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Michaelis R, Tang V, Wagner JL, Modi AC, LaFrance Jr WC, Goldstein LH, Lundgren T, Reuber M

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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 PsycINFO, ClinicalTrials.gov, [WHO International Clinical Trials Registry Platform \(ICTRP\)](http://WHOInternationalClinicalTrialsRegistryPlatform.org). We screened the references from included studies and relevant reviews, and contacted researchers in the field for unpublished studies.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. Consequentially, 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 or 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 *[Explanation]*

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)					
Outcomes	Comparative effect sizes* (95% CI)		No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Usual care or supportive care	Psychological treatments			
QOLIE-31 total score	The range of mean change in the control groups was -1.9 to 8.14 points	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	468 (9 RCTs)	⊕⊕⊕○ MODERATE ¹	
QOLIE-31 emotional well-being subscale	The range of mean change in the control groups was -6.23 to 20 points	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	440 (8 RCTs)	⊕⊕⊕○ MODERATE ¹	
QOLIE-31 energy or fatigue subscale	The range of mean change in the control groups was -5.3 to 8.13 points	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	440 (8 RCTs)	⊕⊕⊕○ MODERATE ¹	

QOLIE-31 overall QoL subscale	The range of mean change in the control groups was - 2.63 to 4.09 points	The 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	440 (8 RCTs)	⊕⊕⊕○ MODERATE ¹
QOLIE-31 seizure worry subscale	The range of mean change in the control groups was - 5.18 to 5.96 points	The mean change from baseline in the intervention groups was on average 5.96 higher (95% CI 2.50 to 9.42). The range of mean change was 2.74 to 28.56 points	440 (8 RCTs)	⊕⊕⊕○ MODERATE ¹
QOLIE-31 cognitive functioning subscale	The range of mean change in the control groups was - 2.71 to 6.9 points	The mean change from baseline in the intervention groups was on average 3.00 higher (95% CI 0.21 to 5.78)	440 (8 RCTs)	⊕⊕⊕○ MODERATE ¹
QOLIE-31 medication effects subscale	The range of mean change in the control groups was - 8.11 to 12.04 points	The mean change from baseline in the intervention groups was on average 3.84 higher (95% CI 0.28 to 7.41). The range of mean change was 0.93 to 5.59 points	440 (8 RCTs)	⊕⊕⊕○ MODERATE ¹
QOLIE-31 social function subscale	The range of mean change in the control groups was - 4.28 to 7.35 points	The mean change from baseline in the intervention groups was on average 2.77 higher (95% CI -1.02 to 6.57). The range of mean change was 2.3 to 10.49 points	438 (8 RCTs)	⊕⊕⊕○ MODERATE ¹

* 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

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

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 refractory 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 psychological comorbidities (e.g. attention deficit hyperactivity disorder (ADHD) and depression (Ott 2001; Ott 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; Cramer 1999; Devinsky 1999; Williams 2003), antiepileptic drug (AED) side effects (Benevente 2004; Gilliam 2004; Loisel 2016), and medication adherence (Wu 2014), as well as socioeconomic status (Loisel 2016), and psychological comorbidities (Loisel 2016; Ramsey 2016). Notably, psychological distress and loneliness show the closest correlation with HRQoL, while seizure-related factors are much less important (Suurmeijer 2001). When investigating the association between medical parameters and HRQoL, side effects (Loisel 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 2006). 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 psychological 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 (Guilfoyle 2015; Gülepek 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 control, 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 (Ecoffery 2015a; Ecoffery 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 adjunctive 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 as add-on 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 visualisation 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 intervention 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 PEARLS group (Ciechanowski 2010). Compared with participants in the control group, participants assigned to the interven-

tion 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 pre-ictal 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 those 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:

Study methods

- 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 Chi^2 test, forest plots, and the I^2 statistic. We judged that an $I^2 > 70\%$ and a Chi^2 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 measurements stated in the study methods to assess reporting bias within the publication. The authors assessed reporting biases 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 this 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 out-

lined, 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.

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; DiIorio 2011; Fraser 2015; Pramuka 2007; Thompson 2010), five in Germany (Jantzen 2009; May 2002; Pfäfflin 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 (Lua 2013), Norway (Helde 2005), Serbia (Martinović 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; Martinović 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 (Martinović 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; Martinović 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 sleep management (DiIorio 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; Lua 2013; May 2002; Pramuka 2007)), increase knowledge and coping (Rau 2006), or satisfaction of participants with information and support (Pfäfflin 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 (Callier 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); supportive 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; Callier 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, 11 studies used the QOLIE-31; (Au 2003; Beretta 2014; Callier 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Lua 2013; 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 the 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 ($\pm$ standard deviation (SD)). Three studies included the mean difference between pre- and post-intervention scores ($\pm$ 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; Callier 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 ($\pm$ SD) for the meta-analysis, rather than post-intervention scores ($\pm$ 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 ($\pm$ SD); Fraser 2015 provided the mean change from baseline ($\pm$ 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 ($\pm$ SD); Callier 2016 provided the unadjusted mean change from baseline ($\pm$ SD). Three studies did not provide the mean change from baseline ($\pm$ 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 ($\pm$ 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: decreasing drug-related problems (Beretta 2014); increasing drug-adherence (Pakpour 2015); and increasing satisfaction with treatment and support (Pfafflin 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

2009; 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; Pfäfflin 2016).

Several studies used the participant's psychological functioning (e.g. depressive symptoms) as one of the inclusion criterion. Four studies included only adults 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 only included 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

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Au 2003	+	+	?	+	+	+	?
Beretta 2014	+	+	+	+	+	+	?
Caller 2016	+	+	+	+	+	+	+
Ciechanowski 2010	+	+	+	+	+	+	+
Dilorio 2011	+	+	+	+	+	+	+
Fraser 2015	+	+	+	+	+	+	+
Gandy 2014	+	+	+	+	+	+	+
Helde 2005	+	+	+	+	+	+	?
Hosseini 2016	?	?	+	+	+	+	+
Jantzen 2009	+	+	+	+	+	+	?
Lua 2013	+	?	?	?	+	+	?
Lundgren 2006	+	+	+	+	+	+	+
Lundgren 2008	+	+	+	+	+	+	+
Martinović 2006	+	+	+	+	+	+	?
May 2002	+	+	+	+	+	+	?
Orjuela-Rojas 2015	+	+	+	+	+	+	?
Pakpour 2015	+	?	?	?	+	+	+
Präflin 2016	+	+	+	+	+	+	+
Pramuka 2007	+	?	+	+	+	+	+
Rau 2006	+	+	+	+	+	+	?
Schröder 2014	+	+	+	+	+	+	+
Tang 2015	+	+	+	+	+	+	+
Thompson 2010	?	+	+	?	+	+	+
Yadegary 2015	+	?	?	?	?	+	+

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; Martinović 2006; May 2002; Pakpour 2015; Pfäfflin 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 (DiIorio 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; DiIorio 2011; Fraser 2015; Gandy 2014; Helde 2005; Lundgren 2006; Lundgren 2008; Martinović 2006; Pfäfflin 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 (DiIorio 2011). Seven studies reported an unconcealed allocation procedure (Au 2003; Caller 2016; Jantzen 2009; May 2002; Rau 2006; Thompson 2010; Orjuela-Rojas 2015), and four studies provided insufficiently descriptions (Lua 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; DiIorio 2011; Fraser 2015; Gandy 2014; Helde 2005; Hosseini 2016; Jantzen 2009; Lundgren 2006; Lundgren 2008; May 2002; Orjuela-Rojas 2015; Pakpour 2015; Pfäfflin 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 (DiIorio 2011; 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 (Martinović 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 (DiIorio 2011; Fraser 2015; Gandy 2014; Helde 2005; Hosseini 2016; Lua 2013; Pfäfflin 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; Martinović 2006; May 2002; Orjuela-Rojas 2015; Pfäfflin 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 (DiIorio 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; DiIorio 2011; Fraser 2015; Gandy 2014; Jantzen 2009; Lundgren 2006; Lundgren 2008; Martinović 2006; May 2002; Orjuela-Rojas 2015).

Incomplete outcome data

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; Martinović 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 (Callier 2016; DiIorio 2011; Gandy 2014; Hosseini 2016; Orjuela-Rojas 2015; Pfäfflin 2016; Pramuka 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; Pramuka 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; Callier 2016; Fraser 2015; Gandy 2014; Helde 2005; Hosseini 2016; Jantzen 2009; Lua 2013; Lundgren 2006; Lundgren 2008; May 2002; Orjuela-Rojas 2015; Pakpour 2015; Pfäfflin 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; Martinović 2006; Pramuka 2007; Schröder 2014; Thompson 2010). Two authors provided additional data (DiIorio 2011; Schröder 2014). Therefore, we ended assessing four studies at high risk of bias due to evidence of selective outcome reporting within the publications (Ciechanowski 2010; Martinović 2006; Pramuka 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; Callier 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; Callier 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-P, 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 (Martinović 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 subscale 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; $P < 0.0001$; $\text{Chi}^2 P = 0.08$; $I^2 = 43\%$); [Analysis 1.1](#); [Figure 4](#)

Figure 4. Forest plot of comparison: I QOLIE-31- Comparison of mean change from baseline, outcome: I.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; $P = 0.002$; $\text{Chi}^2 P = 0.02$; $I^2 = 59\%$); [Analysis 1.2](#); [Figure 5](#).

Figure 5. Forest plot of comparison: I QOLIE-31- Comparison of mean change from baseline, outcome: I.2 QOLIE-31 - emotional well-being subscale.

- Energy and fatigue (eight RCTs, 440 participants): significant mean change of 6.90 points (95% CI 3.49 to 10.31; $P < 0.0001$; $\text{Chi}^2 P = 0.24$; $I^2 = 24\%$); [Analysis 1.3](#); [Figure 6](#).

Figure 6. Forest plot of comparison: I QOLIE-31- Comparison of mean change from baseline, outcome: I.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; $P = 0.0008$; $\text{Chi}^2 P = 0.06$; $I^2 = 49\%$); [Analysis 1.4](#); [Figure 7](#).

Figure 7. Forest plot of comparison: I QOLIE-31- Comparison of mean change from baseline, outcome: I.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; $P = 0.0007$; $\text{Chi}^2 P = 0.86$; $I^2 = 0\%$); [Analysis 1.5](#).

- Cognitive functioning (eight RCTs, 440 participants): significant mean change of 3.00 points (95% CI 0.21 to 5.78; $P = 0.04$; $\text{Chi}^2 P = 0.93$; $I^2 = 0\%$); [Analysis 1.6](#).

- Medication effects (eight RCTs, 440 participants): significant mean change of 3.84 points (95% CI 0.28 to 7.41; $P = 0.0008$); [Analysis 1.7](#).

= 0.03; Chi^2 $P = 0.66$; $I^2 = 0\%$; [Analysis 1.7](#).

- Social function (eight RCTs, 438 participants): non-significant mean change of 2.77 points (95% CI -1.02 to 6.57; $P = 0.15$; Chi^2 $P = 0.98$; $I^2 = 0\%$; [Analysis 1.8](#)).

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 63.00 (SD 15.48) versus control mean 65.04 (SD 14.38); P value was reported to be non-significant, without precise value); [Pfäfflin 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 32.56 (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 ([DiIorio 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; $P = 0.09$; $I^2 = 33\%$; [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; $P = 0.20$; $I^2 = 81\%$; [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. [DiIorio 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](#); [Martinović 2006](#); [Schröder 2014](#); [Tang 2015](#); [Thompson 2010](#)). Five studies used more than one outcome measure ([Callier 2016](#); [Ciechanowski](#)

2010; Gandy 2014; Martinović 2006; Orjuela-Rojas 2015). 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 4.58 (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 5.2; $P = 0.93$; 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 accessing 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 1.2)). 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 wait-list control mean 16.48 (SD 3.81); $P = 0.045$).

Three studies that used other measures found non-significant difference 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 wait-list control mean 12.22 (SD 8.86); 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) 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 were 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 6.00 (SD 3.91); $P < 0.001$). 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 $\times$ 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-31-P, 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; Caller 2016; Ciechanowski 2010; Fraser 2015; Gandy 2014; Helde 2005; Martinović 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 Borghs 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; Lua 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 investigated 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 involved participant groups with comparable underlying epilepsy diagnoses, but differing severities of psychiatric and somatic comorbidities, and diverse cultural, ethnic, and socioeconomic backgrounds. There were differences between the included studies in their stated treatment methods, goals, strategies, and theoretical underpinnings. Psychologists with varying levels of experience delivered most of the treatments; team efforts including a wider range of specialists (doctors, nurses, social workers, etc.) were involved 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 primary outcome measure. Hence, the efforts to pool data were hampered, to some extent, by the wide diversity of outcome measures and interventions used in these trials. These circumstances were addressed by focusing 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-analysis to fairly similar interventions to avoid clinical heterogeneity. Overall, the quality of evidence of the meta-analysis was limited 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 sensitivity 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-

sessed there was no reason to further downgrade the quality of evidence. 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-being.

Potential biases in the review process

Identifying relevant studies that fit our broad operational definition of psychological treatments was challenging. As outlined in the review protocol, we searched a wide variety of databases, including trial registers, and scanned reference lists of relevant systematic 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 possibility that we may have missed a relevant study, or misjudged an included study or study outcome. Since this review will be periodically 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-significant 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 expertise with the implementation of RCTs in this area of research, rather than an increased risk of bias. Lundgren had not been involved 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 improvements in HRQoL in prospective uncontrolled, as well as in controlled 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 RCT 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 in the intervention groups was significantly better than in the control groups (using 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 nonpharmacologic 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; Martinovic 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 that would allow for the evaluation of treatment fidelity (such as recording and scoring sessions), which should also be used. Due to limitations of self-report measures, future study designs could strive to complement these measures with objective measures e.g. biomarkers, functional Magnetic Resonance Imaging (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).

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REFERENCES

References to studies included in this review

Au 2003 {published data only}

Au A, Chan F, Li K, Leung P, Li P, Chan J. Cognitive-behavioral group treatment program for adults with epilepsy in Hong Kong. *Epilepsy & Behavior* 2003;**4**(4):441–446. DOI: 10.1016/S1525-5050(03)00149-5; PUBMED: 12899867

Beretta 2014 {published and unpublished data}

Beretta S, Beghi E, Messina P, Gerardi F, Pescini F, La Licata A, et al. Comprehensive educational plan for patients with epilepsy and comorbidity (EDU-COM): a pragmatic randomised trial. *Journal of Neurology, Neurosurgery, and Psychiatry* 2014;**85**(8):889–94. DOI: 10.1136/jnnp-2013-306553; ISSN: 1468–330X 0022–3050; PUBMED: 24403284

Caller 2016 {published data only}

Caller T, Ferguson R, Roth R, Secore K, Alexandre F, Zhao W, et al. Self-management (HOBSCOTCH) improves cognition and quality of life in epilepsy: a randomised controlled trial. *Neurology* 2016;**86**(16 Supplement): Abstract no: S22.005.

* Caller TA, Ferguson RJ, Roth RM, Secore KL, Alexandre FP, Zhao W, et al. A cognitive behavioral intervention (HOBSCOTCH) improves quality of life and attention in epilepsy. *Epilepsy & Behavior* 2016;**57**(Part A):111–7. DOI: 10.1016/j.yebeh.2016.01.024

Ciechanowski 2010 {published and unpublished data}

Chaytor N, Ciechanowski P, Miller JW, Fraser R, Russo J, Unutzer J, et al. Long-term outcomes from the PEARLS randomised trial for the treatment of depression in patients with epilepsy. *Epilepsy & Behavior* 2011;**20**(3):545–9. DOI: 10.1016/j.yebeh.2011.01.017; ISSN: 1525–5069; PUBMED: 21333607

* Ciechanowski P, Chaytor N, Miller J, Fraser R, Russo J, Unutzer J, et al. PEARLS depression treatment for individuals with epilepsy: a randomised controlled trial. *Epilepsy & Behavior* 2010;**19**(3):225–31. DOI: 10.1016/j.yebeh.2010.06.003; ISSN: 1525–5069; PUBMED: 20609631

DiIorio 2011 {published and unpublished data}

DiIorio C, Bamps Y, Walker E. Results of a randomised controlled trial evaluating WebEase, an online self-management program. *Epilepsy Currents* 2011;**11**(Suppl 1): Abstract no: 2.358.

* DiIorio C, Bamps Y, Walker ER, Escoffery C. Results of a research study evaluating WebEase, an online epilepsy self-management program. *Epilepsy & Behavior* 2011;**22**(3):469–74. DOI: 10.1016/j.yebeh.2011.07.030; ISSN: 1525–5069; PUBMED: 21889413

Fraser 2015 {published data only}

Fraser RT, Johnson EK, Lashley S, Barber J, Chaytor N, Miller J, et al. The program for active consumer engagement in self-management (PACES) in epilepsy.

- Epilepsia* 2015;**56**(Suppl 1):49, Abstract no: p0169. DOI: 10.1111/epi.13241
- * Fraser RT, Johnson EK, Lashley S, Barber J, Chaytor N, Miller JW, et al. PACES in epilepsy: results of a self-management randomised controlled trial. *Epilepsia* 2015; **56**(8):1264–74. DOI: 10.1111/epi.13052; PUBMED: 26122460
- Gandy 2014** {published and unpublished data}
Gandy M, Sharpe L, Nicholson Perry K, Thayer Z, Miller L, Boserio J, et al. Cognitive behaviour therapy to improve mood in people with epilepsy: a randomised controlled trial. *Cognitive Behaviour Therapy* 2014;**43**(2):153–66. DOI: 10.1080/16506073.2014.892530; PUBMED: 24635701
- Helde 2005** {published and unpublished data}
Helde G, Bovim G, Bråthen G, Brodtkorb E. A structured, nurse-led intervention program improves quality of life in patients with epilepsy: a randomised, controlled trial. *Epilepsy & Behavior* 2005;**7**(3):451–7. DOI: 10.1016/j.yebeh.2005.06.008; PUBMED: 16087407
- Hosseini 2016** {published data only (unpublished sought but not used)}
Hosseini N, Mokhtari S, Momeni E, Vossoughi M, Berekatani M. Effect of motivational interviewing on quality of life in patients with epilepsy. *Epilepsy & Behavior* 2016;**55**:70–4. DOI: 10.1016/j.yebeh.2015.10.012
- Jantzen 2009** {published data only}
Jantzen S, Muller-Godeffroy E, Hallfahrt-Krisl T, Aksu F, Pust B, Kohl B, et al. FLIP&FLAP-a training programme for children and adolescents with epilepsy, and their parents. *Seizure* 2009;**18**(7):478–86. DOI: 10.1016/j.seizure.2009.04.007; ISSN: 1532–2688; PUBMED: 19477662
- Lua 2013** {published data only (unpublished sought but not used)}
Lua PL, Neni WS. A randomised controlled trial of an SMS-based mobile epilepsy education system. *Journal of Telemedicine and Telecare* 2013;**19**(1):23–8. DOI: 10.1177/1357633x12473920; PUBMED: 23390210
* Lua PL, Neni WS. Health-related quality of life improvement via telemedicine for epilepsy: printed versus SMS-based education intervention. *Quality of Life Research* 2013;**22**(8):2123–32. DOI: 10.1007/s11136-013-0352-6; PUBMED: 23329469
- Lundgren 2006** {published data only}
Lundgren T, Dahl J, Melin L, Kies B. Evaluation of acceptance and commitment therapy for drug refractory epilepsy: a randomised controlled trial in South Africa - a pilot study. *Epilepsia* 2006;**47**(12):2173–9. DOI: 10.1111/j.1528-1167.2006.00892.x; PUBMED: 17201719
- Lundgren 2008** {published data only}
Dahl JC, Lundgren TL, Yardi N. Evaluation of short term ACT psychotherapy and yoga in a RCT trial for refractory seizures in India. *Epilepsia* 2005;**46** Suppl 6:196, Abstract no: p545.
* Lundgren T, Dahl J, Yardi N, Melin L. Acceptance and Commitment Therapy and yoga for drug-refractory epilepsy: a randomised controlled trial. *Epilepsy & Behavior* 2008;**13**(1):102–8. DOI: 10.1016/j.yebeh.2008.02.009; PUBMED: 18343200
- Martinović 2006** {published data only}
Martinović Z, Simonović P, Djokić R. Preventing depression in adolescents with epilepsy. *Epilepsy & Behavior* 2006;**9**(4):619–24. DOI: 10.1016/j.yebeh.2006.08.017; ISSN: 1525–5050; PUBMED: 17049927
- May 2002** {published data only}
May TW, Pfafflin M. The efficacy of an educational treatment program for patients with epilepsy (MOSES): results of a controlled, randomised study. *Epilepsia* 2002;**43**(5):539–49. ISSN: 0013–9580; PUBMED: 12027917
- Orjuela-Rojas 2015** {published data only}
Orjuela-Rojas JM, Martinez-Juarez IE, Ruiz-Chow A, Crail-Melendez D. Treatment of depression in patients with temporal lobe epilepsy: a pilot study of cognitive behavioral therapy vs. selective serotonin reuptake inhibitors. *Epilepsy & Behavior* 2015;**51**:176–81. DOI: 10.1016/j.yebeh.2015.07.033
- Pakpour 2015** {published data only}
Pakpour AH, Gholami M, Esmaili R, Naghibi SA, Updegraff JA, Molloy GJ, et al. A randomised controlled multimodal behavioral intervention trial for improving antiepileptic drug adherence. *Epilepsy & Behavior* 2015;**52**: 133–42. DOI: 10.1016/j.yebeh.2015.08.036
- Pfafflin 2016** {published data only}
Pfafflin M, Schmitz B, May TW. Efficacy of the epilepsy nurse: results of a randomised controlled study. *Epilepsia* 2016;**57**(7):1190–8. DOI: 10.1111/epi.13424; ISSN: 0013–9580, Print 1528–1167, Electronic; PUBMED: 27265887
- Pramuka 2007** {published data only}
Pramuka M, Hendrickson R, Zinski A, Van Cott AC. A psychosocial self-management program for epilepsy: a randomised pilot study in adults. *Epilepsy & Behavior* 2007;**11**(4):533–45. DOI: 10.1016/j.yebeh.2007.06.013; PUBMED: 17904909
- Rau 2006** {published data only}
Rau J, May TW, Pfafflin M, Heubrock D, Petermann F. [Education of children with epilepsy and their parents by the modular education program epilepsy for families (FAMOSE)--results of an evaluation study]. *Rehabilitation* 2006;**45**(1):27–39. DOI: 10.1055/s-2005-915371; PUBMED: 16468111
- Schröder 2014** {published and unpublished data}
Schröder J, Brückner K, Fischer A, Lindenau M, Köther U, Vettorazzi E, et al. Efficacy of a psychological online intervention for depression in people with epilepsy: a randomised controlled trial. *Epilepsia* 2014;**55**(12): 2069–76. DOI: 10.1111/epi.12833; PUBMED: 25410633
- Tang 2015** {published data only}
Tang V, Kwan P, Poon WS. Mindfulness-based psychological treatment and social support intervention for drug-resistant epilepsy: a randomised, assessor-blinded, controlled trial.

- Epilepsia* 2013;**54**(Suppl 3):324, Abstract no: P1027. DOI: 10.1111/epi.12229
- * Tang V, Poon WS, Kwan P. Mindfulness-based therapy for drug-resistant epilepsy: an assessor-blinded randomised trial. *Neurology* 2015;**85**(13):1100–7. DOI: 10.1212/WNL.0000000000001967; PUBMED: 26333801
- Thompson 2010** *{published data only}*
Thompson NJ, Walker ER, Obolensky N, Winning A, Barmon C, Diiorio C, et al. Distance delivery of mindfulness-based cognitive therapy for depression: project UPLIFT. *Epilepsy & Behavior* 2010;**19**(3):247–54. DOI: 10.1016/j.yebeh.2010.07.031; ISSN: 1525–5069; PUBMED: 20851055
- Yadegary 2015** *{published data only}*
Yadegary MA, Maemodan FG, Nayeri ND, Ghanjekhanlo A. The effect of self-management training on health-related quality of life in patients with epilepsy. *Epilepsy & Behavior* 2015;**50**:108–12. DOI: 10.1016/j.yebeh.2015.04.051; ISSN: 1525–5050; PUBMED: 26232570
- References to studies excluded from this review**
- Aliasgharpour 2013** *{published data only}*
Aliasgharpour M, Dehghani Nayeri N, Yadegary MA, Haghani H. Effects of an educational program on self-management in patients with epilepsy. *Seizure* 2013;**22**(1): 48–52. DOI: 10.1016/j.seizure.2012.10.005; PUBMED: 23122512
- Dahl 1985** *{published data only}*
Dahl J, Melin L, Brorson LO, Schollin J. Effects of a broad-spectrum behavior modification treatment program on children with refractory epileptic seizures. *Epilepsia* 1985; **26**(4):303–9. PUBMED: 4006888]
- Dahl 1992** *{published data only}*
Dahl J, Brorson LO, Melin L. Effects of a broad-spectrum behavioral medicine treatment program on children with refractory epileptic seizures: an 8-year follow-up. *Epilepsia* 1992;**33**(1):98–102. PUBMED: 1733765]
- Dash 2015** *{published data only}*
Dash D, Sebastian TM, Aggarwal M, Tripathi M. Impact of health education on drug adherence and self-care in people with epilepsy with low education. *Epilepsy & Behavior* 2015;**44**:213–7. DOI: 10.1016/j.yebeh.2014.12.030; PUBMED: 25768712
- Davis 1984** *{published data only}*
Davis GR, Armstrong HE Jr, Donovan DM, Temkin NR. Cognitive-behavioral treatment of depressed affect among epileptics: preliminary findings. *Journal of Clinical Psychology* 1984;**40**(4):930–5. PUBMED: 6434595]
- DiIorio 2009** *{published data only}*
DiIorio C, Reisinger EL, Yeager KA, McCarty F. A telephone-based self-management program for people with epilepsy. *Epilepsy & Behavior* 2009;**14**(1):232–6. DOI: 10.1016/j.yebeh.2008.10.016; PUBMED: 19010447
- Helgeson 1990** *{published data only}*
Helgeson DC, Mittan R, Tan SY, Chayasirisobhon S. Sepulveda Epilepsy Education: the efficacy of a psychoeducational treatment program in treating medical and psychosocial aspects of epilepsy. *Epilepsia* 1990;**31**(1): 75–82. PUBMED: 2303015]
- Li 2016** *{published data only}*
Li J, Wang X, Meng H, Zeng K, Quan F, Liu F. Systemic family therapy of comorbidity of anxiety and depression with epilepsy in adolescents. *Psychiatry Investigation* 2016; **13**(3):305–10. DOI: 10.4306/pi.2016.13.3.305
- McLaughlin 2011** *{published data only}*
McLaughlin DP, McFarland K. A randomised trial of a group based cognitive behavior therapy program for older adults with epilepsy: the impact on seizure frequency, depression and psychosocial well-being. *Journal of Behavioral Medicine* 2011;**34**(3):201–7. DOI: 10.1007/s10865-010-9299-z; PUBMED: 20927577
- Modi 2016a** *{published data only}*
Modi AC, Guilfoyle SM, Mann KA, Rausch JR. A pilot randomised controlled clinical trial to improve antiepileptic drug adherence in young children with epilepsy. *Epilepsia* 2016;**57**(3):e69–75. DOI: 10.1111/epi.13289; ISSN: 1528–1167 0013–9580; PUBMED: 26693964
- Olley 2001** *{published data only}*
Olley BO, Osinowo HO, Brieger WR. Psycho-educational therapy among Nigerian adult patients with epilepsy: a controlled outcome study. *Patient Education and Counseling* 2001;**42**(1):25–33. DOI: 10.1016/s0738-3991(00)00087-2; PUBMED: 11080603
- Peterson 1984** *{published data only}*
Peterson GM, McLean S, Millington KS. A randomised trial of strategies to improve patient compliance with anticonvulsant therapy. *Epilepsia* 1984;**25**(4):412–7. PUBMED: 6430689]
- Pfäfflin 2012** *{published data only}*
Hagemann A, Pfäfflin M, Nussbeck F, May TW. The efficacy of an educational program for parents of children with epilepsy (FAMOSEs): results of a controlled multicenter evaluation study [Was bringt das Schulungsprogramm famoses den Eltern epilepsiekranker Kinder? Ergebnisse einer kontrollierten, multizentrischen Evaluationsstudie]. <https://ekvv.uni-bielefeld.de/blog/uniaktuell/resource/Poster2.pdf> (accessed 3 May 2016).
* Pfäfflin M, Petermann F, Rau J, May TW. The psychoeducational program for children with epilepsy and their parents (FAMOSEs): Results of a controlled pilot study and a survey of parent satisfaction over a five-year period. *Epilepsy & Behavior* 2012;**25**(1):11–6. DOI: 10.1016/j.yebeh.2012.06.012; PUBMED: 22980075
- Ridsdale 2000** *{published data only}*
Ridsdale L, Kwan I, Cryer C. Newly diagnosed epilepsy: can nurse specialists help? A randomised controlled trial. Epilepsy Care Evaluation Group. *Epilepsia* 2000;**41**(8): 1014–9. PUBMED: 10961629]
- Tajrishi 2015** *{published data only}*
Tajrishi MP, Abbasi S, Fard TN, Yousefi S, Abadi AMM, Kasmaei HD. Efficacy of attribution retraining on mental health of epileptic children. *Iranian Red Crescent Medical*

Journal 2015;17(10):e19393. DOI: 10.5812/ircmj.19393; ISSN: 2074-1804

Tan 1986 {published data only}

Tan SY, Bruni J. Cognitive-behavior therapy with adult patients with epilepsy: a controlled outcome study. *Epilepsia* 1986;27(3):225-33. PUBMED: 3516668]

Thompson 2015 {published data only}

Thompson NJ, Patel AH, Selwa LM, Stoll SC, Begley CE, Johnson EK, et al. Expanding the efficacy of project UPLIFT: distance delivery of mindfulness-based depression prevention to people with epilepsy. *Journal of Consulting and Clinical Psychology* 2015;83(2):304-13. DOI: 10.1037/a0038404

References to ongoing studies

Kralj-Hans 2014 {published data only}

* Kralj-Hans I, Goldstein LH, Noble AJ, Landau S, Magill N, McCrone P, et al. Self-Management education for adults with poorly controlled epILEpsy (SMILE (UK)): a randomised controlled trial protocol. *BMC Neurology* 2014;14:69. DOI: 10.1186/1471-2377-14-69; PUBMED: 24694207

Ridsdale L. Self-management education for adults with poorly controlled epilepsy: the SMILE trial. *European Journal of Neurology* 2015;22(Suppl 1):118, Abstract no: L101. DOI: 10.1111/ene.12806

Ridsdale L, Kralj-Hans I, Noble A, Landau S, McCrone P, Morgan M, et al. Self-management education for epilepsy: an RCT protocol. *Journal of Neurology, Neurosurgery and Psychiatry* 2014; Vol. 85, issue 10:A20-A21, Abstract no: 076. DOI: 10.1136/jnnp-2014-309236.76

Additional references

Alper 2007

Alper K, Schwartz KA, Kolts RL, Khan A. Seizure incidence in psychopharmacological clinical trials: an analysis of Food and Drug Administration (FDA) summary basis of approval reports. *Biological Psychiatry* 2007;62(4):345-54.

Baldwin 2013

Baldwin SA, Imel Z. Therapist effects. In: Lambert MJ editor(s). *Handbook of Psychotherapy and Behavioral Change*. New York: Wiley, 2013:258-97.

Benevente 2004

Benavente-Aguilar I, Morales-Blancquez C, Rubio EA, Rey JM. Quality of life of adolescents suffering from epilepsy living in the community. *Journal of Paediatric Child Health* 2004;40(3):110-3.

Borghs 2012

Borghs S, de la Loge C, Cramer JA. Defining minimally important change in QOLIE-31 scores: estimates from three placebo-controlled lacosamide trials in patients with partial-onset seizures. *Epilepsy & Behavior* 2012;23(3): 230-4. DOI: 10.1016/j.yebeh.2011.12.023

Boutron 2008

Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, CONSORT Group. Methods and processes of the

CONSORT Group: example of an extension for trials assessing nonpharmacologic treatments. *Annals of Internal Medicine* 2008;148(4):W60-6. [PUBMED: 18283201]

Brown 2009

Brown I, Sheeran P, Reuber M. Enhancing antiepileptic drug adherence: a randomised controlled trial. *Epilepsy & Behaviour* 2009;16:34-9.

Camfield 2001

Camfield C, Breau L, Camfield P. Impact of pediatric epilepsy on the family: a new scale for clinical and research use. *Epilepsia* 2001;42(1):104-12.

CDC 2012

Centers for Disease Control and Prevention (CDC). Epilepsy in adults and access to care - United States, 2010. *MMWR. Morbidity and Mortality Weekly Report* 2012 Nov 16;61(45):909-13. [PUBMED: 23151949]

Chang 2011

Chang YT, Chen PC, Tsai JJ. Bidirectional relation between schizophrenia and epilepsy: a population-based retrospective cohort study. *Epilepsia* 2011;52(11):2036-42.

Cohen 1988

Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Lawrence Erlbaum Associates, 1988.

Crail-Melendez 2013

Crail-Melendez D, Herrera-Melo A, Martinez-Juarez IE, Ramirez-Bermudez J. Cognitive-behavioral therapy for depression in patients with temporal lobe epilepsy: a pilot study. *Epilepsy Behav* 2013;23:52-56.

Cramer 1999

Cramer JA, Westbrook LE, Devinsky O, Perrine K, Glassman MB, Camfield C. Development of the Quality of Life in Epilepsy Inventory for Adolescents: the QOLIE-AD-48. *Epilepsia* 1999;40(8):1114-21.

Cramer 2003

Cramer JA, Van Hammée G, N132 Study Group. Maintenance of improvement in health-related quality of life during long-term treatment with levetiracetam. *Epilepsy & Behavior* 2003;4(2):118-23. DOI: doi.org/10.1016/S1525-5050(03)00004-0

Cull 1997

Cull C, Goldstein LH (eds.). *The Clinical Psychologist's Handbook of Epilepsy: Assessment and Management*. Routledge Press, 1997.

Davies 2003

Davies S, Heyman I, Goodman R. A population survey of mental health problems in children with epilepsy. *Developmental Medicine and Child Neurology* 2003;45(5): 292-5.

Devinsky 1999

Devinsky O, Westbrook L, Cramer J, Glassman M, Perrine K, Camfield C. Risk factors for poor health-related quality of life in adolescents with epilepsy. *Epilepsia* 1999;40(12): 1715-20.

Dilorio 1992

DiIorio C, Faherty B, Manteuffel B. Self-efficacy and social support in self-management of epilepsy. *Journal of Nursing Research* 1992;**14**:292–307.

Ekinci 2009

Ekinci O, Titus JB, Rodopman AA, Berkem M, Trevathan E. Depression and anxiety in children and adolescents with epilepsy. *Epilepsy & Behavior* 2009;**14**(1):8–18.

Eklund 2016

Eklund A, Nichols TE, Knutsson H. Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates.. *Proceedings of the National Academy of Sciences of the United States of America* 2016;**113**(28):7900–5.

Elsas 2011

Elsas SM, Gregory WL, White G, Navarro G, Salinsky MC, Andrews DJ. Aura interruption: the Andrews/Reiter behavioral intervention may reduce seizures and improve quality of life - a pilot trial. *Epilepsy & Behavior* 2011;**22**(4):765–72.

Escoffery 2015a

Escoffery C, Bamps Y, LaFrance WC Jr, Stoll S, Shegog R, Buelow J, et al. Development of the Adult Epilepsy Self-Management Measurement Instrument (AESMMI). *Epilepsy & Behavior* 2015;**50**:172–83.

Escoffery 2015b

Escoffery C, Bamps Y, LaFrance WC Jr, Stoll S, Shegog R, Buelow J, et al. Factor analyses of an Adult Epilepsy Self-Management Measurement Instrument (AESMMI). *Epilepsy & Behavior* 2015;**50**:184–9.

Ferro 2013

Ferro MA, Camfield CS, Levin SD, Smith ML, Wiebe S, Zou G, et al. Trajectories of health-related quality of life in children with epilepsy: a cohort study. *Epilepsia* 2013;**54**(11):1889–97.

Fisher 2014

Fisher RS, Acevedo C, Arzimanoglou A, Bogacz AJ, Cross H, Elger CE, et al. ILAE Official Report: a practical clinical definition of epilepsy. *Epilepsia* 2014;**55**(4):475–82.

Fried 1990

Fried R, Fox MC, Carlton RM. Effect of diaphragmatic respiration with end-tidal CO₂ biofeedback on respiration, EEG, and seizure frequency in idiopathic epilepsy. *Annals of the New York Academy of Sciences* 1990;**602**:67–96.

Gandy 2013

Gandy M, Sharpe L, Perry KN. Cognitive behavior therapy for depression in people with epilepsy: a systematic review. *Epilepsia* 2013;**54**(10):1725–34.

Gilbert 2012

Gilbert F. The burden of normality: from 'chronically ill' to 'symptom free'. New ethical challenges for deep brain stimulation postoperative treatment. *Journal of Medical Ethics* 2012;**38**:408–12.

Gilliam 2002

Gilliam F. Optimizing health outcomes in active epilepsy. *Neurology* 2002;**58**(8):9–20.

Gilliam 2004

Gilliam FG, Fessler AJ, Baker G, Vahle V, Carter J, Attarian H. Systematic screening allows reduction of adverse antiepileptic drug effects: a randomised trial. *Neurology* 2004;**62**(1):23–7.

GRADEPro 2015 [Computer program]

McMaster University (developed by Evidence Prime). GRADEPro GDT. Version (accessed prior to 24 August 2017). Hamilton (ON): McMaster University (developed by Evidence Prime), 2015.

Guilfoyle 2015

Guilfoyle SM, Monahan S, Wesolowski C, Modi AC. Depression screening in pediatric epilepsy: evidence for the benefit of a behavioral medicine service in early detection. *Epilepsy & Behavior* 2015;**44**:5–10.

Gülpek 2011

Gülpek D, Bolat E, Mete L, Arici S, Celebisoy M. Psychiatric comorbidity, quality of life and social support in epileptic patients. *Nordic Journal of Psychiatry* 2011;**65**(6): 373–80.

Hesdorffer 2000

Hesdorffer DC, Hauser WA, Annegers JF, Cascino G. Major depression is a risk factor for seizures in older adults. *Annals of Neurology* 2000;**47**:246–9.

Hesdorffer 2006

Hesdorffer DC, Hauser WA, Olafsson E, Ludvigsson P, Kjartansson O. Depression and suicide attempt as risk factors for incident unprovoked seizures. *Annals of Neurology* 2006;**59**:35–41.

Higgins 2011

Higgins PT, Green S, Altman GD, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Institute of Medicine 2012

Institute of Medicine (U.S.). Committee on the Public Health Dimensions of the Epilepsies. In: England M, Liverman C, Schultz A, Strawbridge L editor(s). *Epilepsy across the spectrum: promoting health and understanding*. Washington, DC: National Academies Press, 2012. [ISBN 978-0-309-25506-6; PUBMED: 22993876]

Jehi 2014

Jehi L. Responsive neurostimulation: the hope and the challenges. *Epilepsy Currents* 2014;**14**(5, September/October):270–1.

Jones 2013

Jones NC, O'Brien TJ. Stress, epilepsy, and psychiatric comorbidity: how can animal models inform the clinic?. *Epilepsy & Behavior* 2013;**26**(3):363–9.

Kanner 2006

Kanner AM. Depression and epilepsy: a new perspective on two closely related disorders. *Epilepsy Currents / American Epilepsy Society* 2006;**6**:141–6.

Kanner 2009

Kanner AM, Byrne R, Chicharro A, Wu J, Frey M. A lifetime psychiatric history predicts a worse seizure outcome following temporal lobectomy. *Neurology* 2009;**72**:793–9.

Kwan 2000

Kwan P, Brodie MJ. Early identification of refractory epilepsy. *New England Journal of Medicine* 2000;**342**:314–9.

Larson 2012

Larson AM, Ryther CCR, Jennesson M, Geoffrey AL, Bruno PL, Anagnos CJ, et al. Impact of pediatric epilepsy on sleep patterns and behaviors in children and parents. *Epilepsia* 2012;**53**(7):1162–9.

Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from <http://handbook.cochrane.org/>.

Loiselle 2016

Loiselle K, Ramsey RR, Rausch JR, Modi AC. Trajectories of health-related quality of life among youth with newly diagnosed epilepsy. *Journal of Pediatric Psychology* 2016;**41**(9):1011–21. [doi: 10.1093/jpepsy/jsw019]

Michaelis 2012

Michaelis R, Schonfeld W, Elsas SM. Trigger self-control and seizure arrest in the Andrews/Reiter behavioral approach to epilepsy: a retrospective analysis of seizure frequency. *Epilepsy & Behavior* 2012;**23**(3):266–71.

Modi 2011

Modi AC, Ingerski LM, Rausch JR, Glauser TA. Treatment factors affecting longitudinal quality of life in new onset pediatric epilepsy. *Journal of Pediatric Psychology* 2011;**36**(4):466–75.

Modi 2012

Modi AC, Pai AL, Hommel KA, Hood KK, Cortina S, Hilliard ME, et al. Pediatric self-management: a framework for research, practice, and policy. *Pediatrics* 2012;**129**(2):473–85.

Modi 2013

Modi AC, Guilfoyle SM, Rausch JR. Preliminary feasibility, acceptability, and efficacy of an innovative adherence intervention for children with newly diagnosed epilepsy. *Journal of Pediatric Psychology* 2013;**38**:605–16.

Modi 2016b

Modi AC, Guilfoyle SM, Mann K, Rausch JR. A pilot randomized controlled clinical trial to improve antiepileptic drug adherence in young children with epilepsy. *Epilepsia* 2016;**7**(3):69–75. [doi: 10.1111/epi.13289]

Novakova 2013

Novakova B, Harris PR, Ponnusamy A, Reuber M. The role of stress as a trigger for epileptic seizures: a narrative review of evidence from human and animal studies. *Epilepsia* 2013;**54**(11):1866–76.

Ott 2001

Ott D, Caplan R, Guthrie D, Siddarth P, Komo S, Shields WD, et al. Measures of psychopathology in children with complex partial seizures and primary generalized epilepsy with absence. *Journal of the American Academy of Child and Adolescent Psychiatry* 2001;**40**(8):907–14.

Ott 2003

Ott D, Siddarth P, Gurbani S, Koh S, Tournay A, Shields WD, et al. Behavioral disorders in pediatric epilepsy: unmet psychiatric need. *Epilepsia* 2003;**44**(4):591–7.

Painter 2014

Painter E, Rausch JR, Modi AC. Patterns of caregivers of children with newly diagnosed epilepsy: a case controlled design. *Epilepsy & Behavior* 2014;**31**:1–9.

Ramaratnam 2008

Ramaratnam S, Baker GA, Goldstein LH. Psychological treatments for epilepsy. *Cochrane Database of Systematic Reviews* 2008, Issue 3. DOI: 10.1002/14651858.CD002029.pub3

Ramsey 2016

Ramsey RR, Loiselle K, Rausch JR, Harrison J, Modi AC. Predictors of trajectories of epilepsy-specific quality of life among children newly diagnosed with epilepsy. *Epilepsy & Behavior* 2016;**57**:202–10. [doi: 10.1016/j.yebeh.2016.02.002]

Reiter 2009

Reiter JM, Andrews DJ. A neurobehavioral approach for treatment of complex partial epilepsy: efficacy. *Seizure* 2000;**9**(3):198–203.

RevMan 2014 [Computer program]

Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Ried 2001

Ried S, Specht U, Thorbecke R, Goecke K, Wohlfarth R. MOSES: An educational program for patients with epilepsy and their relatives. *Epilepsia* 2001;**42**:76–80.

Russ 2012

Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. *Pediatrics* 2012;**129**:256–64. [22271699]

Rutter 1970

Rutter M, Graham P, Yule W. *A Neuropsychiatric Study in Childhood*. Philadelphia: Lippincott, 1970.

Ryan 2015

Ryan JL, McGrady ME, Guilfoyle SM, Follansbee-Junger K, Arnett AD, Modi AC. Health care charges of youth newly diagnosed with epilepsy. *Neurology* 2015;**85**(6):490–7.

Ryan 2016

Ryan JL, McGrady ME, Guilfoyle SM, Follansbee-Junger K, Peugh JL, Loiselle KA, et al. Quality of life changes and health care charges among youth with epilepsy. *Journal of Pediatric Psychology* 2016;**41**(8):888–97. [doi: 10.1093/jpepsy/jsw098]

Schilling 2002

Schilling LS, Grey M, Knafl KA. The concept of self-management of type 1 diabetes in children and adolescents: an evolutionary concept analysis. *Journal of Advanced Nursing* 2002;**37**(1):87–99.

Schulz 2010

Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *Journal of Clinical Epidemiology* 2010;**63**(8):834–40.

Schünemann 2011

Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, et al. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Green S, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org/.

Selassie 2014

Selassie A, Wilson L, Martz G, Smith G, Wagner J, Wannamaker B. Epilepsy beyond seizures: a population-based study of comorbidities. *Epilepsy Research* 2014;**108**:305–15.

Snyder 1990

Snyder M. Stressors, coping mechanisms, and perceived health in persons with epilepsy. *International Disability Studies* 1990;**12**:100–3.

Stevanovic 2007

Stevanovic D. Health-related quality of life in adolescents with well-controlled epilepsy. *Epilepsy & Behavior* 2007;**10**:571–5.

Suurmeijer 2001

Suurmeijer TP, Reuvekamp MF, Aldenkamp BP. Social functioning, psychological functioning, and quality of life in epilepsy. *Epilepsia* 2001;**42**(9):1160–8.

Tang 2014

Tang V, Michaelis R, Kwan P. Psychobehavioral therapy for epilepsy. *Epilepsy & Behavior* 2014;**32**:147–55.

Tanriverdi 2009

Tanriverdi T, Ajlan A, Poulin N, Olivier A. Morbidity in epilepsy surgery: an experience based on 2449 epilepsy surgery procedures from a single institution. *Journal of Neurosurgery* 2009;**110**:1111–23.

Tschuschke 2005

Tschuschke V. Die psychotherapie in zeiten evidenzbasierter medizin. *Psychotherapeutenjournal* 2005;**2**:106–15.

Téllez-Zenteno 2005

Téllez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. *Brain* 2005;**128**:1188–98.

Téllez-Zenteno 2010

Téllez-Zenteno JF, Hernandez Ronquillo L, Moien-Afshari F, Wiebe S. Surgical outcomes in lesional and non-lesional

epilepsy: a systematic review and meta-analysis. *Epilepsy Research* 2010;**89**:310–8.

Velissaris 2012

Velissaris SL. Psychological trajectories in the year after a newly diagnosed seizure. *Epilepsia* 2012;**53**(10):1774–81.

Wagner 2010

Wagner JL, Smith G, Ferguson PL, Van Bakergem K, Hrisko S. Pilot study of an integrated cognitive-behavioral and self-management intervention for youth with epilepsy and caregivers: Coping Openly and Personally with Epilepsy (COPE). *Epilepsy & Behavior* 2010;**18**(3):280–5.

Wagner 2012

Wagner JL, Ferguson PL, Smith G. The relationship of coping behaviors to depressive symptoms in youth with epilepsy: an examination of caregiver and youth proxy report. *Epilepsy & Behavior* 2012;**24**:86–92.

Wagner 2015

Wagner J, Wilson D, Smith G, Malek A, Selassie A. Neurodevelopmental and mental health comorbidities in children and adolescents with epilepsy and migraine: a response to identified research gaps. *Developmental Medicine and Child Neurology* 2015;**57**:45–52.

Wang 2012

Wang J, Wang Y, Wang LB, Xu H, Zhang XL. A comparison of quality of life in adolescents with epilepsy or asthma using the Short-Form Health Survey (SF-36). *Epilepsy Research* 2012;**101**:157–65.

Wellmer 2012

Wellmer J, von der Groeben F, Klarman U, Weber C, Elger CE, Urbach H, et al. Risks and benefits of invasive epilepsy surgery workup with implanted subdural and depth electrodes. *Epilepsia* 2012;**53**(8):1322–32.

WHO 2017

World Health Organization. Epilepsy Fact Sheet. Updated February 2017. www.who.int/mediacentre/factsheets/fs999/en/ (accessed prior to 24 August 2017).

Williams 2003

Williams J, Steel C, Sharp GB, DelosReyes E, Phillips T, Bates S, et al. Parental anxiety and quality of life in children with epilepsy. *Epilepsy & Behavior* 2003;**4**(5):483–6.

Wu 2014

Wu YP, Follansbee-Junger K, Rausch J, Modi A. Parent and family stress factors predict health-related quality in pediatric patients with new-onset epilepsy. *Epilepsia* 2014;**55**(6):866–77.

References to other published versions of this review**Michaelis 2016**

Michaelis R, Tang V, Wagner JL, Modi AC, LaFrance W, Goldstein LH, et al. Psychological treatments for people with epilepsy. *Cochrane Database of Systematic Reviews* 2016, Issue 2. DOI: 10.1002/14651858.CD012081

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Au 2003

Methods	Prospective, randomized, assessor-blinded, controlled trial 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)	
Participants	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 7.9) 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	
Interventions	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	
Outcomes	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)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Allocation was performed using a matched design.

Au 2003 (Continued)

Allocation concealment (selection bias)	High risk	Allocation was not concealed, based on information provided by study authors
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded, based on information provided by study authors
Incomplete outcome data (attrition bias) All outcomes	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	<p>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</p> <p>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</p> <p>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</p> <p>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</p>
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	
Outcomes	Drug-related problems (particularly drug interactions), QoL, measured with the Quality of Life Inventory in Epilepsy inventory 31 (QOLIE-31) Time points measured: 1) Baseline 2) 1-month after baseline 3) 6-month after baseline	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A centralised, computer-generated allocated sequence was used for the randomization. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Information was sought and provided in the study protocol. Assignment to the experimental or control arm was done electronically, via a protected database
Blinding of participants and personnel (performance bias) All outcomes	High risk	Neither the participants nor the physicians providing the intervention were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Physicians assessing outcomes were blind to the assigned arm
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/91 in Treatment and 1/83 in UC withdrew during the study.
Selective reporting (reporting bias)	Low risk	Unpublished data (QOLIE-31 raw data) were sought and provided. No evidence to suggest reporting bias after review of study protocol

Other bias	Unclear risk	Not enough information to evaluate fidelity to intervention protocol and selective recruitment bias
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Caller 2016

Methods	Assessor-blinded, randomized, controlled trial comparing a group receiving HOB-SCOTCH (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	<p>Inclusion criteria: epilepsy, with or without uncontrolled seizures, with subjective memory complaints (QOLIE-31 cognition subset questions ≤ 7) who provided informed consent</p> <p>Exclusion criteria: severe mental disability, estimated IQ < 70, visual impairment precluding reading and writing, and those without a reliable phone access</p> <p>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</p> <p>The study was conducted at Dartmouth-Hitchcock Epilepsy Center between January 2013 and June 2014</p>
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
Outcomes	<p>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)</p> <p>Time points measured:</p> <ol style="list-style-type: none"> 1) Baseline (after randomization) 2) 8 weeks after baseline
Notes	

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was ensured by using a computer-generated random assignment
Allocation concealment (selection bias)	High risk	Allocation concealment was not performed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded to the treatment they received
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome measures were collected by a research co-ordinator blinded to treatment arms
Incomplete outcome data (attrition bias) All outcomes	High risk	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%)
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting within publication.
Other bias	Low risk	Low risk for infidelity to intervention protocol. Not enough information to evaluate selective recruitment bias

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	<p>Inclusion criteria: ICD-9 epilepsy diagnosis and significant depression based on PHQ-9 score ≥ 10</p> <p>Exclusion criteria: pregnant women, bipolar or psychotic disorder, active psychiatric treatment, substance abuse history based on questionnaire, cognitive impairment based on screening test</p> <p>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</p> <p>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</p>

	had seizures without LOC in PEARLS/TAU The study was conducted in the University of Washington Regional Epilepsy Center. Subject recruitment took place between April 2007 and April 2008	
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 month), participants received monthly 5- to 10-minutes 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		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random assignment and block randomizations were used. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Concealment was ensured.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded to the treatment they received
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded.

Ciechanowski 2010 (Continued)

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

Dilorio 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 antiepileptic 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

	and 29/18/12/6 in WCL	
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	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quasi-randomization by assigning participants alternatively.
Allocation concealment (selection bias)	Low risk	Concealment was ensured.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded to their treatment; personnel were blinded since this was a web-based intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	The assessors were not blinded at any assessment, based on information provided by study authors
Incomplete outcome data (attrition bias) All outcomes	High risk	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
Selective reporting (reporting bias)	Low risk	Unpublished data (QOLIE-10 outcomes) were sought and provided. No evidence to suggest reporting bias

Other bias	Low risk	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
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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	<p>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)</p> <p>Exclusion criteria: severe mental illness or psychosis, or known cognitive impairment (IQ < 70)</p> <p>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</p> <p>All participants were recruited through the UW Regional Epilepsy Center and Swedish Epilepsys Center, both in Seattle. Recruitment took place from 2010 to 2013</p>	
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	<p>Epilepsy Self-Management Scale (ESMS), Epilepsy Self-Efficacy Scale (ESES), Quality of Life Inventory in Epilepsy inventory 31 (QOLIE-31), Patient Health Questionnaire-9 (PHQ-9), and the Generalized Anxiety Disorder-7 (GAD-7)</p> <p>Time points measured:</p> <p>1) Baseline (after randomizations)</p> <p>2) Post-intervention (8 weeks)</p> <p>3) 6-months follow-up</p>	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Fraser 2015 (Continued)

Random sequence generation (selection bias)	Low risk	A random number generator was used for randomized assignment. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Information was sought and provided; allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to the treatment they received or provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Information was sought and provided. According to authors, outcome assessment was blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	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
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting bias within study, or after review of documentation of outcome measures used in the study
Other bias	Low risk	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

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 ≥ 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

	<p>in years was 15 (SD 13; range 5 to 37) in CBT, and 9 (SD 13; range 5 to 32) in WLC. 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</p> <p>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</p>	
Interventions	<p>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</p>	
Outcomes	<p>The Neurological Depressive Disorders Inventory-Epilepsy (NDDI-E), the Hospital Anxiety Depression Scale (HADS), Quality of Life Inventory in Epilepsy-31 (QOLIE-31)</p> <p>Time points measured:</p> <p>1) Baseline (before randomizations)</p> <p>2) Post-treatment</p> <p>3) 3-month follow-up</p>	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A list of random numbers, using the Bernoulli function, was generated and used consecutively for randomization. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Concealment was ensured.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded to their treatment.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessment was not blinded, based on information provided by study authors

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/primarily 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		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated block randomization was used. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Allocation concealment was ensured.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Neither participants nor service providers were blinded, based on information provided by study authors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/58 and 2/56 withdrew from the study. No evidence to suggest attrition bias
Selective reporting (reporting bias)	Low risk	Unpublished data (QOLIE-89 raw data) were sought and provided. No evidence to suggest selective reporting
Other bias	Unclear risk	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

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	<p>Randomized 56 participants (age 18 and above) with willingness to participate, epilepsy diagnosis for at least 1 year, with primary generalized tonic-clonic 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</p> <p>Exclusion criteria: immigrants, missing more than one intervention session, recent tragic life events (such as loss of life, divorce, etc.)</p> <p>All participants were diagnosed with epilepsy at the Nour and Kashani Hospitals in Isfahan, Iran</p>	
Interventions	<p>Intervention comprised 5 group sessions, each separated by 4 days. The structure of the motivational interviewing sessions was extracted from the book <i>Motivational Interviewing Group Intervention</i> for each session. Motivational interviewing is a strategy for fortification and enhancement of internal motivation, for changing through 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</p> <p>The WLC was offered conventional treatment, according to individual needs</p>	
Outcomes	<p>The Quality of Life Inventory in Epilepsy inventory-89 (QOLIE-89)</p> <p>Time points measured:</p> <p>1) Baseline (before randomization)</p> <p>2) 2 months after the intervention and randomization</p>	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The described procedure remained unclear, but suggested quasi-randomization by assigning participants alternatively
Allocation concealment (selection bias)	Unclear risk	Unclear if allocation was concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to the treatment they received and provided

Hosseini 2016 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessment was blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	The drop-out rate in the treatment group was 5/28 (17.9%). Attrition was considered high. Furthermore, the reason for exclusion (missing > 1 treatment session) indicated that the model of analysis was not ITT
Selective reporting (reporting bias)	Low risk	No evidence to suggest selective reporting.
Other bias	Low risk	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

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 children's ability to explain epilepsy to others. Outcome measures were obtained at baseline and 6-month after treatment
Participants	<p>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</p> <p>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 participant</p> <p>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. 19/15/4/13/3/11 participants in IG and 22/15/7/3/1/10 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</p> <p>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</p>
Interventions	<p>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</p>

	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	
Outcomes	DISABKIDS modular HRQOL questionnaire, disclosure of epilepsy, seizure-free episode Time points measured: 1) Baseline (immediately before intervention for IG and at recruitment for WLC) 2) Follow-up assessment (6 months after intervention)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	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
Allocation concealment (selection bias)	High risk	Allocation was not concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and therapists were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessment was blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The attrition was less than 10% in all sub-groups of the sample
Selective reporting (reporting bias)	Low risk	No evidence for selective reporting within publication.
Other bias	Unclear risk	Not enough information to evaluate fidelity to intervention protocol and selective recruitment bias

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	<p>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</p> <p>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</p> <p>The study was conducted in the Neurology Clinics of 3 public hospitals in the states of Terengganu, Pahang, and Kelantan in Malaysia</p>	
Interventions	<p>The intervention for both the 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</p> <p>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</p>	
Outcomes	<p>Malay Quality of Life Inventory in Epilepsy-30 (MQOLIE-30)</p> <p>Time points measured:</p> <p>1) Baseline (at recruitment)</p> <p>2) 3 months (after intervention)</p>	
Notes	Data was sought but not provided.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	An interactive voice response system was used for randomization. No evidence to suggest selection bias

Lua 2013 (Continued)

Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided regarding blinding of personnel delivering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1/72 (1%) and 7/72 (10%) withdrew from the study (both < 20%, which was our cut-off). No evidence to suggest attrition bias
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

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 12-month following the end of interventions
Participants	27 participants (aged 27 to 55years) 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 a 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 and 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

	<p>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</p> <p>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</p>	
Outcomes	Satisfaction with Life Scale (SWLS), World Health Organization Quality of Life instrument, short version (WHOQOL-BREF), seizure frequency, seizure index Time points measured: 1) Baseline 2) Post-intervention 3) 6-month follow-up 4) 12-month follow-up	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computerized randomization table was used. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Allocation concealment was ensured, according to information provided by study authors
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to the treatment they received or provided
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no drop-outs.
Selective reporting (reporting bias)	Low risk	No evidence to suggest selective reporting.
Other bias	Low risk	Low risk of infidelity to intervention protocol, since the intervention was provided by the therapists who had developed the

Lundgren 2006 (Continued)

		intervention. Not enough information to evaluate selective recruitment bias
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Lundgren 2008

Methods	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	
Participants	<p>.</p> <p>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</p> <p>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</p>	
Interventions	<p>Refer to Lundgren 2006 for the structure and intervention details of ACT</p> <p>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</p>	
Outcomes	<p>Satisfaction with Life Scale (SWLS), World Health Organization Quality of Life instrument, short version (WHOQOL-BREF), seizure frequency, seizure index</p> <p>Time points measured:</p> <p>1) Baseline</p> <p>2) Post-intervention</p> <p>3) 6-month follow-up</p> <p>4) 12-month follow-up</p>	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computerized randomization table was used. No evidence to suggest selection bias

Lundgren 2008 (Continued)

Allocation concealment (selection bias)	Low risk	Allocation concealment was ensured, according to information provided by study authors
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to the treatment they received and provided
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no drop-outs.
Selective reporting (reporting bias)	Low risk	No evidence to suggest selective reporting.
Other bias	Low risk	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

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

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		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computer-generated list of numbers were used for randomization. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Allocation concealment was ensured.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	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
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded, according to information provided by study authors

Incomplete outcome data (attrition bias) All outcomes	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 on 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	<p>Inclusion criteria: epilepsy, regardless of syndrome, duration, or severity</p> <p>Exclusion criteria: mental retardation, acute psychiatric illness, non-epileptic seizures only</p> <p>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)</p> <p>Participants were drawn from 22 epilepsy centers in Germany, Austria, and Switzerland</p>
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		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence generation was ensured, according to information provided by study authors
Allocation concealment (selection bias)	High risk	Allocation was not concealed, according to information provided by study authors
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded, according to information provided by study authors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded, according to information provided by study authors
Incomplete outcome data (attrition bias) All outcomes	High risk	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
Selective reporting (reporting bias)	Low risk	No evidence to suggest selective reporting.
Other bias	Unclear risk	Not enough information to evaluate fidelity to the intervention protocol and selective recruitment

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	<p>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</p> <p>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</p> <p>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 SSRI. 3 participants in each group had a comorbid anxiety disorder.</p> <p>The study was conducted at the National Institute of Neurology and Neurosurgery in Mexico City. Recruitment took place between January 2013 and December 2013</p>	
Interventions	<p>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</p> <p>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</p>	
Outcomes	<p>Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale (HADS), Quality of Life Inventory in Epilepsy-31 (QOLIE-31), Mini International Neuropsychiatric Interview (MINI)</p> <p>Time-points measured</p> <p>1) Baseline</p> <p>2) 6-week during treatment</p> <p>3) 12-week (immediately after treatment)</p>	
Notes	Original data were sought and provided by study authors.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement

Orjuela-Rojas 2015 (Continued)

Random sequence generation (selection bias)	High risk	Group assignment was not random. Allocation to CBT group was based on participant's ability to attend the weekly sessions; the rest were assigned to the SSRI group
Allocation concealment (selection bias)	High risk	Allocation was not concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Psychiatrists who applied monitoring scales were blinded to the study
Incomplete outcome data (attrition bias) All outcomes	High risk	2/7 (28.5%) in CBT 1/8 (12.5%) in SSRI lost to follow-up. We considered the overall attrition rate (20%) high for this short-term intervention
Selective reporting (reporting bias)	Low risk	No evidence to suggest selective reporting.
Other bias	Unclear risk	Not enough information to evaluate fidelity to the intervention protocol and selective recruitment

Pakpour 2015

Methods	Unblinded, randomized controlled multi-center trial comparing motivational interviewing intervention (MI) with usual care (UC) in adults with epilepsy on their drug adherence, drug-taking behaviors, seizure severity and HRQOL. Outcome measures were obtained at baseline, 3 months, and 6 months following delivery of the intervention
Participants	<p>Inclusion criteria: adults (aged 18 or above), diagnosis of epilepsy according to the ILAE criteria, independent in daily living activities or were responsible for taking their medications, prescribed AEDs</p> <p>Exclusion criteria: rapidly progressing neurological or medical condition, were not prescribed AEDs, diagnosis of an intellectual disability, major cognitive impairment (MMSE < 23), unable to read and write Persian</p> <p>Recruited 275 adults with epilepsy. 137 and 138 were randomly assigned to MI and UC, respectively. The mean age was 41.37 (SD 16.25) years in MI, and 39.86 (SD 15.01) years in UC. There were 45 in MI and 49 women in UC. 41 (MI) and 96 (UC) were on polytherapy. 55/34/48 in MI and 60/38/40 in UC had idiopathic/cryptogenic/symptomatic epilepsy. 60/38/32 in MI and 64/39/30 in UC had focal seizures/generalized seizures/absence seizures; the rest were unknown in either group</p> <p>The study involved 8 neurologic clinics from Qazvin (N = 2) and Teheran (N = 6). Recruitment took place between June 2014 and February 2015</p>

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 Automaticity 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		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	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
Allocation concealment (selection bias)	Unclear risk	Insufficient information was provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information on the blinding of participants was provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear - insufficient information was provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	4/275 drop-outs at follow-up. Attrition rate was considered low

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 infidelity to intervention protocol low. Not enough information to evaluate selective recruitment

Pfafflin 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: incapable 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 ($\pm$ 14.8), and 44.9 ($\pm$ 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 ($\pm$ 16.8) in EN, and 23.5 ($\pm$ 17.1) in WLC Two outpatient clinics that specialized in epilepsy participated
Interventions	The two certified epilepsy nurses ('epilepsy specialist assistant' or 'epilepsy specialist counsellor') 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

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

Pramuka 2007

Methods	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
Participants	<p>Inclusion criteria: adults (18 or above) with a diagnosis of epilepsy made by a neurologist, ability to understand and participant in the consent process</p> <p>Exclusion criteria: not specified</p> <p>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</p> <p>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)</p>

Interventions	<p>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, a rehabilitation psychologist, an exercise physiologist, and a behavioral interventionist). Therapeutic 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</p> <p>Those in the TAU maintained their regular schedule of follow-up appointments with their neurologists and the epilepsy nurse in the clinic</p>	
Outcomes	<p>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)</p> <p>Time points measured:</p> <p>1) Baseline</p> <p>2) 1-month follow-up</p> <p>3) 6-month follow-up</p>	
Notes	Data were sought but not provided.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A table of random number was used to generate a randomization sequence. No evidence to suggest selection bias
Allocation concealment (selection bias)	Unclear risk	Insufficient information.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and investigators who led the group were not blinded to group assignment
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded.
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-

		ered high for this short-term intervention
Selective reporting (reporting bias)	High risk	Baseline scores for both groups, and data for 6-month after baseline assessment for the TAU group were unavailable. Data were sought but not provided
Other bias	High risk	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

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	<p>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</p> <p>Exclusion criteria: children with non-epileptic seizures only, and their families</p> <p>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 in 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</p> <p>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</p>
Interventions	<p>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)</p> <p>The WLC group was offered conventional treatment according to individual needs</p>

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)	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	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
Allocation concealment (selection bias)	High risk	Unclear in publication. According to information sought from authors, the allocation was not concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinded to final assessor only. Neither participants nor service providers were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The participating research institutes that assessed the data received an anonymous set of collected data
Incomplete outcome data (attrition bias) All outcomes	High risk	76.4% of all study participants returned the questionnaires (parents: 78.6%; children: 71.4%; FAMOSES (children): 18, 4%; WLC (children): 40,6%)
Selective reporting (reporting bias)	Low risk	All outcomes were reported at all measured times.
Other bias	Unclear risk	Not enough information to evaluate fidelity to the intervention protocol and selective recruitment

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	<p>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</p> <p>Exclusion criteria: acute suicidal ideation, diagnosis of psychosis, bipolar disorder, or suicidality, insufficient time to take part in the online program for 9 weeks</p> <p>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 $1/2/\geq 3$ different seizure types</p> <p>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</p>	
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	<p>Beck Depression Inventory (BDI-I), The World Health Organization (WHO) Quality of Life questionnaire (WHOQOL-BREF), Quality of Life Inventory in Epilepsy (QOLIE-31)</p> <p>Time points measured:</p> <p>1) Baseline</p> <p>2) 9 weeks after the baseline</p>	
Notes		
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement

Schröder 2014 (Continued)

Random sequence generation (selection bias)	Low risk	Allocation was done in consecutive order, using a computer-generated randomized number table. No evidence to suggest selection bias
Allocation concealment (selection bias)	Low risk	Allocation concealment was ensured.
Blinding of participants and personnel (performance bias) All outcomes	High risk	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
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All assessments and outcome measures were obtained online.
Incomplete outcome data (attrition bias) All outcomes	High risk	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
Selective reporting (reporting bias)	Low risk	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
Other bias	Low risk	Low risk of infidelity to intervention protocol, since the intervention was provided via a web-based program Not enough information to evaluate selective recruitment.

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	
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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%/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)

Allocation concealment (selection bias)	Low risk	Allocation concealment was ensured, based on information provided by study authors
Blinding of participants and personnel (performance bias) All outcomes	High risk	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
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant in the SS group withdrew. No evidence to suggest attrition bias
Selective reporting (reporting bias)	Low risk	No evidence to suggest selective reporting.
Other bias	Low risk	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

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	<p>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</p> <p>Exclusion criteria: active suicidal ideation and cognitive impairment (i.e. score lower or equal to 20 on the telephone MMSE)</p> <p>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</p> <p>Recruitment and screening were coordinated by the physicians and nurses at the participating hospital-based epilepsy clinic from June 2007 to November 2008</p>

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

Thompson 2010 (Continued)

		outs in each group (13/53 = 24.5%). In addition, the number of participants in the telephone group (N = 13) and web group (N = 12) participating in UPLIFT did not match the total number of UPLIFT (N = 26) reported. Evidence of attrition bias noted for this short-term intervention
Selective reporting (reporting bias)	High risk	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
Other bias	Low risk	Low risk for infidelity to intervention protocol since all therapists were supervised by a licensed clinical psychologist. Not enough information to evaluate selective recruitment

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	<p>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</p> <p>Exclusion criteria: conditions in which intensive care was needed, enrolled in other research studies, were absent from each training session</p> <p>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</p> <p>The study took place in a teaching hospital in Zanjan, Iran.</p>
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

	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	
Outcomes	Quality of Life Inventory in Epilepsy-31-P (QOLIE-31-P). Time points measured 1) Baseline 2) 1-month after intervention	
Notes		
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A table of random numbers was used. No evidence to suggest selection bias
Allocation concealment (selection bias)	Unclear risk	Insufficient information was provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information was provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information was provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information was provided.
Selective reporting (reporting bias)	Low risk	No evidence to suggest selective reporting.
Other bias	High risk	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

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

Study	Reason for exclusion
Aliasgharpour 2013	No HRQOL outcome measures
Dahl 1985	No HRQOL outcome measures
Dahl 1992	No HRQOL outcome measures
Dash 2015	No HRQOL outcome measures
Davis 1984	No HRQOL outcome measures
DiIorio 2009	No HRQOL outcome measures
Helgeson 1990	No HRQOL outcome measures
Li 2016	No HRQOL outcome measures
McLaughlin 2011	No HRQOL outcome measures
Modi 2016a	No HRQOL outcome measures
Olley 2001	No HRQOL outcome measures
Peterson 1984	No HRQOL outcome measures
Pfäfflin 2012	No HRQOL outcome measures
Ridsdale 2000	No HRQOL outcome measures
Tajrishi 2015	No HRQOL outcome measures
Tan 1986	No HRQOL outcome measures
Thompson 2015	No HRQOL outcome measures

Characteristics of ongoing studies *[ordered by study ID]*[Kralj-Hans 2014](#)

Trial name or title	Self-Management education for adults with poorly controlled epILEpsy (SMILE (UK): a randomized controlled trial protocol
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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, a 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

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

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

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 WHOQOL-BREF - score	2	45	Mean Difference (IV, Random, 95% CI)	0.39 [-5.49, 6.28]

Comparison 3. SWLS - Comparison of post-intervention outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 SWLS - score	2	45	Mean Difference (IV, Random, 95% CI)	5.46 [-2.97, 13.89]

Analysis 1.1. Comparison 1 QOLIE-31- Comparison of mean change from baseline, Outcome 1 QOLIE-31- total score.

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

Outcome: 1 QOLIE-31- total score

Analysis 1.2. Comparison 1 QOLIE-31- Comparison of mean change from baseline, Outcome 2 QOLIE-31 - emotional well-being subscale.

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

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

Analysis 1.3. Comparison 1 QOLIE-31- Comparison of mean change from baseline, Outcome 3 QOLIE-31 - energy and fatigue subscale.

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

Outcome: 3 QOLIE-31 - energy and fatigue subscale

Analysis 1.4. Comparison 1 QOLIE-31 - Comparison of mean change from baseline, Outcome 4 QOLIE-31 - overall QoL subscale.

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

Outcome: 4 QOLIE-31 - overall QoL subscale

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

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

Outcome: 5 QOLIE-31 - seizure worry subscale

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

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

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

Outcome: 8 QOLIE-31 - social function subscale

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

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

ADDITIONAL TABLES

Table 1. Intervention methods, strategies, and treatment goals

	Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Setting	Delivery	Timing	Participants
Psychological Interventions	Au 2003	Cognitive behavioral therapy (CBT)	Seizure frequency	Stress management, cognitive restructuring, communication skills	Clinic	Group	8 weekly 2-h sessions	N = 17 adults with at least 2 seizures per month, with subjectively reported psychological distress
	Ciechanowski 2010 (PEARLS)	Cognitive behavioral therapy (CBT)	Depressive symptoms	Cognitive restructuring to address negative depressive thinking + behavioral activation	Home-based + telephone calls	Individual	8 50-min in-home sessions in 5 months + 7 monthly 5- to 10-min telephone calls	N = 80 adults with epilepsy with significant depression
	Gandy 2014	Cognitive behavioral therapy (CBT)	Depressive symptoms	Cognitive restructuring to address negative depressive thinking + behavioral activation	Clinic	Individual	1 1 to 2 h assessment session + 8 weekly 1-h sessions	N = 59 adults with epilepsy
	Martinovic 2006	Cognitive behavioral therapy (CBT)	Depressive symptoms	Cognitive restructuring to address negative depressive thinking + behavioral activation	Clinic	Group	8 weekly sessions + 4 monthly sessions	N = 32 adolescents with epilepsy and subthreshold depression

Table 1. Intervention methods, strategies, and treatment goals (Continued)

			tion				
Orjuela-Rojas 2015	Cognitive behavioral therapy (CBT)	Depressive symptoms	Cognitive restructuring to address negative depressive thinking + behavioral activation	Clinic	Group	12 weekly 90-min sessions	N = 15 adults with epilepsy and major depression
Schröder 2014 (Deprexis)	Cognitive behavioral therapy (CBT)	Depressive symptoms	Cognitive restructuring to address negative depressive thinking + behavioral activation	Internet-based	Individual	9 weekly modules (10 to 60 min)	N = 78 adults with self-reported depressive symptoms
Thompson 2010 (UPLIFT)	Cognitive behavioral therapy (CBT)	Depressive symptoms	Cognitive restructuring to address negative depressive thinking + behavioral activation	Internet-based + telephone calls	Group	8 weekly 1-h sessions	N = 53 adults with epilepsy and depression (but not severe depression)
Hosseini 2016	Motivational interviewing (MI)	Quality of life	Enhancement of internal motivation for change, by overcoming dualism	Clinic	Group	5 sessions in 20 days	N = 56 adults with epilepsy.
Lundgren 2006 ; Lundgren 2008	Mindfulness therapy (MT)	Quality of life	Acceptance and commitment therapy (ACT) + seizure management	Clinic	Group + individual	5 individual 90-min sessions + 2 group 3-h sessions + 2 1-h boosters at 6 and 12 months	N = 27 (Lundgren 2006) N = 18 adults with epilepsy (Lundgren 2008)

Table 1. Intervention methods, strategies, and treatment goals (Continued)

	Tang 2015	Mindfulness therapy (MT)	Quality of life	Epilepsy management + mindfulness techniques + seizure-related acceptance	Clinic	Group	4 bi-weekly 2.5-h sessions	N = 61 adults with drug-resistant epilepsy
Self-management Interventions	DiIorio 2011 (WebEase)	Motivational interviewing (MI)	Medication adherence + perceived stress	Medication adherence + stress and sleep management	Internet-based	Individual	3 biweekly modules	N = 194 adults with epilepsy
	Fraser 2015 (PACES)	Consumer-driven psychoeducation	Self-management	Medical and psychosocial self-management + epilepsy-related communication	Clinic	Group	8 weekly 75-min sessions	N = 83 adults with epilepsy
	Yadegary 2015	Self-management training program	Quality of life	Medical and psychosocial self-management + seizure communication	Clinic	Group	4 weekly 120-min sessions	N = 60 adults with epilepsy
Adherence interventions	Pakpour 2015	Motivational interviewing (MI)	Medication adherence	MI techniques	Clinic	Individual	3 weekly 40-min to 60-min sessions	N = 275 adults with epilepsy
Educational interventions	Jantzen 2009 (FLIP&FLAP)	Epilepsy education program	Quality of life	Disease knowledge, advocacy topics, self-management, psychosocial aspects	Clinic	Group	2-day course (14 h)	N = 192 children and adolescents with epilepsy, including parents
	May 2002 (MOSES)	Epilepsy education program	Quality of life	Disease knowledge, advocacy topics, self-man-	Clinic	Group		N = 383 adolescents and adults with

Table 1. Intervention methods, strategies, and treatment goals (Continued)

				agement, psychosocial aspects				epilepsy
Lua 2013	Epilepsy education program	Quality of life	Dis- ease knowl- edge, advoca- cy topics, self-man- agement, psychosocial aspects	SMS-based	Individual	11 weekly modules	N = 144 adults with epilepsy	
Pramuka 2007	Epilepsy education program	Quality of life	Dis- ease knowl- edge, advoca- cy topics, self-man- agement, psychosocial aspects	Clinic	Group	6 weekly 2-h sessions	N = 55 adults with epilepsy	
Rau 2006 (FAMOSEs)	Epilepsy education program	Knowledge + coping	Dis- ease knowl- edge, advoca- cy topics, self-man- agement, psychosocial aspects	Clinic	Group	2 -day course (14 h)	N = 70 chil- dren with epilepsy	
Pfäfflin 2016	Counseling	Satisfaction with information and support	Dis- ease knowl- edge, advoca- cy topics, self-man- agement, psychosocial aspects	Clinic	Individual	Delivery during routine visits	N = 187 adults with epilepsy	
Beretta 2014 (EDU-COM)	Patient-tailored medication education	Drug-related problems	Personal- ized educa- tion on drug interac- tion and tol- erability	Clinic	Individual	1-h session + booster ses- sion after 1 month	N = 174 adults with epilepsy and chronic co- morbidity	

Table 1. Intervention methods, strategies, and treatment goals (Continued)

Com- bined inter- ventions	Caller 2016 (HOB- SCOTCH)	Cognitive, memory + self manage- ment train- ing	Quality of life	Problem solving ther- apy and be- havior mod- ification strategies + seizure man- agement + social skills	Home- based + tele- phone calls	Group + in- dividual	8 weekly 40- min to 60 min sessions	N = 66 ado- lescents and adults with epilepsy and self-reported memory complaints
	Helde 2005	Epilepsy ed- ucation + nurse-led counselling	Quality of life	Person- alized coun- selling + dis- ease knowl- edge + drug adherence	Clinic + phone calls	Group + in- dividual	1-day group + phone calls every 3 months for 2 yrs	N = 114 adults with epilepsy

Table 2. Effects of interventions

	Study (inter- vention acronym)	HRQOL	Depression	Anxiety	Seizure- related outcomes	Additional outcomes	Time points measured
Psychological interventions	Au 2003	QOLIE-31 ²	NA	NA	seizure frequency ¹	ESES	1) base- line, 2) post-in- tervention
	Ciechanowski 2010 (PEARLS)	QOLIE-31 ²	HSCL- 20 ¹ , suicidal ideation ¹	NA	seizure frequency	NA	1) baseline, 2) post- intervention 3) 12-month fol- low-up 4) 18- month follow- up
	Gandy 2014	QOLIE-31 ²	HADS-D ¹ , NDDI-E ¹	HADS-A ¹	NA	NA	1) baseline, 2) post-inter- vention, 3) 3- month follow- up
	Hosseini 2016	QOLIE-89 ¹	NA	NA	NA	NA	1) base- line, 2) post-in- tervention
	Lundgren 2006	SWLS ¹ , WHOQOL- BREF ^{1 2}	NA	NA	seizure fre- quency, seizure index	NA	1) base- line, 2) post-in- tervention,

Table 2. Effects of interventions (Continued)

							3) 6-month follow-up, 4) 12-month follow-up
	Lundgren 2008	SWLS ¹ , WHOQOL-BREF ^{1 2}	NA	NA	seizure frequency, seizure index	NA	1) baseline, 2) post-intervention, 3) 6-month follow-up, 4) 12-month follow-up
	Martinović 2006	QOLIE-31 ²	BDI ¹ , CES-D ¹ , HAMD ¹	NA	NA	NA	1) baseline, 2) post-intervention, 3) 9-month follow up
	Orjuela-Rojas 2015	QOLIE-31 ²	BDI ¹ , HADS-D ¹ , MINI ¹	HADS-A ¹	NA	NA	1) baseline, 2) mid-intervention, 3) post-intervention
	Schröder 2014 (Deprexis)	QOLIE-31, WHOQOL-BREF	BDI ¹	NA	NA	NA	1) baseline, 2) post-intervention
	Tang 2015	QOLIE-31-P ^{1 2}	BDI-II	BAI	seizure frequency, SSI	NA	1) baseline, 2) post-intervention
	Thompson 2010 (UPLIFT)	SWLS	BDI ¹	NA	NA	DCSES, SCS, knowledge and skills, BRFS	1) baseline, 2) post-intervention, 3) 4-month follow-up
Self-management interventions	DiIorio 2011 (WebEase)	QOLIE-10	NA	NA	NA	ESI-R ¹ , ESMS ¹ , MAS ¹ , PSQI ¹ , PSS ¹ , Epilepsy Knowledge Profile	1) baseline, 2) post-intervention, 3) 12-week follow-up
	Fraser 2015 (PACES)	QOLIE-31 ²	PHQ-9	GAD-7	NA	ESES ¹ , ESMS ¹	1) baseline, 2) post-intervention, 3) 6-months follow-

Table 2. Effects of interventions (Continued)

							up
	Yadegary 2015	QOLIE-31-P ¹	NA	NA	NA	NA	1) baseline, 2) post-intervention
Adherence intervention	Pakpour 2015	QOLIE-31	NA	NA	LSSS	MARS ¹ , for additional outcomes please see 'Characteristics of included studies' table	1) baseline, 2) post-intervention, 3) 6-month follow-up
Educational interventions	Beretta 2014 (EDU-COM)	QOLIE-31	NA	NA	NA	Drug-related problems ¹	1) baseline, 2) post-intervention, 3) 6-month follow-up
	Jantzen 2009 (FLIP&FLAP)	DISABKIDS	NA	NA	Seizure-free episode	Disclosure of epilepsy	1) baseline, 2) post-intervention
	Lua 2013	MQOLIE-30 ¹	NA	NA	NA	NA	1) baseline, 2) post-intervention
	May 2002 (MOSES)	SF-36 ¹	Depression Scale D-S'	NA	Seizure frequency	For additional outcomes please see 'Characteristics of included studies' table	1) baseline, 2) post-intervention
	Pfäfflin 2016	QOLIE-31 (Overall QoL)	HADS-D	HADS-A	NA	Satisfaction with information and support ¹	1) baseline, 2) post-intervention
	Pramuka 2007	QOLIE-89 ¹	NA	NA	NA	ESES, WPSI, LOC	1) baseline, 2) post-intervention, 3) 6-month follow-up
	Rau 2006 (FAMOSSES)	KINDL	NA	NA	Seizure frequency	Epilepsy knowledge ¹ , for additional	1) baseline, 2) post-intervention

Table 2. Effects of interventions (Continued)

						outcomes please see ' Characteristics of included studies ' table	
Combined interventions	Caller 2016 (HOB- SCOTCH)	QOLIE-31 ^{1 2}	PHQ-9 NDDI-E	NA	NA	Self-report cog- nitive and exec- utive function	1) base- line, 2) post-in- tervention
	Helde 2005	QOLIE-89 ^{1 2}	NA	NA	NA	VAS scale	1) base- line, 2) post-in- tervention

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

BAI - Beck Anxiety Inventory

BDI or BDI II - Beck Depression Inventory or Beck Depression Inventory II

BRFSS - Behavioral Risk Factor Surveillance System

CES-D - Center for Epidemiological Study on Depression scale

DISABKIDS - Modular HRQOL questionnaire

DCSES - Depression Coping Self-Efficacy Scale

ESES - Epilepsy Self-Efficacy Scale

ESMS - Epilepsy Self-Management Scale

ESI-R - Revised Epilepsy Stressor Inventory

GAD-7 - Generalized Anxiety Disorder-7

HADS - Hospital Anxiety Depression Scale

HAMD - Hamilton Depression Scale

HSCL-20 - Hopkins Symptom Checklist-20

KINDL - Gesundheitsbezogene Lebensqualität und psychosoziale Auswirkungen der Epilepsie (Health-related Quality of Life and psychosocial consequences of epilepsy)

LOC - Locus of Control Scale

LSSS - Liverpool Seizure Severity Scale

MARS - Medication Adherence Report Scale

MAS - Medication Adherence Scale

mBDI - Modified Beck Depression Inventory

MCMI-III - Millon Clinical Multiaxial Inventory-III

MINI - Mini International Neuropsychiatric Interview

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

NDDI-E - Neurological Depressive Disorders Inventory-Epilepsy

PHQ-9 - Patient Health Questionnaire-9

PSQI - Pittsburgh Sleep Quality Index

PSS - Perceived Stress Scale

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

SCS - Self-compassion Scale

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 I. 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 counsel?ing OR "crisis intervention" OR desensiti?ation OR "early intervention" OR "emotional freedom tapping" OR ("eye movement" NEAR2 (desensiti?ation OR reprocessing)) OR (feedback NEAR1 (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 restructur*"

#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 colo?r 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 mentali?ation 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 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) 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 NOT #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?ing OR "crisis intervention" OR desensiti?ation OR "early intervention" OR "emotional freedom tapping" OR ("eye movement" NEAR2 (desensiti?ation OR reprocessing)) OR (feedback NEAR1 (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 restructur*"):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 colo?r 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 mentali?ation 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 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) NEAR2 (therap* OR treatment* OR train* OR retrain* OR rehabilitat* OR adapt* OR intervention* OR manag*)):TI,AB,KY
#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*)):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 aromatherap* or "behav* modification" or bibliotherap* or biofeedback or catharsis or conditioning or counsel?ing or "crisis intervention" or desensiti?ation or "early intervention" or "emotional freedom tapping" or ("eye movement" adj2 (desensiti?ation or reprocessing)) or (feedback adj1 (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 restructur*").tw.
3. (((acceptance adj2 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 colo?r 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 mentali?ation 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 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) adj2 (therap* or treatment* or train* or retrain* or rehabilitat* or adapt* or intervention* or manag*)).tw.

5. ((adjustment or attention or confidence or "day to day" or loss or physical or reality or suggestion) adj1 (therap* or treatment* or train* or retrain* or rehabilitat* or adapt* or intervention* or manag*)).tw.
6. 1 or 2 or 3 or 4 or 5
7. exp Epilepsy/
8. Seizures/
9. epilep\$.tw.
10. 7 or 8 or 9
11. exp *Pre-Eclampsia/ or exp *Eclampsia/
12. 10 not 11
13. (nonepileptic or "non-epileptic").ti.
14. 6 and 12
15. 14 not 13
16. (randomized controlled trial or controlled clinical trial or pragmatic clinical trial).pt. or (randomi?ed or placebo or randomly).ab.
17. clinical trials as topic.sh.
18. trial.ti.
19. 16 or 17 or 18
20. exp animals/ not humans.sh.
21. 19 not 20
22. 15 and 21
23. remove duplicates from 22

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 cross-over 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 cross-over 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 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 behav* or "client cent*" or cognitive or colo#r 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 mentali#ation or music or narrative or nondirective or non-directive or nonpharmacol* or non-pharmacol*) W2 (therap* or treatment or train* or retrain* or rehabilitat* or adapt* or intervention or manag*)

S8 abreaction or aromatherap* or "behav* modification" or bibliotherap* or biofeedback or catharsis or conditioning or counsel#ing or "crisis intervention" or desensiti#ation or "early intervention" or "emotional freedom tapping" or ("eye movement" N2 (desensiti#ation or reprocessing)) or (feedback N1 (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 restructur*"

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 "Cootherapy" 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

MM “Intervention” OR MM “Crisis Intervention” OR MM “Early Intervention” OR MM “Family Intervention” OR MM “Group Intervention” OR MM “School Based Intervention” OR MM “Rehabilitation Counseling” OR MM “Self Care Skills” OR MM “Support Groups” OR MM “Twelve Step Programs”

S5 MM “Psychotherapy” OR MM “Adlerian Psychotherapy” OR MM “Adolescent Psychotherapy” OR MM “Analytical Psychotherapy” OR MM “Autogenic Training” OR MM “Behavior Therapy” OR MM “Brief Psychotherapy” OR MM “Brief Relational Therapy” OR MM “Child Psychotherapy” OR MM “Client Centered Therapy” OR MM “Cognitive Behavior Therapy” OR MM “Cognitive Therapy” OR MM “Conversion Therapy” OR MM “Eclectic Psychotherapy” OR MM “Emotion Focused Therapy” OR MM “Existential Therapy” OR MM “Experiential Psychotherapy” OR MM “Expressive Psychotherapy” OR MM “Eye Movement Desensitization Therapy” OR MM “Feminist Therapy” OR MM “Geriatric Psychotherapy” OR MM “Gestalt Therapy” OR MM “Group Psychotherapy” OR MM “Guided Imagery” OR MM “Humanistic Psychotherapy” OR MM “Hypnotherapy” OR MM “Individual Psychotherapy” OR MM “Insight Therapy” OR MM “Integrative Psychotherapy” OR MM “Interpersonal Psychotherapy” OR MM “Logotherapy” OR MM “Narrative Therapy” OR MM “Network Therapy” OR MM “Persuasion Therapy” OR MM “Primal Therapy” OR MM “Psychoanalysis” OR MM “Psychodrama” OR MM “Psychodynamic Psychotherapy” OR MM “Psychotherapeutic Counseling” OR MM “Rational Emotive Behavior Therapy” OR MM “Reality Therapy” OR MM “Relationship Therapy” OR MM “Solution Focused Therapy” OR MM “Supportive Psychotherapy” OR MM “Transactional Analysis”

S4 MM “Neuropsychology” OR MM “Health Care Psychology” OR MM “Medical Psychology”

S3 S1 OR S2

S2 epilep* OR seizure* OR convuls*

S1 MM “Epilepsy” OR MM “Epileptic Seizures” OR MM “Experimental Epilepsy” OR MM “Grand Mal Seizures” OR MM “Petit Mal Seizures” OR MM “Status Epilepticus”

WHAT’S NEW

Date	Event	Description
25 July 2018	Amended	Minor edits have been made to the text.

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* Cull 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.

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Internal sources

- No sources of support supplied

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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 (≥ 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.

INDEX TERMS

Medical Subject Headings (MeSH)

Bias; Energy Metabolism; Epilepsy [*psychology; *therapy]; Fatigue [therapy]; Psychotherapy; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Adult; Child; Humans; Young Adult