Epilepsia®

Cochrane systematic review and meta-analysis of the impact of psychological treatments for people with epilepsy on health-related quality of life

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Summary

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

Methods: The operational definition of *psychological treatments* included a broad range of interventions that use psychological or behavioral techniques designed to improve HRQoL, psychiatric comorbidities, and seizure frequency and severity for adults and children with epilepsy. A systematic literature search was conducted in line with Cochrane criteria for randomized controlled trials (RCTs) and quasi-RCTs investigating psychological treatments and using HRQoL outcome measures as primary or secondary outcome measures. Standard methodological procedures required by the Cochrane Collaboration were used for data collection and analysis.

Results: Twenty-four completed RCTs were included in this review (2439 participants). Based on satisfactory methodological homogeneity, data from 9 studies (468 participants) providing Quality of Life in Epilepsy-31 (QOLIE-31) outcomes were pooled for meta-analyses, showing significant mean changes for QOLIE-31 total score and 6 subscales. The significant mean changes of QOLIE-31 total score (mean improvement of 5.68 points; 95% confidence interval = 3.11-8.24, $P < .0001$) and 3 subscales (emotional well-being, energy/fatigue, overall quality of life [QoL]) exceeded the threshold of minimally important change, indicating a clinically meaningful postintervention improvement of QoL. Overall, the meta-analysis quality of evidence was characterized as "moderate" due to the risk of

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bias present in 8 of the 9 included studies (Handbook for Systematic Reviews of Interventions, Version 5.1.0, 2011, Chapters 8 and 12). A narrative synthesis was conducted for all trials and outcomes that were not entered in the meta-analysis.

Significance: These results provide moderate-quality evidence that psychological treatments for adults with epilepsy may enhance HRQoL in people with epilepsy.

KEYWORDS

anxiety, depression, nonadherence, psychoeducation, self-management

1 | INTRODUCTION

People with epilepsy (PWE) are at increased risk of psychiatric comorbidities compared to the general population and nonneurological medical conditions,[3,4] as well as to people with other neurological diseases,[5] and the profound physical, psychological, and social consequences of epilepsy impact health-related quality of life (HRQoL). HRQoL is a patient-reported outcome measure that encompasses several domains, including physical, social, emotional, and school/work.[6–8] Epilepsy-specific HRQoL measures are more salient to specific aspects of epilepsy and its treatments and thus constitute a particularly sensitive and responsive patient-reported outcome for PWE.[9,10] Unlike in patients with psychogenic nonepileptic seizures, there remains a significant relationship between HRQoL and epilepsy severity markers when psychopathology is introduced as a covariate.[11] Both population-based and experimental studies in human and animal models have demonstrated a robust relationship between seizures and psychiatric disorders. This relationship has been interpreted by some as a sign of bidirectionality, suggesting that psychological/psychiatric disorders can be consequences of as well as predispose to or precipitate epilepsy and that psychiatric disorders can exacerbate seizures, leading to a vicious cycle.[12–14] Other authors, however, criticize the interpretation of a varying temporal relationship as evidence of a bidirectional relationship.[15] Overall, these findings have prompted further research on the use and benefit of psychological treatments for PWE.

A wide array of psychological approaches have been used to target the enhancement of HRQoL, seizure management, and reduction of psychiatric comorbidity in children and adults with epilepsy. Cognitive and behavioral treatments, mind-body therapies, and educational interventions are the most common approaches.[16] A 2008 Cochrane Review[17] assessed the findings of 16 randomized controlled trials (RCTs) and quasi-RCTs of psychological treatments in PWE and found no reliable evidence for the

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Key Points

- A systematic search of databases for RCTs investigating psychological treatments using HRQoL outcome measures yielded 24 RCTs
- Data from 9 studies were pooled for meta-analyses showing significant mean changes for Quality of Life in Epilepsy-31 total score and 6 subscales
- These results provide evidence of moderate quality that psychological treatments for adults with epilepsy may enhance HRQoL in PWE

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efficacy of psychological treatments in terms of seizure control. Over the past decade, additional trials with substantially improved designs have become available that have been critically appraised in a number of recent reviews,[16,18] providing growing evidence for the positive effects of psychological treatments on wider HRQoL, psychiatric symptoms (ie, anxiety, depression), psychological functioning (ie, self-management), and seizure control in PWE.

A Psychology Task Force was set up under the Medical Therapies Committee comprising experts selected by the International League Against Epilepsy (ILAE) to review and reappraise the role of psychological treatments for PWE. The purpose of this review was twofold. First, we aimed to examine the effectiveness of psychological treatments on HRQoL in PWE. To address this, the Task Force was charged with performing a meta-analysis of RCTs and quasi-RCTs investigating the effects of psychological treatments on HRQoL in PWE. Second, we explored the effects of psychological treatments on psychiatric symptoms and seizure control in these trials. This article summarizes the findings of a Cochrane Review that is the outcome of an international collaboration process and has been approved by the ILAE Executive Committee.[19]

1.1 | Operational definition of psychological treatments for PWE

The operational definition of *psychological treatments* includes a broad range of interventions that use psychological techniques for children and adults with epilepsy. These interventions may be given singly or in combination, either alone or as add-on to antiepileptic drugs, and can be categorized into 4 groups:

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

2. Self-management/family management. This is 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 encompass individual, family, community, or health care system domains. Behaviors include relaxation, physical exercise, and coping skills.

3. Adherence interventions. These are defined as efforts to assist patients to adhere to the advice of health care providers, including taking prescribed self-administered medications, following a ketogenic diet, and avoiding seizure triggers. Medication taking can be broken down into several components, including optimal dose timing and frequency of dosing. Strategies to improve adherence include visual reminders, organizational strategies, behavioral strategies (eg, pair medication with a daily routine), and problem-solving around adherence barriers.

4. (Psycho-)educational interventions. These are defined as interventions that aim to increase knowledge about epilepsy, its comorbidities, and its treatments or the functions and activities of the brain.

2 | MATERIALS AND METHODS

2.1 | Types of studies

Because HRQoL is the primary outcome of interest in this review, we included all RCTs and quasi-RCTs that investigated psychological treatments, as operationally defined, for children and adults with epilepsy and that reported validated HRQoL outcome measures as primary or secondary outcome measures. Other quality of life (QoL)-related parameters, such as symptoms of psychiatric comorbidities and seizure-related outcome measures, were also interpreted in the included studies.

2.2 | Search methods and identification of studies

The process of study selection is displayed in Figure 1. The following databases were searched on September 20,
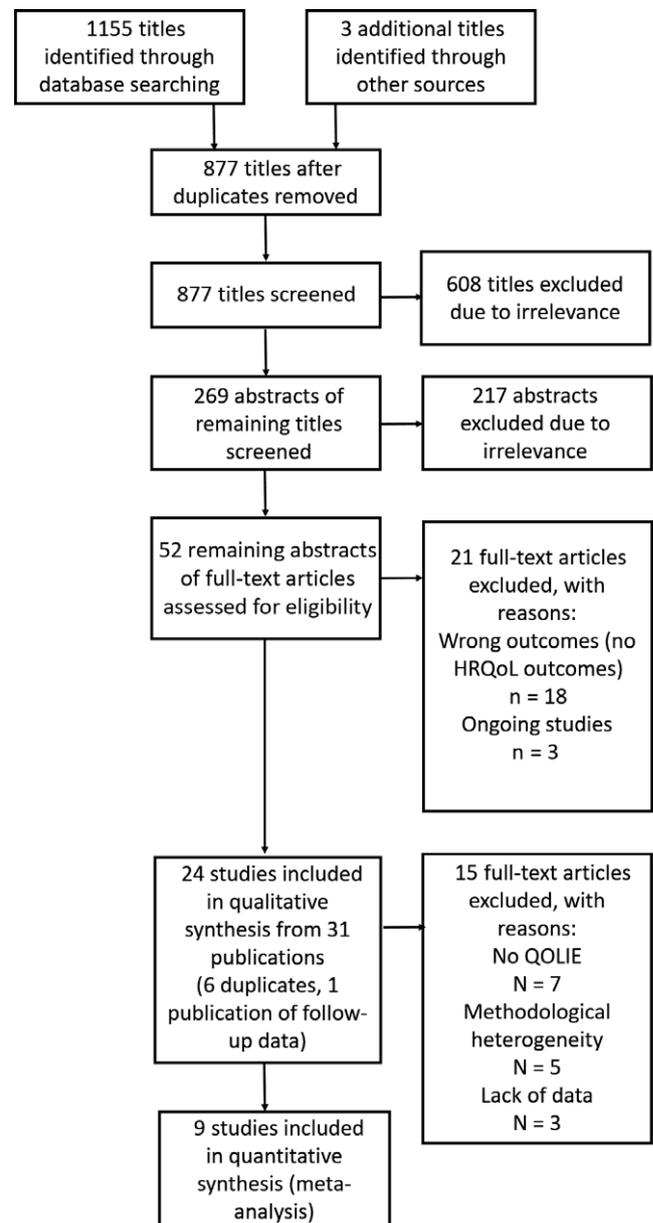

FIGURE 1 Flow chart of study selection. HRQoL, health-related quality of life; QOLIE, Quality of Life in Epilepsy

2016 for RCTs and quasi-RCTs investigating psychological treatments without language restrictions: Cochrane Epilepsy Group Specialized Register, Cochrane Central Register of Controlled Trials via the Cochrane Register of Studies Online, MEDLINE (Ovid) from 1946 onward, and Psy-INFO (EBSCO) from 1887 onward. The search strategies for each of these databases are shown in Appendices S1-S4. ClinicalTrials.gov was searched using the search terms (psychological OR psychotherapy) AND epilepsy. The World Health Organization International Clinical Trials Registry Platform was searched using the search terms (psychological OR psychotherapy) AND epilepsy. In addition, the reference lists of retrieved studies and relevant reviews were reviewed to identify additional reports of relevant studies.

In line with the standard Cochrane selection process,[20] all titles and abstracts were reviewed independently to determine their relevance by 2 review authors, a neurology resident specializing in epilepsy and psychotherapy (R.M.) and a clinical psychologist specializing in neuropsychology and psychotherapy (V.T.), resolving disagreements through discussion with the wider group of authors or the Epilepsy Review Group. Relevance was defined by the operational definition of psychological treatments for PWE and the inclusion of a validated HRQoL measure as a primary or secondary outcome. The full text of all studies was examined if initial screening suggested that they may be suitable for inclusion. Reasons for exclusion at the level of full-text review are included in Figure 1.

2.3 | Data analysis and management

Data of all included studies were extracted by R.M. and V.T. independently using an electronic Cochrane data collection form that had been adapted and pilot tested to fit the scope of this review.[21] Risk of bias (ROB) assessment was conducted using the Cochrane Collaboration's recommended domain-based evaluation tool for randomized trials.[1] Critical assessments were made separately for type of bias, namely selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias. Discrepancies were resolved by mutual discussion. The original investigators were contacted to request missing information (eg, missing data) and clarification of methodology (eg, procedure of randomization). All study investigators were contacted for their original protocols or comparable documents to assess reporting bias.

Methodological heterogeneity, that is, variability in study design,[22] was assessed by R.M. and V.T. by examining the trial designs. Statistical heterogeneity was assessed by applying the I^2 and χ^2 tests. The authors judged a I^2 result of >70% and a χ^2 result of $P < .01$ as indicative of statistical heterogeneity.[23] The types of interventions and outcome measures used in the included studies were compared by tabulation to assess whether meta-analysis was appropriate. Meta-analysis was performed using Review Manager software.[24] The inverse variance method for continuous outcomes and a random-effects model was employed. $P < .05$ was used as a statistical significance level.

The mean change from baseline (±standard deviation [SD]) of the most commonly used HRQoL outcome measure was used for meta-analysis. For studies that were excluded from the meta-analysis due to methodological heterogeneity or insufficient data, the available postintervention scores of validated HRQoL measures were compiled and presented via narrative synthesis. Postintervention scores of secondary outcomes consisting of validated measures of psychiatric symptoms and seizure-related outcomes were also compiled. The treatment effect for each continuous outcome was expressed as a mean difference (MD) with 95% confidence interval (CI). This review used the GRADE approach[25] to interpret findings.[2]

3 | RESULTS

3.1 | Description of studies

3.1.1 | Search results

The electronic search yielded 1155 titles from the databases, with an additional 3 titles obtained from hand-searching. Following the removal of duplicates, 877 titles remained. Six hundred eight titles were excluded due to irrelevance (that is, the titles clearly indicated that the studies were not related to the investigation of psychological interventions for PWE). The authors reviewed the abstracts of the remaining 269 titles for eligibility, leaving 52 full texts to be assessed for inclusion. Twenty-one full texts were excluded following full-text analysis (Figure 1). Finally, this review included 24 completed RCTs from 31 publications. One publication[26] described follow-up measurements of the same study population[27]; it was therefore not considered as a separate RCT (Figure 1).

3.1.2 | Psychological treatment methods

Psychological interventions
Table 1 groups the studies' characteristics and intervention components according to the operational definition of psychological treatments. Intervention components may appear in multiple groups due to the broad spectrum of treatment techniques that are commonly used to realize the goals of psychological interventions. The majority of psychological interventions were cognitive and/or behaviorally based interventions (11 studies, 46%) with the primary goal of

TABLE 1 Characteristics and intervention components of included studies

Study (intervention acronym), country	Treatment method	Treatment goal	Main treatment strategies	Timing	Participants
Psychological interventions					
Ciechanowski 2010 & Chaytor 2011 (PEARLS), USA[26,27]	CBT	Depressive symptoms	Cognitive restructuring, social/behavioral activation	8 × 50-min in-home sessions/ 5 mo + 7 monthly telephone calls	n = 80 adults with epilepsy with significant depression (PHQ-9 score ≥ 10)
Gandy 2014, Australia[28]				1 × 2 h assessment + 8 weekly 1 h sessions	n = 59 adults with epilepsy
Martinović 2006, Serbia[29]				8 weekly sessions + 4 monthly sessions	n = 32 adolescents with newly diagnosed epilepsy and subthreshold depression
Orjuela-Rojas 2015, Mexico[30]				12 weekly 90-min sessions	n = 15 adults with epilepsy with major depression
Schröder 2014 (Deprexis), Germany[32]				9 weekly 10- to 60-min modules	n = 78 adults with self-reported depressive symptoms
Thompson 2010 (UPLIFT), USA[31]				8 weekly 1-h sessions	n = 53 adults with epilepsy and mild or moderate depression (CES-D score > 13 and < 38)
Au 2003, Hong Kong[33]		Seizure frequency	Stress management, communication skills	8 weekly 2-h sessions	n = 17 adults with ≥ 2 seizures per month + psychological distress
Hosseini 2016, Iran[37]	MI	Quality of life	MI techniques	5 sessions in 20 d	n = 56 adults with primary generalized tonic–clonic epilepsy and uncontrolled seizures
Lundgren 2006, South Africa[34] Lundgren 2008, India[35]	ACT		ACT, seizure self-management	5 individual 90-min sessions + 2 group 3-h sessions + 2 1-h boosters at 6 and 12 mo	n = 27 & n = 18 adults with epilepsy with ≥4 seizures/3 mo
Tang 2015, Hong Kong[36]	MT		Epilepsy-specific mindfulness practices	4 biweekly 2.5-h sessions	n = 61 adults with drug-resistant epilepsy
Self-management interventions					
DiIorio 2011 (WebEase), USA[45]	MI	Medication adherence	Stress/sleep management	3 biweekly modules	n = 194 adults with epilepsy
Fraser 2015 (PACES), USA[46]	Consumer-driven psychoeducation	Self-management	Epilepsy-self management, communication strategies	8 weekly 75-min sessions	n = 83 adults with epilepsy
Yadegary 2015, Iran[47]	Self-management	Quality of life		4 weekly 120-min sessions	n = 60 adults with epilepsy with ≥1 seizure during the past year
Adherence					

(Continues)

TABLE 1 (Continued)

Study (intervention acronym), country	Treatment method	Treatment goal	Main treatment strategies	Timing	Participants
Pakpour 2015, Iran[48]	MI	Medication adherence	MI techniques	3 weekly 40- to 60-min sessions	n = 275 adults with epilepsy
Psychoeducation					
Jantzen 2009 (FLIP&FLAP), Germany[38]	Epilepsy education program	Quality of life	Epilepsy-specific education, psychosocial aspects, self-management	2- to 2.5-d course (14-16 h)	n = 192 children and adolescents with epilepsy including parents
May & Pfäfflin 2002 (MOSES), Austria, Germany, Switzerland[40]				2-d course (14 h)	n = 383 adolescents and adults with epilepsy
Lua & Neni 2013, Malaysia[39]				11 weekly modules	n = 144 adults with epilepsy
Pramuka 2007, USA[41]				6 weekly 2-h sessions	n = 55 adults with epilepsy
Rau 2006 (FAMOSES), Germany[42]		Knowledge + coping		2-d course (14 h)	n = 70 children with epilepsy
Pfäfflin 2016, Germany[43]	Counseling	Satisfaction with information and support		Delivery during routine visits	n = 187 adults with epilepsy
Beretta 2014 (EDU-COM), Italy[44]	Patient-tailored medication education	Drug-related problems	Personalized medication counseling	1-h session + booster session after 1 mo	n = 174 adults with epilepsy and chronic comorbidity
Combined interventions					
Caller 2016 (HOBSCOTCH), USA[50]	Cognitive, memory + self-management training	Quality of life	Problem-solving therapy, seizure management, social skills	8 weekly 40- to 60-min sessions	n = 66 adolescents and adults with epilepsy and self-reported memory complaints
Helde 2005, Norway[49]	Epilepsy education + nurse-led counseling	Personalized counseling		1-d group + phone calls every 3 mo for 2 y	n = 114 adolescents and adults with epilepsy

The included studies' characteristics and intervention components are grouped according to the operational definition of psychological treatments. The studies that are included in the meta-analysis are highlighted in gray. ACT, acceptance and commitment therapy; CBT, cognitive behavioral therapy; CES-D, Center for Epidemiologic Studies Depression; MI, motivational interviewing; MT, mindfulness therapy; PHQ-9, Patient Health Questionnaire-9.

treating depressive symptoms in adolescents and/or adults with epilepsy, with varying levels of depression severity defined as the inclusion criterion (n = 6, 54%).[26–32] The most common treatment strategies were cognitive restructuring to address depressive thoughts and behavioral and social activation. Two of these interventions (18%) included mindfulness techniques.[31,32] Only 1 study (9%) targeted seizure frequency as a primary treatment goal.[33] Treatment components included general and epilepsy-specific stress management strategies. Four studies (36%) focused on the primary treatment goal of improving HRQoL. Three (27%) of them employed mindfulness interventions[34–36] and evaluated mindfulness techniques in combination with seizure management techniques. One of these studies (4%)[37] investigated motivational interviewing (MI), which focused on enhancement of internal motivation for coping with epilepsy.

(Psycho-)educational interventions

There were 7 studies (29%) examining the benefit of educational interventions. All of them comprised epilepsy knowledge, advocacy topics, daily self-management behaviors, and psychosocial aspects primarily to enhance QoL (n = 4, 57%),[38–41] increase knowledge and coping,[42] increase satisfaction of patients with information and support,[43] or reduce drug-related problems.[44]

Self-management interventions

Three self-management/family management programs (12%) were identified. One Internet-based self-management program[45] focused on improving adherence and perceived stress levels. One consumer-driven psychoeducation intervention[46] focused on self-management behaviors by discussing medical and psychosocial aspects of epilepsy self-management and epilepsy-related communication. Another self-management intervention[47] applied similar techniques but primarily evaluated the impact of the intervention on HRQoL outcomes.

Adherence intervention

There was only 1 study (4%) that investigated an adherence intervention using MI aiming to improve medication adherence, medication-taking behaviors, seizure severity, and HRQoL.[48]

Combined interventions

There were 2 combined interventions (8%). One combined an epilepsy education group session covering epilepsy knowledge and nurse-led personalized counseling with the primary goal of enhancing QoL.[49] The other was a home- and telephone-based intervention[50] combining self-management and cognitive training to enhance QoL, mood, and objective and subjective neurocognitive functions.

3.1.3 | Participants

The majority of studies examined interventions for adults with epilepsy (75%); only 2 studies investigated educational interventions for children with epilepsy.[38,42] One study investigated a psychological intervention for adolescents and young adults with epilepsy,[29] 2 studies investigated mixed interventions for adolescents and adults,[49,50] and 2 studies investigated educational interventions for adolescents and adults.[40,43]

Severity of depressive symptoms was used as an inclusion criterion in 5 studies (21%; see Table 1).[26,27,29–32] One study only included adults with epilepsy and other chronic comorbidities,[44] because the intervention targeted adverse effects stemming from drug interactions. Another study[50] included adolescents and adults with subjective memory complaints, because the intervention included special cognitive and memory training.

Seizure-related parameters (eg, minimum seizure frequency) constituted an inclusion criterion in 6 studies (25%; see Table 1).[33–37,47] Altogether, the numbers of seizure-free individuals and individuals with primary generalized epilepsy were comparably small in the study populations of all included studies (mean number of participants = 102). Many studies excluded individuals with intellectual disability, and none of the studies reported whether individuals experienced nocturnal or diurnal seizures or whether individuals experienced seizure warnings.

3.1.4 | Trial design

Almost half of all study designs included a wait list control (WLC) group (n = 11, 46%).[28,31–33,37,38,40,42,43,45,46] Six studies (25%) included an immediate active control group (paper-based education intervention,[39] supportive therapy,[34] yoga,[35] counseling as usual,[29] pharmacotherapy with a selective serotonin reuptake inhibitor,[30] social support[36]). The remaining 7 studies (29%) employed a usual care (UC)/treatment as usual (TAU) control group.[26,27,31,41,44,48–50] The employment of a UC/TAU design instead of a WLC group was especially reasonable in long-term interventions (≥6 months).[26,27,49]

3.1.5 | Treatment delivery

Of the 24 studies, 11 examined group therapy (46%),[20,29,30,33,37,38,40–42,46,47] 6 interventions (25%) were delivered through individual sessions,[9,15,26,27,43,44,48] and 4 interventions (17%) combined group therapy with individual sessions.[34,35,49,50] Two studies (8%) used an Internet-based delivery method,[32,45] and 1 study (4%) used an Short Message Service (SMS)-based approach.[39] A specialized team, usually consisting of medical (doctors, nurses) and

mental health specialists (eg, psychologists, psychiatric nurses, social workers) delivered most of the educational interventions. Psychologists with different levels of clinical experience and training delivered most of the psychological and self-management interventions. Two interventions (8%) included peer coaches with epilepsy.[31,46] One pragmatic design (4%) left the delivery of the educational intervention to the treating physician.[44]

3.2 | Trial quality

The ROB assessment is summarized in Table 2. All studies were subject to at least 1 form of bias, as described below.

3.2.1 | Allocation (selection bias)

The majority of studies (71%) reported an adequate method of random sequence generation. Reasons for a rating as

high ROB included quasirandomized trial designs such as a matched design (n = 1, 4%),[33] alternating assignment (n = 1, 4%),[45] and allocation based on participants' application to 1 of 2 available courses and availability of spaces in offered courses in a WLC design (n = 2, 8%).[38,42] One study[30] was rated with very serious ROB because the allocation depended on the participants' "feasibility to attend the meetings." The majority of the studies reported proper procedure for allocation concealment.

3.2.2 | Blinding (performance bias and detection bias)

Blinding of participants and personnel is almost impossible to achieve when studying psychological treatments; hence the majority of studies had a high ROB (92%). Four studies (17%)[34–36,39] managed to blind the participants in both the treatment group and the active control group by telling

TABLE 2 Summary of risk of bias assessment

Study	Random sequence generation	Allocation concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other biases
Au[33]	↑	↑	?	↓	↓	↓	?
Beretta[44]	↓	↓	↑	↓	↓	↓	?
Caller[50]	↓	↑	↑	↓	↑	↓	↓
Chaytor[26]	↓	↓	↑	↓	↑	↑	↓
Ciechanowski[27]	↓	↓	↑	↓	↑	↑	↓
DiIorio[45]	↑	↓	↑	↑	↑	↓	↓
Fraser[46]	↓	↓	↑	↓	↑	↓	↓
Gandy[28]	↓	↓	↑	↑	↑	↓	↓
Helde[49]	↓	↓	↑	↓	↓	↓	?
Hosseini[37]	?	?	↑	↓	↑	↓	↓
Jantzen[38]	↑	↑	↑	↓	↓	↓	?
Lua & Neni[39]	↓	?	?	?	↓	↓	?
Lundgren[34]	↓	↓	↑	↑	↓	↓	↓
Lundgren[35]	↓	↓	↑	↑	↓	↓	↓
Martinović[29]	↓	↓	↓	↓	↓	↑	?
May & Pfäfflin[40]	↓	↑	↑	↓	↑	↓	?
Orjuela-Rojas[30]	↑	↑	↑	↓	↑	↓	?
Pakpour[48]	↓	?	?	?	↓	↓	↓
Pfäfflin[43]	↓	↓	↑	↓	↑	↓	↓
Pramuka[41]	↓	?	↑	↑	↑	↑	↑
Rau[42]	↓	↑	↑	↓	↑	↓	↓
Schröder[32]	↓	↓	↑	↓	↑	↓	↓
Tang[36]	↓	↓	↑	↓	↓	↓	↓
Thompson[31]	?	↑	↑	?	↑	↑	↓
Yadegary[47]	↓	?	?	?	?	↓	↑

↓, low risk of bias; ↑, high risk of bias; ? = unclear risk of bias.

them that they would participate in an intervention to improve coping with epilepsy. There were no personnel involved to be blinded in 2 studies (8%) investigating a Web-based intervention.[32,45] One study (4%)[29] was classified as having a very low risk as the therapists who delivered the treatment (cognitive behavioral intervention and counseling as usual) were blinded to the participants' group status; the researchers told both therapists only that they would deliver psychological means to improve coping with epilepsy. Blinding of the assessment of patient-reported outcome data was adequate in the majority of studies (62%). Five studies (21%) had a high detection bias because the personnel conducting the outcome assessment were aware of the treatment allocation.[28,34,35,41,45]

3.2.3 | Incomplete outcome data (attrition bias)

Three studies (12%)[33–35] were rated as low risk because they reported no dropout throughout. Eight studies (33%)[27,29,36,38,39,44,48,49] were rated as low risk as there was only a small number of missing data, which were balanced across the groups with justifiable reasons. A high ROB was suggested in 10 studies (42%) because of larger numbers of missing data (a cutoff of ≥15% for short-term interventions <6 months and ≥20% for long-term interventions of ≥6 months was applied) that were, however, balanced in 1 study (4%)[46] and unbalanced in 7 studies (29%).[28,30.37,41,43,45,50] One study (4%) excluded participants who had missed >1 intervention session, which indicated that no intention-to-treat analysis had been undertaken.[37] An unclear risk was assigned to 1 study (4%) that did not provide data on the attrition rate.[47] There were 2 studies (8%) that reimbursed their participants for participation in the study, but these studies had a high attrition rate nonetheless.[41,45]

3.2.4 | Selective reporting (reporting bias)

Sixteen studies (67%) were rated as low ROB as there was no evidence of selective outcome reporting within the publications. Four studies (17%)[26,27,29,31,41] were rated as high ROB due to evidence of selective outcome reporting within the publications. A rating of low ROB was confirmed based on document review of registered protocols provided by the authors for 9 studies (37%).[32,36,40,42,44–46,49,50]

3.2.5 | Other potential sources of bias

Other potential sources of biases included language bias, selective recruitment, and fidelity to the intervention protocol. Language bias remained unclear. We included 1 non-English publication, which was published in German

(4%).[42] In general, we did not have enough evidence to judge the biases in regard to selective recruitment and fidelity to the intervention protocol. As a result, the bias judgment remained unclear in most cases. Three studies (12%), however, provided details regarding the attempt to ensure fidelity to the intervention protocol by employing standard training protocols and supervision.[26–28,31] Furthermore, the risk of infidelity to the intervention protocol was considered to be relatively low whenever the therapist delivering the intervention coincided with the developer of the intervention protocol (n = 6, 25%)[25–27,34,46,48,49] and very low when the delivery of the intervention was Internet-based only (n = 2, 8%).[32,45]

3.2.6 | Effects of interventions

HRQoL

The most commonly used scale for assessing HRQoL was the Quality of Life in Epilepsy-31/-31-P/-89 (QOLIE-31/-31-P/-89).[51,52] It was used in 17 studies (71%), of which 12 (70%) were considered for meta-analyses due to satisfactory methodological homogeneity.[26,27,29,30,33,36,37,41,46,47,49,50] Five studies (29%) were not included in the meta-analysis due to methodological heterogeneity regarding intervention delivery that was not face-to-face (n = 2, 40%; Web-based intervention delivery,[32] SMS-based intervention delivery[39]) or comparatively narrow intervention goals (n = 3, 60%; decreasing medication-related problems,[44] increasing medication adherence,[48] increasing satisfaction with treatment and support[43]). Of the 12 studies being considered for meta-analysis, 3 studies (25%) were eventually excluded due to the lack of raw QOLIE-89 data (n = 2)[37,41] or QOLIE-31-P data (n = 1),[47] which prevented the conversion of the results into the cross-study summary QOLIE-31 scores used for the meta-analysis.*

Consequently, the meta-analysis comprised data from 9 studies (37%)[26–30,33,36,46,49,50] with a total of 468 participants (see studies highlighted in gray in Table 1). Due to substantial baseline differences between intervention and control groups, the mean change from baseline (±SD) was used for quantitative synthesis (meta-analysis) rather than postintervention scores (±SD), and required data were sought from all study authors. Because Martinović et al.[29] only provided the total score, subscale results can only be presented for 8 studies (89%), with a total of 440 participants. A positive mean change indicated a postintervention improvement.

Significant differences of mean improvement between the treatment group and the control group were found in the total score (9 RCTs, n = 468 participants, MD = +5.68 points, 95% CI = 3.11-8.24, $P < .0001$, χ^2 $P = .08$, $I^2 = 43\%$) and all subscales except social functioning (8 RCTs, n = 440 participants, MD = +2.77 points, 95%

CI = −1.02 to 6.57, P = .15, χ^2 P = .98, I^2 = 0%; Figures 2A-D).

1. Emotional well-being: 8 RCTs, n = 440 participants, MD = +7.03 points, 95% CI = 2.51-11.54, P = .002, χ^2 P = .02, I^2 = 59%;
2. Energy/fatigue: 8 RCTs, n = 440 participants, MD = +6.90 points, 95% CI = 3.49-10.31, P < .0001, χ^2 P = 0.24, I^2 = 24%;
3. Overall QoL: 8 RCTs, n = 440 participants, MD = +6.47 points, 95% CI = 2.68-10.25, P = .0008, χ^2 P = .06, I^2 = 49%;
4. Seizure worry: 8 RCTs, n = 440 participants, MD = +5.96 points, 95% CI = 2.50-9.42, P = .0007, χ^2 P = .86, I^2 = 0%;
5. Cognitive functioning: 8 RCTs, n = 440 participants, MD = +3.00 points, 95% CI = 0.21, 5.78, P = .04, χ^2 P = .93, I^2 = 0%;
6. Medication effect: 8 RCTs, n = 440 participants, MD = 3.84 points, 95% CI = 0.28-7.41, P = .03, χ^2 P = .66, I^2 = 0%.

Results indicated that participants in the treatment group showed significantly more postintervention improvement in terms of QOLIE-31 total score and 6 of 7 subscales, compared to their counterparts in the control group. The mean improvement of the total score and 3 subscales, namely, emotional well-being, energy/fatigue, and overall QoL, exceeded the minimally important change (MIC) threshold established by Borghs et al.[53] for a small effect size (Cohen d = 0.3), indicating a clinically meaningful postintervention improvement.[53]

Of the 8 studies (47%) that were excluded from the meta-analysis, 4 studies (50%)[37,39,47,48] reported significant improvements in the treatment group when comparing the postintervention outcomes of treatment and control groups in terms of QOLIE total score (Table 3A). The remaining 4 studies (50%) did not report a significant difference between postintervention total scores when comparing treatment and control groups (Table 3A).[25,32,43,44] The

potential impact of the 3 studies (25%)[37,41,47] that did not provide data that would have allowed the study to be included in data synthesis is probably small, especially because 2 (67%) studies[37,47] also reported significantly higher QoL in the treatment group when comparing postintervention outcomes of treatment and control groups.

Eight studies (33%) used HRQoL scales other than the QOLIE outcome measures (Table 3B). All of them showed a nonsignificant postintervention mean difference between the intervention and control group except for Jantzen et al.,[38] who reported that children and adolescents of the treatment group showed a significantly greater increase on the "social exclusion" subscale in DISABKIDS, indicating better QoL, compared to the controls (Table 3B).

3.2.7 | Psychiatric comorbidities outcome measures

Depression
A total of 11 studies (46%) measured depressive symptoms as an outcome measure. The most commonly used scale was the Beck Depression Inventory/Beck Depression Inventory-II, which was used in 5 studies (45%).[29–32,36] All studies indicated that there were no statistically significant differences between the treatment and control groups at baseline. Postintervention means were used to compare the difference between the 2 groups. Seven studies (64%) reported a significant postintervention difference between the intervention and the control groups.[26–29,31,32,36,46] Two of these studies (28%) used >1 outcome measure.[28,29] Four of the 11 studies (36%) reported nonsignificant results[24,30,43,50]; Caller et al.[50] and Orjuela-Rojas et al.[30] used >1 outcome measure (Table 4A).
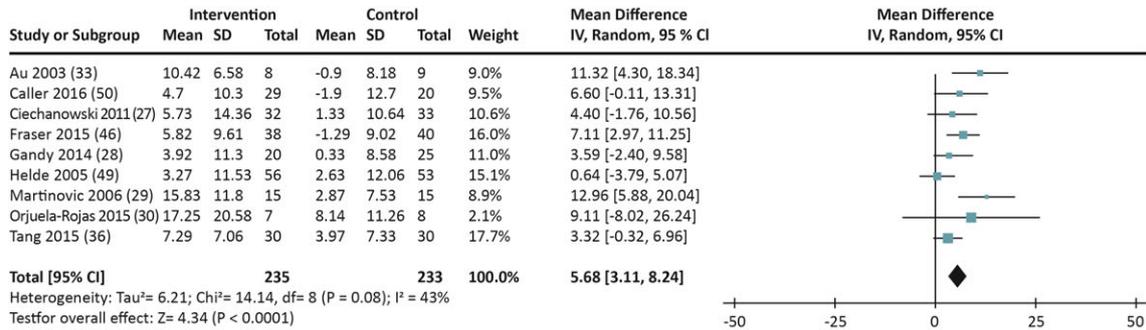
Suicidal ideation
Two studies (8%) reported suicidal ideation as an outcome measure. Whereas Ciechanowski et al.[27] reported a significantly smaller proportion of patients reporting suicidal ideation at follow-up (decreasing 24% in the intervention group

FIGURE 2 Forest plots of comparisons of mean change from baseline of Quality of Life in Epilepsy (QOLIE)-31 total score and subscale scores. A, QOLIE-31 total score. B, QOLIE-31 emotional well-being. C, QOLIE-31 energy/fatigue. D, QOLIE-31 overall quality of life. Sample size information can be found in the columns labeled "Total." Effect sizes are stated in the columns labeled "Mean Difference." Five study authors provided unpublished data to allow inclusion in the meta-analysis: Orjuela-Rojas et al.[30] provided raw data to calculate the mean change from baseline (±standard deviation [SD]), Fraser et al.[46] provided the mean change from baseline (±SD) for the control group, Helde et al.[49] provided raw data to allow for the conversion of results from QOLIE-89 to QOLIE-31, Tang et al.[36] provided all converted scores from QOLIE-31-P to QOLIE-31 and the mean change from baseline (±SD), and Caller et al.[50] provided unadjusted mean change from baseline (±SD). Three studies did not provide the mean change from baseline (±SD).[15,17,21] The mean change from baseline was calculated as a difference between pre- and postintervention means. To calculate an adjusted SD, these 3 studies were grouped with studies investigating interventions comparable in terms of intervention method, treatment setting (group vs individual), and total treatment time: Au et al.[33] with Tang et al.,[36] Ciechanowski et al.[27] with Gandy et al.,[28] and Martinović et al.[29] with Orjuela-Rojas et al.[30] This allowed for the calculation of the adjusted SD of the mean change from baseline based on the correlation between pre- and postintervention means (±SD) of the studies with which they were grouped. Because Martinović et al.[29] could not provide QOLIE-31 subscale outcomes, only the total score was included from this study. CI, confidence interval; IV, inverse variance
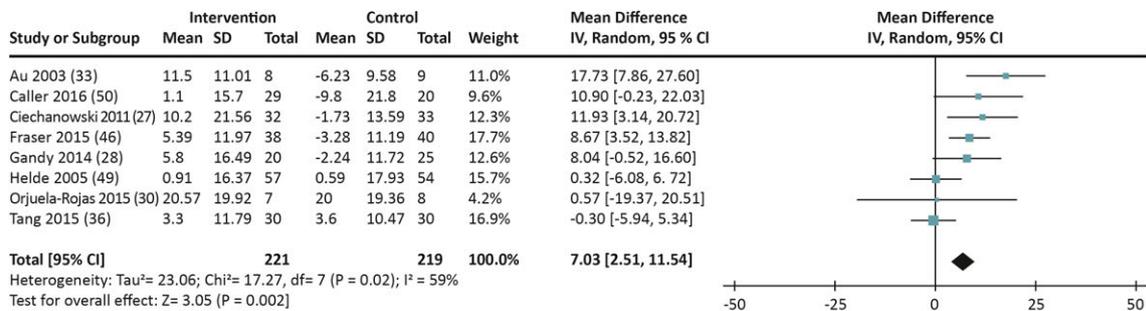
and increasing 12% in the usual care group [$P = .025$]; post-treatment outcomes were not reported), Orjuela-Rojas et al.[30] did not find a between-group difference in terms of suicide risk using the Mini International Neuropsychiatric Interview (intervention mean = 1.1 vs control mean = 0.6, $P = .42$; SD was not reported).
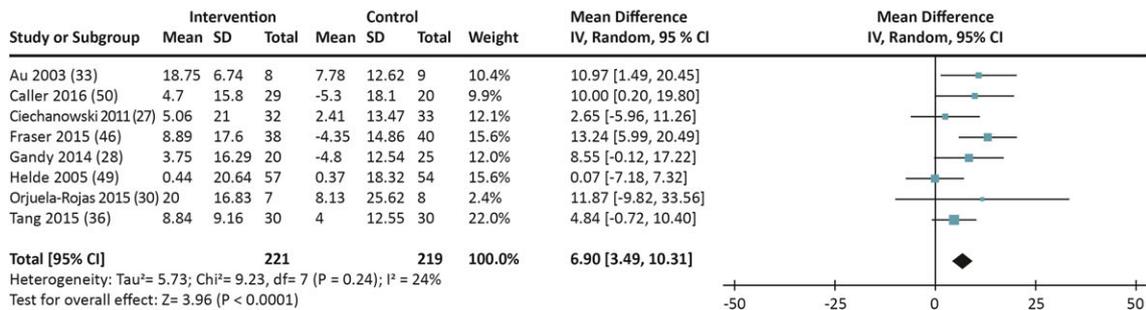
A

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95 % CI
Au 2003 (33)	10.42	6.58	8	-0.9	8.18	9	9.0%	11.32 [4.30, 18.34]
Caller 2016 (50)	4.7	10.3	29	-1.9	12.7	20	9.5%	6.60 [-0.11, 13.31]
Ciechanowski 2011 (27)	5.73	14.36	32	1.33	10.64	33	10.6%	4.40 [-1.76, 10.56]
Fraser 2015 (46)	5.82	9.61	38	-1.29	9.02	40	16.0%	7.11 [2.97, 11.25]
Gandy 2014 (28)	3.92	11.3	20	0.33	8.58	25	11.0%	3.59 [-2.40, 9.58]
Helde 2005 (49)	3.27	11.53	56	2.63	12.06	53	15.1%	0.64 [-3.79, 5.07]
Martinovic 2006 (29)	15.83	11.8	15	2.87	7.53	15	8.9%	12.96 [5.88, 20.04]
Orjuela-Rojas 2015 (30)	17.25	20.58	7	8.14	11.26	8	2.1%	9.11 [-8.02, 26.24]
Tang 2015 (36)	7.29	7.06	30	3.97	7.33	30	17.7%	3.32 [-0.32, 6.96]
Total [95% CI]			235			233	100.0%	5.68 [3.11, 8.24]

Heterogeneity: Tau² = 6.21; Chi² = 14.14, df= 8 (P = 0.08); I² = 43%
Test for overall effect: Z= 4.34 (P < 0.0001)

B

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95 % CI
Au 2003 (33)	11.5	11.01	8	-6.23	9.58	9	11.0%	17.73 [7.86, 27.60]
Caller 2016 (50)	1.1	15.7	29	-9.8	21.8	20	9.6%	10.90 [-0.23, 22.03]
Ciechanowski 2011 (27)	10.2	21.56	32	-1.73	13.59	33	12.3%	11.93 [3.14, 20.72]
Fraser 2015 (46)	5.39	11.97	38	-3.28	11.19	40	17.7%	8.67 [3.52, 13.82]
Gandy 2014 (28)	5.8	16.49	20	-2.24	11.72	25	12.6%	8.04 [-0.52, 16.60]
Helde 2005 (49)	0.91	16.37	57	0.59	17.93	54	15.7%	0.32 [-6.08, 6.72]
Orjuela-Rojas 2015 (30)	20.57	19.92	7	20	19.36	8	4.2%	0.57 [-19.37, 20.51]
Tang 2015 (36)	3.3	11.79	30	3.6	10.47	30	16.9%	-0.30 [-5.94, 5.34]
Total [95% CI]			221			219	100.0%	7.03 [2.51, 11.54]

Heterogeneity: Tau² = 23.06; Chi² = 17.27, df= 7 (P = 0.02); I² = 59%
Test for overall effect: Z= 3.05 (P = 0.002)

C

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95 % CI
Au 2003 (33)	18.75	6.74	8	7.78	12.62	9	10.4%	10.97 [1.49, 20.45]
Caller 2016 (50)	4.7	15.8	29	-5.3	18.1	20	9.9%	10.00 [0.20, 19.80]
Ciechanowski 2011 (27)	5.06	21	32	2.41	13.47	33	12.1%	2.65 [-5.96, 11.26]
Fraser 2015 (46)	8.89	17.6	38	-4.35	14.86	40	15.6%	13.24 [5.99, 20.49]
Gandy 2014 (28)	3.75	16.29	20	-4.8	12.54	25	12.0%	8.55 [-0.12, 17.22]
Helde 2005 (49)	0.44	20.64	57	0.37	18.32	54	15.6%	0.07 [-7.18, 7.32]
Orjuela-Rojas 2015 (30)	20	16.83	7	8.13	25.62	8	2.4%	11.87 [-9.82, 33.56]
Tang 2015 (36)	8.84	9.16	30	4	12.55	30	22.0%	4.84 [-0.72, 10.40]
Total [95% CI]			221			219	100.0%	6.90 [3.49, 10.31]

Heterogeneity: Tau² = 5.73; Chi² = 9.23, df= 7 (P = 0.24); I² = 24%
Test for overall effect: Z= 3.96 (P < 0.0001)

D

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95 % CI
Au 2003 (33)	14.07	11.7	8	-1.39	9.75	9	9.1%	15.46 [5.15, 25.77]
Caller 2016 (50)	2.2	11.9	29	-6	16.9	20	11.4%	8.20 [-0.38, 16.78]
Ciechanowski 2011 (27)	5.62	21.22	32	2	12	33	11.7%	3.62 [-4.80, 12.04]
Fraser 2015 (46)	7.43	15.56	38	-2.63	13.64	40	15.2%	10.06 [3.55, 16.57]
Gandy 2014 (28)	0.13	13.49	20	-0.78	11.3	25	13.5%	0.91 [-6.48, 8.30]
Helde 2005 (49)	3.29	17.37	57	4.09	16.34	54	15.7%	-0.80 [-7.07, 5.47]
Orjuela-Rojas 2015 (30)	19.64	16.29	7	2.82	18.44	8	4.0%	16.82 [-0.76, 34.40]
Tang 2015 (36)	8.5	10.59	30	0.75	7.49	30	19.5%	7.75 [3.11, 12.39]
Total [95% CI]			221			219	100.0%	6.47 [2.68, 10.25]

Heterogeneity: Tau² = 13.54; Chi² = 13.61, df = 7 (P = 0.06); I² = 49%
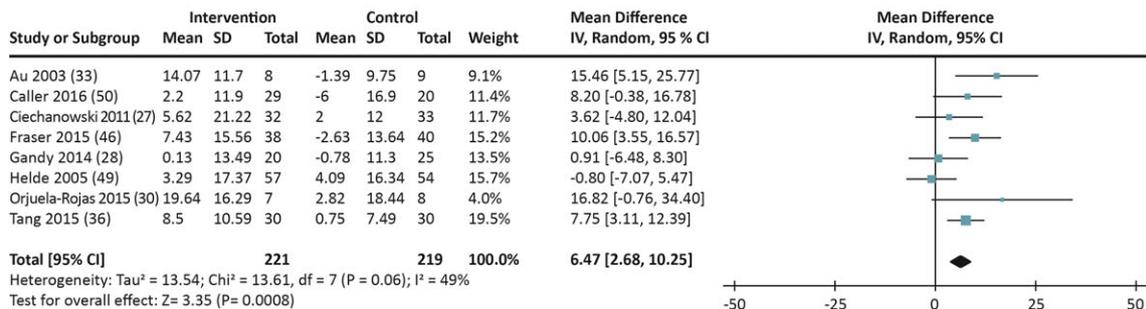Test for overall effect: Z= 3.35 (P= 0.0008)

TABLE 3 (A) Postintervention QOLIE-31/-31-P/-89 total scores of studies not included in meta-analysis and (B) mean postintervention scores of all studies using health-related quality of life scales other than the QOLIE-31/-89

	Intervention group		Control group		
Study	**Mean**	**SD**	**Mean**	**SD**	**P**
A					
QOLIE-31					
Beretta[44]	63.00	15.48	65.04	14.38	.0070
Lua & Neni[39]	69.2	17.4	58.4	13.7	
Pakpour[48]	62.14	13.21	56.01	12.12	<.001
Schröder[32]	31.72	13.37	32.56	13.37	.755
QOLIE-31-P					
Yadegary[47]	72.18	11.34	53.49	15.97	<.001
QOLIE-89					
Pramuka[41]	67.3	2.6	65	2.8	Not significant
	Mean change	SD	Mean change	SD	P
Hosseini[37]	35.95	8.74	−8.07	8.91	<.001
B					
DiIorio[45]					
QOLIE-10	33.8	8.0	33.3	7.5	.7310
Jantzen[38]					
DISABKIDS	Reported significant increase in the "social exclusion" subscale				
Lundgren[34]					
WHOQOL-BREF	58.4	9.7	55.3	6.6	
SWLS	23.3	4.6	13.9	6.0	
Lundgren[35]					
WHOQOL-BREF	57.2	7.2	60.2	8.6	
SWLS	21.8	6.3	21.0	7.1	
May & Pfäfflin[40]					
SF-36 Mental	43.7	11.5	42.5	11.8	
SF-36 Physical	50.4	9.4	52.0	8.7	.0750
Rau[42]					
KINDL	70.6	13.3	77.3	15.0	.075
Schröder[32]					
WHOQOL-BREF	75.9	15.0	78.6	17.4	Not significant
Thompson[31]					
SWLS	21.0	Not reported	18.0	Not reported	.0900

A, Postintervention QOLIE-31/-31-P/-89 total scores of all 8 studies that were not included in the meta-analysis due to the uniqueness of the intervention protocol and incompatible data. QOLIE, Quality of Life in Epilepsy; SD, standard deviation. B, QOLIE-10: Quality of Life in Epilepsy-10[57]; DISABKIDS: Quality of Life in Children and Adolescents with Disabilities and Their Family[54,55]; WHOQOL-BREF: World Health Organization Quality of Life instrument, short version[60]; SWLS: Satisfaction with Life Scale;[59]SF-36: Short-Form 36 (Mental: mental health, Physical: physical functioning)[58]; KINDL: Gesundheitsbezogene Lebensqualität und Psychosoziale Auswirkungen der Epilepsie (Health-Related Quality of Life and Psychosocial Consequences of Epilepsy).[56] The epilepsy-specific HRQoL outcome measures are highlighted in gray. References to the questionnaires' psychometric properties and validation are included.

Anxiety

A total of 5 studies (21%) included anxiety level as an outcome measure[28,30,36,43,46]; all of them reported no significant baseline difference between the treatment and control groups. The Beck Anxiety Inventory was used in 4 studies (80%). Only Tang et al.[36] reported significantly fewer anxiety symptoms in the treatment group compared to control at postintervention ($P = .008$; Table 4B).

TABLE 4 (A) Mean postintervention scores of depression outcomes and (B) mean postintervention scores of anxiety outcomes

Study		Intervention group		Control group		
		Mean	SD	Mean	SD	P
A						
Gandy[28]	HADS-D	4.58	3.59	5.5	5.26	.048
Orjuela-Rojas[30]		5.4	Not reported	5.2	Not reported	.93
Pfäfflin[43]		9% with HADS-D ≥ 11		5.5% with HADS-D ≥ 11		Nonsignificant
Martinović[29]	BDI/BDI-II	5.4	2.97	7.8	2.66	<.05
Schröder[32]		15.84	13	18.37	10.23	.01
Thompson[31]		5.5	Not reported	10.6	Not reported	<.01
Orjuela-Rojas[30]		17.2	Not reported	14.6	Not reported	.58
		Mean	95% CI	Mean	95% CI	P
Tang[36]		6.9	4.49, 9.31	9.47	6.26, 12.67	.045
Fraser[46]	PHQ-9	6.3	5.5	8.6	6	.02
Gandy[28]	NDDI-E	14.3	3.4	16.48	3.81	.045
Martinović[29]	CES-D	9.8	4.2	13.6	4.64	<.05
	HAMD	3.3	1.29	5.8	1.98	<.05
May & Pfäfflin[40]	D-S'	13.63	8.99	12.22	8.86	Nonsignificant
		Mean change	SD	Mean change	SD	P
Caller[50]	NDDI-E	−0.4	0.6	0.7	0.8	.3000
Caller[50]	PHQ-9	−0.7	1	1.2	1.2	Nonsignificant
Ciechanowski[27] and Chaytor[26]	HSCL-20	−0.18	0.7	−0.48	0.7	.09
B						
Gandy[28]	HADS-A	6.11	2.96	7.45	3.78	.089
Orjuela-Rojas[30]		9.7	Not reported	9.2	Not reported	.800
Pfäfflin[43]		20.9% with HADS-A ≤ 11		17.8% with HADS-A ≥ 11		Nonsignificant
Fraser[46]	GAD-7	5.4	6.6	6.1	5.1	.282
		Mean	95% CI	Mean	95% CI	
Tang[36]	BAI	9.73	6.35, 13.22	10.7	7.24, 14.16	.008

BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CES-D, Center for Epidemiologic Studies Depression; CI, confidence interval; D-S', Depressive Mood Scale; GAD-7, Generalized Anxiety Disorder-7; HADS-A, Hospital Anxiety Depression Scale (Anxiety); HADS-D, Hospital Anxiety Depression Scale (Depression); HAMD, Hamilton Depression Scale; HSCL-20, Hopkins Symptom Checklist-20; NDDI-E, Neurological Depressive Disorders Inventory-Epilepsy; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

3.2.8 | Seizure-related outcomes

A total of 9 studies (37%) had seizure-related variables as an outcome measure.[26,27,33–36,38,40,42,48] Seizure-related outcomes included seizure frequency, seizure severity, and seizure index (seizure frequency × seizure duration in seconds) as operationally defined by Lundgren et al.[34,35] Three studies (33%) reported a significantly greater reduction of seizure frequency in the treatment compared to the control group at postintervention,[34,36,40] whereas the other 5 studies (55%) found no significant differences between the groups.[26,27,33,35,38,42] In terms of seizure severity, Pakpour et al.[48] reported a significantly greater reduction in the treatment group compared to controls at postintervention using the Liverpool Seizure Severity Scale, whereas Tang et al.[36] reported no significant group differences using the Seizure Severity Index. Significantly greater reduction in terms of seizure index in the treatment group at postintervention compared to controls was reported in both studies by Lundgren et al.[34,35] (Table 5).

4 | DISCUSSION

This critical review yielded a meta-analysis consisting of 9 RCTs with 468 participants that indicated significant postintervention improvement for the total scores and 6 of

TABLE 5 Mean postintervention scores of seizure outcomes

Study	Measure	Intervention group		Control group		
		Mean	SD	Mean	SD	*P*
Lundgren[34]	Mean seizures/mo	0.71	0.91	6.00	3.91	<.001
May & Pfäfflin[40]		2.77	1.64	2.74	1.62	<.041
Pakpour[48]	LSSS	47.24	17.41	58.09	21.75	<.05
Lundgren[34]	Seizure index[a]	23	35	2087	3539	<.001
Lundgren[35]		62	104	15	23	<.05
		Mean	95% CI	Mean	95% CI	
Tang[36]	Mean seizures/6 wk	5.9	2.88-8.92	7.33	3.46-11.21	.018
	SSI	2.55	2.06-3.03	2.91	2.44-3.38	>.05

CI, confidence interval; LSSS, Liverpool Seizure Severity Scale; SD, standard deviation; SSI, Seizure Severity Index.

[a]Seizure frequency × seizure duration in seconds.

7 QOLIE-31 subscales. The mean improvement of the total score and 3 subscales, namely, emotional well-being, energy/fatigue, and overall QoL, exceeded the MIC threshold established by Borghs et al.[53] for a small effect size (Cohen *d* = 0.3), indicating a clinically meaningful postintervention improvement. Although the 2008 Cochrane Review[17] found no reliable evidence for the efficacy of psychological treatment in PWE, this reappraisal, with many new intervention studies in the past decade, draws a more optimistic conclusion that psychological treatments can be beneficial to adults with epilepsy in terms of improved HRQoL. Furthermore, this pattern of improvement was reported by 4 additional RCTs that were excluded from our meta-analysis.

In terms of psychiatric symptoms and seizure-related outcomes, the majority of studies (n = 7 of 11) examining depressive symptoms reported more improvement in the treatment (significant decrease in depressive symptoms) compared to the control group. In contrast, only 1 of 5 studies examining anxiety found a significantly greater reduction of anxiety symptoms in the treatment condition compared to control at postintervention. Slightly more than half of the studies (n = 5 of 9) investigating seizure-related outcomes reported significantly better seizure control in the treatment condition compared to control at posttreatment, although 2 studies by the same leading author used an outcome parameter that was not a validated tool.[34,35]

4.1 | Agreement with other studies or reviews

The results of this review reinforce the conclusions of a recent systematic review of psychological treatments for epilepsy,[16] which suggested that cognitive-behavioral therapy and mindfulness-based interventions have consistently demonstrated significant effects on improving HRQoL in prospective uncontrolled as well as in controlled study designs. Furthermore, this review is in keeping with a systematic review of cognitive behavior therapy for depression in PWE[18] that suggested interventions tailored toward improving depression are possibly efficacious. Our results are also in line with the previous Cochrane Review[17] with respect to a lack of reliable support for the efficacy of psychological treatments in controlling seizures.

4.2 | Overall completeness and applicability of evidence

The studies in this review evaluated complex psychological treatments typically applied in tertiary care settings and involved patient groups with different underlying epilepsy diagnoses, severities of psychiatric and somatic comorbidities, and 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 education interventions. In some cases, the work of these therapists was carefully structured and supervised based on specific treatment protocols, whereas some studies presumably relied on briefer training courses. Nine different outcome measures had been used to investigate our primary outcome. Hence, the efforts to extract data for meta-analysis were hampered to some extent by the wide diversity of outcome measures. These circumstances were addressed by focusing our meta-analysis mainly on psychological and self-management interventions, 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 believe that the results from this meta-analysis should not be applicable in similar settings and patient groups. Unfortunately, the variability of outcome measures has plagued efforts to review and critique

the psychological treatment literature,[61] and development and use of common data elements for psychological research trials is recommended.[62]

Because many psychological treatments involve patient-oriented goal setting, it would be interesting to explore whether the extended QOLIE-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. The use of HRQoL outcomes for which an MIC has been established allows for the evaluation of the clinical relevance in addition to statistical outcomes. The percentage of participants whose results reached MIC was only provided in 1 study.[36] The recent validation of the PedsQL Epilepsy Module may provide a necessary psychometrically sound HRQoL outcome for pediatric trials.[63]

4.3 | Quality of reporting

In many cases, the trial quality and its implementation were better than the actual publication suggested. This is easily understandable in studies that were published prior to the update of CONSORT guidelines for nonpharmacologic studies by Schulz et al.[64] During our review process, the ROB assessments were shared with all study authors and their methodological details were clarified. Thirteen authors contributed additional information that had been omitted or remained unclear in the publication.

4.4 | Implications for research

Although there is a growing body of research to support use of psychological interventions in individuals with epilepsy, particularly adults, several research gaps still remain. Well-designed multisite RCTs that employ evidence-based interventions and standardized behavioral health outcome measures appropriate to the intervention components are necessary to evaluate the benefit of psychological interventions. A recent commentary in *Epilepsy & Behavior* highlights considerations and challenges to conducting and reporting on psychological RCTs in adult and pediatric epilepsy and offers potential solutions for improving the quality of evidence.[62]

4.5 | Limitations

There are some fundamental limitations in reviewing RCTs on using psychological treatment for epilepsy. First, the feasibility of using RCTs to study psychological interventions has been challenged repeatedly. It is questionable that the multifaceted characteristics, including clinical factors, psychological readiness, motivation, and psychopathological states can be realistically balanced across intervention and control groups.[65] Furthermore, it has been demonstrated that only a small percentage of the therapeutic effect in face-to-face psychological treatment could be attributed to treatment methods and treatment strategies. One of the strongest therapeutic components was suggested to be therapeutic relationship and working alliance.[66,67] None of the studies investigating face-to-face psychological interventions in this review has included these as variables, which prevents the comparative investigation of their contribution to outcome variance. Another limitation of the meta-analysis is that the majority of available studies focused on adults with epilepsy; therefore, our overall conclusions should not be generalized to the pediatric population. Seventeen studies (71%) exhibited larger amounts of missing data, although their participants were reimbursed for study participation.[29,33] High attrition rates challenge the feasibility of psychological treatments, because they require motivation and active participation. One additional limitation is the timeliness of reviews that are copublished with the Cochrane Review system. This review will be updated in 2-3 years to include newer psychological trials.

4.6 | Quality of evidence

Although studies included in this review had a range of limitations, most trials were rated as having low ROB in terms of randomization procedures, allocation concealment, blinding of assessors, and selective reporting. A high or unclear ROB was assigned in half of our studies due to attrition bias. This appeared to be a common limitation in psychological intervention studies, as participants' motivation and cooperation are highly important but unpredictable. Blinding of participants was performed in only 4 studies.[34–36,39] Blinding of therapists is intrinsically difficult in psychological intervention studies, but it was nevertheless achieved by 1 study, in which the therapists were not aware of the study hypotheses.[29] In general, we did not have enough evidence to judge the biases in regard to selective recruitment and fidelity to the intervention protocol. We limited the meta-analysis to fairly similar interventions to avoid methodology heterogeneity. Even so, the inclusion of complex multicomponent interventions with diverse primary treatment goals still resulted in substantial clinical and statistical heterogeneity and the quality of evidence of the meta-analysis was downgraded by a few serious risks of bias in some of the studies (eg, Orjuela-Rojas et al.[30] with 4 high-risk and 1 unclear rating of a total of 7 ROB parameters). Because the majority of included studies had at least some bias issues, we did not perform a

sensitivity analysis comparing studies with low ROB with studies with high ROB. Considering the above, we are moderately confident in the effect estimate that psychological interventions and self-management interventions may enhance overall QoL in PWE, and in subdomains of epilepsy-related QoL, namely energy/fatigue, overall QoL, and emotionally well-being. In conclusion, the analysis reveals that in the past 10 years, psychological interventions have demonstrated improvement in QoL in PWE. Results of this meta-analysis support the use of psychological interventions as an adjunctive treatment for adults with epilepsy.

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DISCLOSURE

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ENDNOTE

* Seven of 9 studies used the QOLIE-31. Conversion to QOLIE-31 total score and subscales was needed for 1 study that used the QOLIE-31-P and 1 study that used the QOLIE-89. For the QOLIE-31-P, conversion was performed by recalculation using the QOLIE-31 scoring manual and algorithm while excluding the patient-weighted items. For the QOLIE-89, conversion to QOLIE-31 was performed by reorganizing single items into subscales based on the QOLIE-31 scoring manual, and recalculation based on the QOLIE-31 algorithm.

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SUPPORTING INFORMATION

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