>
<td>Group</td>
<td>5 sessions in 20 days</td>
<td>N = 56 adults with epilepsy.</td>
</tr>
<tr>
<td>Lundgren 2006; Lundgren 2008</td>
<td>Mindfulness therapy (MT)</td>
<td>Acceptance and commitment therapy (ACT) + seizure management</td>
<td>Quality of life</td>
<td>Clinic</td>
<td>Group + individual</td>
<td>5 individual 90-min sessions + 2 group 3-h sessions + 2 1-h boosters at 6 and 12 months</td>
<td>N = 27 (Lundgren 2006) N = 18 adults with epilepsy (Lundgren 2008)</td>
</tr>
<tr>
<td>Table 1. Intervention methods, strategies, and treatment goals (Continued)</td>
<td></td>
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<tr>
<td><strong>Self-management Interventions</strong></td>
<td>Tang 2015</td>
<td>Mindfulness therapy (MT)</td>
<td>Quality of life</td>
<td>Epilepsy management + mindfulness techniques + seizure-related acceptance</td>
<td>Clinic</td>
<td>Group</td>
<td>4 bi-weekly 2.5-h sessions</td>
</tr>
<tr>
<td></td>
<td>Dilorio 2011 (WebEase)</td>
<td>Motivational interviewing (MI)</td>
<td>Medication adherence + perceived stress</td>
<td>Medication adherence + stress and sleep management</td>
<td>Internet-based</td>
<td>Individual</td>
<td>3 biweekly modules</td>
</tr>
<tr>
<td></td>
<td>Fraser 2015 (PACES)</td>
<td>Consumer-driven psychoeducation</td>
<td>Self-management</td>
<td>Medical and psychosocial self-management + epilepsy-related communication</td>
<td>Clinic</td>
<td>Group</td>
<td>8 weekly 75-min sessions</td>
</tr>
<tr>
<td></td>
<td>Yadegary 2015</td>
<td>Self-management training program</td>
<td>Quality of life</td>
<td>Medical and psychosocial self-management + seizure communication</td>
<td>Clinic</td>
<td>Group</td>
<td>4 weekly 120-min sessions</td>
</tr>
<tr>
<td><strong>Adherence interventions</strong></td>
<td>Pakpour 2015</td>
<td>Motivational interviewing (MI)</td>
<td>Medication adherence</td>
<td>MI techniques</td>
<td>Clinic</td>
<td>Individual</td>
<td>3 weekly 40-min to 60-min sessions</td>
</tr>
<tr>
<td><strong>Educational interventions</strong></td>
<td>Jantzen 2009 (FLIP &amp; FLAP)</td>
<td>Epilepsy education program</td>
<td>Quality of life</td>
<td>Disease knowledge, advocacy topics, self-management, psychosocial aspects</td>
<td>Clinic</td>
<td>Group</td>
<td>2-day course (14 h)</td>
</tr>
<tr>
<td></td>
<td>May 2002 (MOSES)</td>
<td>Epilepsy education program</td>
<td>Quality of life</td>
<td>Disease knowledge, advocacy topics, self-management</td>
<td>Clinic</td>
<td>Group</td>
<td>N = 383 adolescents and adults with</td>
</tr>
<tr>
<td>Study</td>
<td>Intervention</td>
<td>Outcomes</td>
<td>Setting</td>
<td>Delivery</td>
<td>N</td>
<td></td>
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<td>---------------</td>
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<td>-----------------------------------------------</td>
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<td></td>
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</tr>
<tr>
<td>Lua 2013</td>
<td>Epilepsy education program</td>
<td>Quality of life</td>
<td>SMS-based</td>
<td>Individual</td>
<td>11 weekly modules</td>
<td>144 adults with epilepsy</td>
<td></td>
</tr>
<tr>
<td>Pramuka 2007</td>
<td>Epilepsy education program</td>
<td>Quality of life</td>
<td>Clinic Group</td>
<td>6 weekly 2-h sessions</td>
<td>55 adults with epilepsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rau 2006 (FAMOSES)</td>
<td>Epilepsy education program</td>
<td>Knowledge + coping</td>
<td>Clinic Group</td>
<td>2-day course (14 h)</td>
<td>70 children with epilepsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfafflin 2016</td>
<td>Counseling</td>
<td>Satisfaction with information and support</td>
<td>Clinic Individual</td>
<td>Delivery during routine visits</td>
<td>187 adults with epilepsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Berton 2014 (EUD-COM)</td>
<td>Patient-tailored medication education</td>
<td>Drug-related problems</td>
<td>Clinic Individual</td>
<td>1-h session + booster session after 1 month</td>
<td>174 adults with epilepsy and chronic co-morbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined interventions</td>
<td>Caller 2016 (HOB-SCOTCH)</td>
<td>Cognitive, memory + self management training</td>
<td>Quality of life</td>
<td>Problem solving therapy and behavior modification strategies + seizure management + social skills</td>
<td>Home-based + telephone calls</td>
<td>Group + individual</td>
<td>8 weekly 40-min to 60-min sessions</td>
</tr>
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<td>-----------------------------------------------------------------</td>
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</tr>
<tr>
<td></td>
<td>Helde 2005</td>
<td>Epilepsy education + nurse-led counselling</td>
<td>Quality of life</td>
<td>Personalized counselling + disease knowledge + drug adherence</td>
<td>Clinic + phone calls</td>
<td>Group + individual</td>
<td>1-day group + phone calls every 3 months for 2 yrs</td>
</tr>
</tbody>
</table>

Table 2. Effects of interventions

<table>
<thead>
<tr>
<th>Study (intervention acronym)</th>
<th>HRQOL</th>
<th>Depression</th>
<th>Anxiety</th>
<th>Seizure-related outcomes</th>
<th>Additional outcomes</th>
<th>Time points measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological interventions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Au 2003</td>
<td>QOLIE-31²</td>
<td>NA</td>
<td>NA</td>
<td>seizure frequency¹</td>
<td>ESES</td>
<td>1) baseline, 2) post-intervention</td>
</tr>
<tr>
<td>Ciechanowski 2010 (PEARLS)</td>
<td>QOLIE-31²</td>
<td>HSCL-20¹</td>
<td>NA</td>
<td>seizure frequency</td>
<td>NA</td>
<td>1) baseline, 2) post-intervention 3) 12-month follow-up 4) 18-month follow-up</td>
</tr>
<tr>
<td>Gandy 2014</td>
<td>QOLIE-31²</td>
<td>HADS-D¹, NDDI-E¹</td>
<td>HADS-A¹</td>
<td>NA</td>
<td>NA</td>
<td>1) baseline, 2) post-intervention, 3) 3-month follow-up</td>
</tr>
<tr>
<td>Hosseini 2016</td>
<td>QOLIE-89¹</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1) baseline, 2) post-intervention</td>
</tr>
<tr>
<td>Lundgren 2006</td>
<td>SWLS¹</td>
<td>WHOQOL-BREF¹</td>
<td>NA</td>
<td>seizure frequency, seizure index</td>
<td>NA</td>
<td>1) baseline, 2) post-intervention</td>
</tr>
</tbody>
</table>

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Table 2. Effects of interventions  
(Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Measure(s)</th>
<th>Domain(s)</th>
<th>Time Points</th>
<th>Follow-up Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lundgren 2008</strong></td>
<td>SWLS¹⁺, WHOQOL-BREF¹ ²</td>
<td>NA</td>
<td>NA</td>
<td>1) baseline, 2) post-intervention, 3) 6-month follow-up, 4) 12-month follow-up</td>
</tr>
<tr>
<td><strong>Martinovic 2006</strong></td>
<td>QOLIE-31²</td>
<td>BDI¹, CES-D¹, HAMD¹</td>
<td>NA</td>
<td>1) baseline, 2) post-intervention, 3) 9-month follow up</td>
</tr>
<tr>
<td><strong>Orjuela-Rojas 2015</strong></td>
<td>QOLIE-31²</td>
<td>BDI¹, HADS-D¹, MINI²</td>
<td>HADS-A¹</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Schröder 2014 (Deprexis)</strong></td>
<td>QOLIE-31, WHOQOL-BREF</td>
<td>BDI¹</td>
<td>NA</td>
<td>1) baseline, 2) post-intervention</td>
</tr>
<tr>
<td><strong>Tang 2015</strong></td>
<td>QOLIE-31- P¹ ²</td>
<td>BDI-II</td>
<td>BAI</td>
<td>seizure frequency, SSI</td>
</tr>
<tr>
<td><strong>Thompson 2010 (UPLIFT)</strong></td>
<td>SWLS</td>
<td>BDI¹</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Self-management interventions</strong></td>
<td>QOLIE-10</td>
<td>NA</td>
<td>NA</td>
<td>ESI-R¹, ESMS², MAS³, PSQI⁴, PSS², Epilepsy Knowledge Profile</td>
</tr>
<tr>
<td><strong>Fraser 2015 (PACES)</strong></td>
<td>QOLIE-31²</td>
<td>PHQ-9</td>
<td>GAD-7</td>
<td>NA</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Table 2. Effects of interventions  (Continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yadegary 2015</strong></td>
</tr>
<tr>
<td><strong>Adherence</strong></td>
</tr>
<tr>
<td><strong>Pakpour 2015</strong></td>
</tr>
<tr>
<td><strong>Educational</strong></td>
</tr>
<tr>
<td><strong>Beretta 2014</strong></td>
</tr>
<tr>
<td><strong>Jantzen 2009 (FLIP&amp; FLAP )</strong></td>
</tr>
<tr>
<td><strong>Lua 2013</strong></td>
</tr>
<tr>
<td><strong>May 2002 (MOSES)</strong></td>
</tr>
<tr>
<td><strong>Pfäfflin 2016</strong></td>
</tr>
<tr>
<td><strong>Pramuka 2007</strong></td>
</tr>
<tr>
<td><strong>Rau 2006 (FAMOSES)</strong></td>
</tr>
</tbody>
</table>

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Table 2. Effects of interventions (Continued)

<table>
<thead>
<tr>
<th>Combined interventions</th>
<th>Caller 2016 (HOB-SCOTCH)</th>
<th>QOLIE-31¹²</th>
<th>PHQ-9</th>
<th>NDDI-E</th>
<th>NA</th>
<th>NA</th>
<th>Self-report cognitive and executive function</th>
<th>1) baseline, 2) post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Helde 2005</td>
<td>QOLIE-89¹²</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>VAS scale</td>
<td>1) baseline, 2) post-intervention</td>
</tr>
</tbody>
</table>

¹ - primary outcome measure(s) in study
² - included in meta-analysis

Interpretation of post-intervention outcomes

- Significant improvement in treatment group when comparing post-intervention outcomes of treatment and control group
- No significant difference between treatment and control group at post-intervention based on mean comparisons

Outcome Measures

<table>
<thead>
<tr>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAI - Beck Anxiety Inventory</td>
</tr>
<tr>
<td>BDI or BDI II - Beck Depression Inventory or Beck Depression Inventory II</td>
</tr>
<tr>
<td>BRFSS - Behavioral Risk Factor Surveillance System</td>
</tr>
<tr>
<td>CES-D - Center for Epidemiological Study on Depression scale</td>
</tr>
<tr>
<td>DISABKIDS - Modular HRQOL questionnaire</td>
</tr>
<tr>
<td>DCSES - Depression Coping Self-Efficacy Scale</td>
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<tr>
<td>ESES - Epilepsy Self-Efficacy Scale</td>
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<tr>
<td>ESMS - Epilepsy Self-Management Scale</td>
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<tr>
<td>ESI-R - Revised Epilepsy Stressor Inventory</td>
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<tr>
<td>GAD-7 - Generalized Anxiety Disorder-7</td>
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<tr>
<td>HADS - Hospital Anxiety Depression scale</td>
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<td>HAMD - Hamilton Depression Scale</td>
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<td>HSCL-20 - Hopkins Symptom Checklist-20</td>
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<tr>
<td>KINDL - Gesundheitsbezogene Lebensqualität und psychosoziale Auswirkungen der Epilepsie (Health-related Quality of Life and psychosocial consequences of epilepsy)</td>
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<tr>
<td>LOC - Locus of Control Scale</td>
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<td>LSSS - Liverpool Seizure Severity Scale</td>
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<tr>
<td>MARS - Medication Adherence Report Scale</td>
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<tr>
<td>MAS - Medication Adherence Scale</td>
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<tr>
<td>mBDI - Modified Beck Depression Inventory</td>
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<tr>
<td>MCMI-III - Millon Clinical Multiaxial Inventory-III</td>
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<tr>
<td>MINI - Mini International Neuropsychiatric Interview</td>
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<tr>
<td>MQOLIE-30 - Malay Quality of Life Inventory in Epilepsy-30</td>
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<tr>
<td>NDDI-E - Neurological Depressive Disorders Inventory-Epilepsy</td>
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<tr>
<td>PHQ-9 - Patient Health Questionnaire-9</td>
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<td>PSQI - Pittsburgh Sleep Quality Index</td>
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<tr>
<td>PSS - Perceived Stress Scale</td>
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<tr>
<td>QOLIE-31, QOLIE-31-P, QOLIE-89 - Quality of Life in Epilepsy-31, Patient-weighted Quality of Life in Epilepsy-31, Quality of Life in Epilepsy-89</td>
</tr>
<tr>
<td>SCS - Self-compassion Scale</td>
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</tbody>
</table>
SF-36 - Short-Form 36
SSI - Seizure Severity Index
SWLS - Satisfaction with Life Scale
VAS scale (Helde 2005) - General satisfaction with the follow-up by the Neurological Clinic during the last 2 years
WHOQOL-BREF - World Health Organization Quality of Life instrument, short version
WPSI - Washington Psychosocial Seizure Inventory
4-point Likert scale (Martinović, 2006) - Rating of positive and negative thoughts

APPENDICES

Appendix 1. Cochrane Epilepsy Group Specialized Register search strategy
#1 MeSH DESCRIPTOR Neuropsychology Explode All
#2 MeSH DESCRIPTOR Rehabilitation Explode All
#3 MeSH DESCRIPTOR Mind-Body Therapies Explode All
#4 MeSH DESCRIPTOR Psychotherapy Explode All
#5 MeSH DESCRIPTOR Psychology, Applied Explode All
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 abreaction OR aromatherap* OR "behav* modification" OR bibliotherap* OR biofeedback OR catharsis OR conditioning OR counselling OR "crisis intervention" OR desensitization OR "early intervention" OR "emotional freedom tapping" OR ("eye movement" NEAR2 (desensitization OR reprocessing)) OR (feedback NEAR 1 (psycholog* OR sensory)) OR flooding OR "free association" OR hypnosis OR hypnotherapy OR imagery OR logotherapy OR meditation OR mindfulness OR "post traumatic stress" OR PTSD OR psychodrama OR psychotherap* OR "residential treatment" OR "rewind technique?" OR "stress manag*" OR "transactional analysis" OR "thought restructuring"
#8 ((acceptance NEAR2 commitment) OR (adaptation NOT "non-adherence") OR anxiety OR art OR assertive OR autogenic OR autosuggestion OR aversive OR behav* OR "client centered" OR cognitive OR color OR compassion* OR coping OR couples OR dance OR depression OR directive OR exercise OR family OR gestalt OR "human givens" OR humanistic OR implosive OR interpersonal OR language OR marital OR message OR memory OR mentalization OR music OR narrative OR nondirective OR "non-directive" OR nonpharmacol* OR "non-pharmacol*") NEAR2 (therap* OR treatment* OR train* OR retrain* OR rehabilitat* OR adapt* OR intervention* OR manag*)
#9 (panic OR "patient centered" OR "quality of life" OR QOL OR "rational emotive" OR relaxation OR self OR socioeconomic OR "socio-environmental" OR stigma OR systemic OR systems OR "therapeutic community" OR trauma) NEAR2 (therap* OR treatment* OR train* OR retrain* OR rehabilitat* OR adapt* OR intervention* OR manag*)
#10 (adjustment OR attention OR confidence OR "day to day" OR loss OR physical OR reality OR suggestion) NEAR1 (therap* OR treatment* OR train* OR retrain* OR rehabilitat* OR adapt* OR intervention* OR manag*)
#11 #6 OR #7 OR #8 OR #9 OR #10
#12 (nonepileptic OR "non-epileptic"):TI
#13 #11 OR #12
#14 INREGISTER
#15 #13 AND #14
Appendix 2. CENTRAL via CRSO search strategy

#1 MESH DESCRIPTOR Neuropsychology EXPLODE ALL TREES
#2 MESH DESCRIPTOR Rehabilitation EXPLODE ALL TREES
#3 MESH DESCRIPTOR Mind-Body Therapies EXPLODE ALL TREES
#4 MESH DESCRIPTOR Psychotherapy EXPLODE ALL TREES
#5 MESH DESCRIPTOR Psychology, Applied EXPLODE ALL TREES
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 (abreaction OR aromatherap* OR "behav* modification" OR bibliotherap* OR biofeedback OR catharsis OR conditioning OR counsel*OR c*ussor OR "c*sis intervention" OR desensitization OR "early intervention" OR "emotional freedom tapping" OR ("eye movement" NEAR2 (desensitization OR reprocessing)) OR (feedback NEAR1 (psycholog* OR sensori* OR training OR "free association" OR hypnosis OR hypnotherapy OR imagery OR logotherapy OR meditation OR mindfulness OR "post traumatic stress" OR PTSD OR psychodrama OR psychotherap* OR "residential treatment?" OR "rewind technique?" OR stress manag* OR "transactional analysis" OR "thought restruct*")):TI,AB,KY
#8 (((acceptance NEAR2 commitment) OR (adherence NOT "non-adherence") OR anxiety OR art OR assertive OR autogenic OR autosuggestion OR aversive OR behav* OR "client cent*" OR cognitive OR color OR compassion OR coping OR couples OR dance OR depression OR directive OR exercise OR family OR gestalt OR "human givens" OR humanistic OR implosive OR interpersonal OR language OR marital OR massage OR memory OR mentalization OR music OR narrative OR nondirective OR "non-directive" OR nonpharmacol* OR "non-pharmacol*") NEAR2 (therap* OR treatment* OR train* OR retrain* OR rehabilitat* OR adapt* OR intervention* OR manag*)):TI,AB,KY
#9 ((panic OR "patient cent*" OR psyche* OR "quality of life" OR QOL OR "rational emotive" OR relaxation OR self* OR socioenvironmental OR "socio-environmental" OR stigma OR systems OR "therapeutic community" OR trauma) NEAR2 (therap* OR treatment* OR train* OR retrain* OR rehabilitat* OR adapt* OR intervention* OR manag*)):TI,AB,KY
#10 (ad*justment OR attention OR confidence OR "day to day" OR loss OR physical OR reality OR suggestion) NEAR1 (therap* OR treatment* OR train* OR retrain* OR rehabilitat* OR adapt* OR intervention* OR manag*)):TI,AB,KY
#11 #6 OR #7 OR #8 OR #9 OR #10
#12 MESH DESCRIPTOR Epilepsy EXPLODE ALL TREES
#13 MESH DESCRIPTOR Seizures
#14 epilep*:TI,AB,KY
#15 #12 OR #13 OR #14
#16 (nonepileptic OR "non-epileptic"):TI
#17 #11 AND #15
#18 #17 NOT #16
#19 * NOT INMEDLINE
#20 #18 AND #19

Appendix 3. MEDLINE search strategy

This strategy is based on the Cochrane Highly Sensitive Search Strategy for identifying randomized trials (Lefebvre 2011).

1. exp Neuropsychology/ or exp Rehabilitation/ or exp Mind-Body Therapies/ or exp psychotherapy/ or exp Psychology, Applied/
2. (abreaction or art or assertive or "behav* modification" or bibliotherap* or biofeedback or catharsis or conditioning or counsel* or "c*sis intervention" or desensitization or "early intervention" or "emotional freedom tapping" or ("eye movement" adj2 (desensitization or reprocessing)) or (feedback adj1 (psycholog* or sensori*)) or flooding or "free association" or hypnosis or hypnotherapy or imagery or logotherapy or meditation or mindfulness or "post traumatic stress" or PTSD or psychodrama or psychotherap* or "residential treatment?" or "rewind technique?" or stress manag* or "transactional analysis" or "thought restruct*")):tw.
3. (((acceptance AND commitment) or (adherence not "non-adherence") or anxiety or art or assertive or autogenic or autosuggestion or aversive or behav* or "client cent*" or cognitive or color* or compassion* or coping or couples or dance or depression or directive or exercise or family or gestalt or "human givens" or humanistic or implosive or interpersonal or language or marital or massage or memory or mentalization or music or narrative or nondirective or "non-directive" or nonpharmacol* or "non-pharmacol*") adj2 (therap* or treatment* or train* or retrain* or rehabilitat* or adapt* or intervention* or manag*)):tw.
4. ((panic or "patient cent*" or psyche* or "quality of life" or QOL or "rational emotive" or relaxation or self* or socioenvironmental or "socio-environmental" or stigma or systems or "therapeutic community" or trauma) adj2 (therap* or treatment* or train* or retrain* or rehabilitat* or adapt* or intervention* or manag*)):tw.
Appendix 4. PsycINFO search strategy

S14 S3 AND S12 AND S13
S13 TI ((randomiz* OR randomis* OR controlled OR placebo OR blind* OR unblind* OR "parallel group" OR crossover OR crossover OR cluster OR "head to head") N2 (analy* OR method OR procedure OR study OR studies OR trial) ) OR AB ((randomiz* OR randomis* OR controlled OR placebo OR blind* OR unblind* OR "parallel group" OR crossover OR crossover OR cluster OR "head to head") N2 (analy* OR method OR procedure OR study OR studies OR trial) )
S12 S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
S11 (adjustment or attention or confidence or "day to day" or loss or physical or reality or suggestion) W1 (therap* or treatment or train* or retrain* or rehabilitat* or adapt* or intervention or manag*)
S10 (panic or "patient cent*" or psycho* or "quality of life" or QOL or rational-emotive or relaxation or self* or socioenvironmental or socio-environmental or stigma or systemic or systems or "therapeutic community" or trauma) W2 (therap* or treatment or train* or retrain* or rehabilitat* or adapt* or intervention or manag*)
S9 ((acceptance W2 commitment) or (adherence not "non-adherence") or anxiety or art or assertive or autogenic or autosuggestion or aversive or behavior* or "client cent*" or cognitive or color* or compassion* or coping or couples or dance or depression or directive or exercise or family or genetic or "human givens" or humanistic or implosive or interpersonal or language or marital or massage or memory or mentalization or music or narrative or non-directive or non-directive or non-pharmacol* or non-pharmacol*) W2 (therap* or treatment or train* or retrain* or rehabilitat* or adapt* or intervention or manag*)
S8 abreaction or aromatherap* or "behavior modification" or bibliotherap* or biofeedback or catharsis or conditioning or counseling or crisis intervention* or desensitization* or "early intervention*" or "emotional freedom tapping*" or ("eye movement" N2 (desensitization or reprocessing)) or (feedback N1 (psycholog* or sensory)) or flooding or "free association" or hypnosis or hypnotization or "humanistic therapy" or meditation or mindfulness or "post traumatic stress" or PTSD or psychodrama or psychotherap* or "residential treatment*" or "rewind technique*" or "stress manage*" or "transactional analysis*" or "thought restructuring*
S7 MM "Mind Body Therapy" OR MM "Aromatherapy"
S6 MM "Rehabilitation" OR MM "Psychotherapeutic Techniques" OR MM "Active Listening" OR MM "Animal Assisted Therapy" OR MM "Co-therapy" OR MM "Dream Analysis" OR MM "Empty Chair Technique" OR MM "Ericksonian Psychotherapy" OR MM "Mirroring" OR MM "Morita Therapy" OR MM "Motivational Interviewing" OR MM "Mutual Storytelling Technique" OR MM "Network Therapy" OR MM "Paradoxical Techniques" OR MM "Cognitive Rehabilitation" OR MM "Neuropsychological Rehabilitation" OR MM "Neurorehabilitation" OR MM "Occupational Therapy" OR MM "Physical Therapy" OR MM "Psychosocial Rehabilitation" OR MM "Therapeutic Social Clubs" OR MM "Vocational Rehabilitation" OR MM "Activities of Daily Living" OR MM "Adaptive Behavior" OR MM "Disability Management" OR MM "Habilitation" OR MM "Independent Living Programs" OR
CONTRIBUTIONS OF AUTHORS

Rosa Michaelis: protocol, literature search, ‘risk of bias’ assessment of studies, contacting authors for missing data, data analysis, interpretation and presentation of results

Venus Tang: protocol, literature search, ‘risk of bias’ assessment of studies, contacting authors for missing data, data analysis, interpretation and presentation of results

Janelle Wagner: review and modification of protocol, critical review of treatment methods, contacting authors for missing data, interpretation and discussion of results

Avani Modi: review and modification of protocol, critical review of treatment methods, interpretation and discussion of results

W. Curt LaFrance Jr: review and modification of protocol, critical review of treatment methods, interpretation and discussion of results

Laura Goldstein: review and modification of protocol, critical review of treatment methods, interpretation and discussion of results

Tobias Lundgren: review and modification of protocol, critical review of treatment methods, interpretation and discussion of results

Markus Reuber: Eligibility and ‘risk of bias’ assessment of Tang’s study, review and modification of protocol, critical review of treatment methods, interpretation and discussion of results

DECLARATIONS OF INTEREST

RM: Dr. Michaelis has a research position at the Gemeinschaftskrankenhaus Herdecke/CURAM/University Witten/Herdecke that allows her to follow her scientific interests, which included working on the Cochrane review. The research position is funded by a grant from the MAHLE foundation and the ICURAM. The grant includes the reimbursement of travel expenses that are related to the content of her scientific work. Prior to the MAHLE foundation (July 2014), the grant money was provided by the Christophorus foundation.

VT: Dr. Tang received a travel stipend from the ILAE to attend the 31st International Epilepsy Congress in Istanbul Turkey (September 2015), during which the Task Force had a one-day meeting related to the study.

JW: Dr. Wagner received a travel stipend from the ILAE to attend the 31st International Epilepsy Congress in Istanbul Turkey (September 2015), during which the Task Force had a one-day meeting related to the study.
AM: Dr. Modi received research funding from NIH and was a consultant to Fish and Richardson regarding adherence to medications in adults with multiple sclerosis. She received a travel stipend from the ILAE to attend the 31st International Epilepsy Congress in Istanbul Turkey (September 2015), during which the Task Force had a one-day meeting related to the study.

WCL: Dr. LaFrance works on this Cochrane project that addressed evidence-based interventions for epilepsy reviewed by the ILAE committee. He received travel stipend from the ILAE to attend the 31st International Epilepsy Congress in Istanbul Turkey (September 2015), during which the Task Force had a one-day meeting related to the study. Dr. LaFrance receives author royalties for the seizure treatment book, Taking Control of Your Seizures: Workbook, Oxford University Press, 2015. He studies evidence-based non-pharmacological interventions for patients with seizures that are ethics committee approved and peer reviewed to address any potential bias.

LG: Dr. Goldstein has received honoraria for speaking, and educational activities not funded by industry; she receives royalties from the publication of Clinical Neuropsychology (Wiley, 2004, 2013) and The Clinical Psychologist’s Handbook of Epilepsy Call 1997. This work represents independent research part-funded by the NIHR Maudsley Biomedical Research Centre (BRC) at South London and Maudsley NHS Foundation Trust and the Institute of Psychiatry, Psychology and Neuroscience, King’s College London. The views expressed are those of the author, and not necessarily those of the NHS, the NIHR or the Department of Health. The views expressed are those of the authors, and not necessarily those of the NHS, the NIHR, or the Department of Health.

TL: None known.

MR: Dr Reuber is responsible for developing and supervising a team of psychotherapists working in a clinical neurology department and provides treatment to patients with epilepsy. Therefore, he has an interest in demonstrating the effectiveness of psychotherapy. However, this potential bias is outweighed by his interest in the development of evidence-based treatments, encouraging him to assess the existing evidence as objectively and impartially as possible.

**Sources of Support**

**Internal sources**
- No sources of support supplied

**External sources**
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- Mahle foundation, Germany.
  For supporting the fellowship and fellowship-related travels of Rosa Michaelis
- Integrated Curriculum Anthroposophical Medicine (ICURAM), Germany.
  For supporting the fellowship and fellowship-related travels of Rosa Michaelis
- National Institute for Health Research, UK.
  This review was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure funding to the Epilepsy Group. The views and opinions expressed herein are those of the authors and do not necessarily reflect those of the Systematic Review Programme, NIHR, National Health Service or the Department of Health.
DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We further clarified the assessment of attrition bias. During the process of assessing attrition bias, we used a cut-off value of $\geq 15\%$ attrition for short-term interventions (< 6 months) and a cut-off value of $\geq 20\%$ attrition for long-term interventions ($\geq 6$ months).

We amended the section on assessment of heterogeneity. Since many diverse treatment types with expected differences in the designs and included populations were considered for this review, and some level of heterogeneity was to be expected, we assumed Chi$^2$ results with $P < 0.01$, and $I^2$ over 70$\%$ as cut-offs for a degree of heterogeneity of concern.

We amended the section on assessment of reporting bias. Rather than only comparing the reported outcomes with the outcome measures and points of measurements stated in the study methods to assess reporting bias within the publication, reporting biases were also assessed by comparing the reported outcomes with the original study protocol or comparable documents.