Psychological treatments for adults and children with epilepsy: Evidence-based recommendations by the International League Against Epilepsy Psychology Task Force

Rosa Michaelis1,2,3 | Venus Tang4,5 | Laura H. Goldstein6 | Markus Reuber7 | William Curt LaFrance Jr.8 | Tobias Lundgren9 | Avani C. Modi10 | Janelle L. Wagner11

1Department of Neurology, Herdecke Community Hospital, University of Witten/Herdecke, Herdecke, Germany
2Integrated Curriculum for Anthroposophical Medicine (ICURAM), Witten/Herdecke University, Herdecke, Germany
3Department of Neurology, Center for Cognitive Neuroscience, Paracelsus Medical University, Salzburg, Austria
4Division of Neurosurgery, Department of Surgery, Faculty of Medicine, Chinese University of Hong Kong, Shatin, Hong Kong
5Department of Clinical Psychology, Prince of Wales Hospital, Shatin, Hong Kong
6Department of Psychology, Institute of Psychiatry, Psychology, and Neuroscience, King’s College London, London, UK
7Academic Neurology Unit, Royal Hallamshire Hospital, University of Sheffield, Sheffield, UK
8Departments of Psychiatry and Neurology, Rhode Island Hospital, Brown University, Providence, RI, USA
9Department of Clinical Neuroscience, Center for Psychiatry Research, Karolinska Institute, Stockholm, Sweden
10Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children’s Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH, USA
11College of Nursing and Department of Pediatrics, Medical University of South Carolina, Charleston, SC, USA

Correspondence
Rosa Michaelis, Department of Neurology, Herdecke Community Hospital, University of Witten/Herdecke, Herdecke, Germany. Email: rosa.michaelis@uni-wh.de

Summary
Given the significant impact that psychosocial factors and epilepsy treatments can have on the health-related quality of life (HRQOL) of individuals with epilepsy and their families, there is great clinical interest in the role of psychological evaluation and treatments to improve HRQOL and comorbidities. Therefore, the International League Against Epilepsy (ILAE) charged the Psychology Task Force with the development of recommendations for clinical care based on evaluation of the evidence from their recent Cochrane review of psychological treatments in individuals with epilepsy. The literature search for a recent Cochrane review of randomized controlled trials investigating psychological treatments for individuals with epilepsy constitutes the key source of evidence for this article. To provide practical guidance to service providers, we provide ratings on study research designs based on (1) the American Academy of Neurology’s Level of Evidence system and (2) the Grading of Recommendations, Assessment, Development, and Evaluation system. This paper is the culmination of an international collaboration process involving pediatric and adult psychologists, neurologists, psychiatrists, and neuropsychiatrists. The process and conclusions were reviewed and approved by the ILAE Executive Committee. The strongest evidence for psychological

A.C.M. and J.L.W. contributed in equal measure to this article and should be considered joint last authors of this contribution.
interventions was identified for the most common mental health problems, including depression, neurocognitive disturbances, and medication adherence. Psychological interventions targeting the enhancement of HRQOL and adherence and a decrease in comorbidity symptoms (anxiety, depression) should be incorporated into comprehensive epilepsy care. There is a range of psychological strategies (ie, cognitive behavioral therapy and mindfulness-based therapies) that show promise for improving the lives of persons with epilepsy, and clinical recommendations are provided to assist epilepsy health care providers in treating the comorbidities and challenges associated with epilepsy and its treatments.

**Key points**

- There are no previous specific recommendations for clinical practice based on the quality of the evidence for psychological treatments in patients with epilepsy
- Ratings on study research designs were based on the American Academy of Neurology’s Level of Evidence system
- Evidence-based recommendations were based by the Grading of Recommendations, Assessment, Development, and Evaluation system
- The best evidence of effectiveness of psychological interventions was identified for depression, medication nonadherence, and neurocognitive disturbances
- Evidence supports that psychological therapies should be considered in the treatment of individuals with epilepsy to improve HRQOL and comorbidities

The findings are intended for health care practitioners around the world.

**2 | METHOD OF EVALUATING THE QUALITY OF PSYCHOLOGICAL TREATMENTS**

**2.1 | Operational definition of psychological treatments**

“Psychological treatment” refers to a broad range of interventions for children and adults that encompass psychological or psychiatric nonpharmacological interventions for individuals, families, and groups, as well as self-/family
management, adherence, and educational interventions (see Table 1). Intervention elements may be administered on their own or in combination. Whereas some intervention elements are universally applicable, other elements address epilepsy and seizures more specifically. Interventions can target specific mental health disorders (anxiety, depression) or particular behaviors related to the management of epilepsy (adherence, coping). Although differences in theoretical underpinnings and treatment targets limit the scope of comparisons, there is overlap among the psychological treatments that can be applied to individuals with epilepsy.

2.2 | Source of evidence for recommendations

The literature search for a recent Cochrane review of randomized controlled trials (RCTs) investigating psychological treatments for individuals with epilepsy constitutes the key source of evidence for this article. Whereas the Cochrane review focused on HRQOL and therefore excluded studies that did not include HRQOL as an outcome parameter, the present evidence-based recommendations included all RCTs investigating psychological interventions in individuals with epilepsy (Figure 1).

2.3 | Method of evaluation

To provide practical guidance to service providers, we provide ratings on study research designs based on (1) the American Academy of Neurology (AAN) Level of Evidence (LOE) system and (2) the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system. GRADE has been modified by Tolin et al to include 3 levels (VERY STRONG, STRONG, and WEAK recommendation) for evaluation of the quality of evidence for RCTs in the clinical psychology literature. Using Tolin’s 3 levels (see Table 2), we evaluate the quality of evidence for psychological treatments for specific disorders (eg, depression, anxiety) in addition to

<table>
<thead>
<tr>
<th>TABLE 1 Terminology for psychological interventions</th>
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<tr>
<td><strong>Intervention</strong></td>
</tr>
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| Psychological interventions             | • To reduce psychological distress (eg, depressive or anxiety symptoms)  
                                           • To improve adjustment and coping with epilepsy and its treatments | • Cognitive-behavioral therapies  
                                           • Behaviorally based therapies  
                                           • Acceptance and commitment therapy  
                                           • Motivational interviewing |
| Self-/family management and adherence intervention | • Activities or steps that an individual or family can perform that are known to either influence 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 health care system domains | • Cognitive-behavioral  
                                           • Motivational interviewing  
                                           • Family therapy |
| Adherence interventions                 | • Helping patients adhere to the advice of health care providers, including taking antiepileptic drugs, following a ketogenic diet, and avoiding seizure triggers  
                                           • Medication taking can be broken down into several components, including optimal dose timing and adequate frequency of dosing | • Problem solving  
                                           • Intention  
                                           • Motivational interviewing  
                                           • Family therapy |
| Educational interventions               | • Increase knowledge of epilepsy and its treatments or the working of the brain | • Psychoeducation (group or individual formats) |
seizure outcomes, adherence, and epilepsy education and provide clinical recommendations for use of indicated treatments. If the evidence base for a given treatment is of low quality or lacking entirely, we highlight the need for further research in this area. We also provide a brief overview of treatment delivery, including options for resource-poor settings, as well as service considerations including recommendations for inpatient and outpatient treatment facilities and for training.

### 2.4 | Notable considerations

Psychological treatments tend to be complex multicomponent interventions, that is, several intervention components may be incorporated in diverse therapeutic approaches (eg, education plus skills training) and studies with different treatment targets, and therefore the same intervention components will be mentioned in various sections throughout this article. Special issues relating to pediatric populations will be included in each subsection. Level 3 and Level 4 Specialized Epilepsy Centers are required to have a psychologist and social worker as part of their centers; however, which psychosocial services are offered are not specified. Because psychological treatment delivery varies within and across countries and settings, we will mostly refer to “mental health care providers” without specifying their professional groups. Mental health care providers can include psychiatrists, psychologists, psychotherapists, licensed clinical social workers, neurologists with therapy training, neuropsychiatrists, and psychiatric nurses, among other mental health professionals. Cultural issues and differences that may affect implementation and utilization will be mentioned; however, an elaborate discussion of cultural considerations and implications is beyond the scope of this paper.

The authors are aware of the challenges of clinical translation marked by the gap between ideal care and real care constraints in busy clinical settings, in which trained staff often necessary to deliver evidence-based interventions are lacking. However, it is relevant for all providers to focus on early identification and prevention of comorbidity, which could be time- and cost-effective, as HRQOL is a significant predictor of health care charges in epilepsy, with poorer HRQOL predicting greater health care charges.21–23

### 3 | AVAILABLE EVIDENCE FOR PSYCHOLOGICAL TREATMENT ACROSS THE EPILEPSY SPECTRUM: RELEVANCE TO CLINICAL PRACTICE AND RECOMMENDATIONS

#### 3.1 | Evidence-based screening: Selecting patients for psychological treatment in the clinical setting

Psychological disorders are at least twice as common in individuals with epilepsy as the general population; therefore, standard screening procedures for patients newly

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**TABLE 2** Modified GRADE recommendations for psychological treatments based on systematic reviews

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Details</th>
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<tbody>
<tr>
<td><strong>VERY STRONG recommendation</strong></td>
<td>All of the following:</td>
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<td></td>
<td>• There is high-quality evidence that the treatment produces a clinically meaningful effect on symptoms of the disorder being treated</td>
</tr>
<tr>
<td></td>
<td>• There is high-quality evidence that the treatment produces a clinically meaningful effect on functional outcomes</td>
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<tr>
<td></td>
<td>• There is high-quality evidence that the treatment produces a clinically meaningful effect on symptoms and/or functional outcomes at least 3 mo after treatment discontinuation</td>
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<tr>
<td></td>
<td>• At least 1 well-conducted study has demonstrated effectiveness in nonresearch settings</td>
</tr>
<tr>
<td><strong>STRONG recommendation</strong></td>
<td>At least 1 of the following:</td>
</tr>
<tr>
<td></td>
<td>• There is moderate- to high-quality evidence that the treatment produces a clinically meaningful effect on symptoms of the disorder being treated</td>
</tr>
<tr>
<td></td>
<td>• There is moderate- to high-quality evidence that the treatment produces a clinically meaningful effect on functional outcomes</td>
</tr>
<tr>
<td><strong>WEAK recommendation</strong></td>
<td>Any of the following:</td>
</tr>
<tr>
<td></td>
<td>• There is only low- or very low-quality evidence that the treatment produces a clinically meaningful effect on symptoms of the disorder being treated</td>
</tr>
<tr>
<td></td>
<td>• There is only low- or very low-quality evidence that the treatment produces a clinically meaningful effect on symptoms of the disorder being treated as well as on functional outcomes</td>
</tr>
<tr>
<td></td>
<td>• There is moderate- to high-quality evidence that the effect of the treatment, although statistically significant, may not be of a magnitude that is clinically meaningful</td>
</tr>
</tbody>
</table>

Adapted from Guyatt et al.18 Reproduced with permission from Tolin et al.19
GRADE, Grading of Recommendations, Assessment, Development, and Evaluation.
diagnosed with epilepsy, as well as for patients with chronic epilepsy, should be integrated into routine epilepsy care.\textsuperscript{15,21,26} Symptom screening assists in the identification of individuals who may benefit from psychological treatments. To address the issue, the AAN has included screening for psychiatric or behavioral disorders at each epilepsy encounter as a new quality measure for the delivery of optimal care and better outcomes for individuals with epilepsy.\textsuperscript{27}

Epilepsy-specific measures are now available to evaluate psychosocial functioning, including depressive symptoms and HRQOL. For example, the 6-item self-report survey, Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), is an epilepsy-specific screening tool for major depression,\textsuperscript{28} and its feasibility has been demonstrated in a routine clinical setting.\textsuperscript{29} Annual use of the NDDI-E has previously been recommended by the ILAE neuropsychiatric commission.\textsuperscript{26} It has been validated in many languages, is freely available, and has been tailored for use in young people (NDDI-E-Y).\textsuperscript{30}

Screening measures for other aspects of psychological functioning (eg, HRQOL, AED side effects) may provide beneficial information regarding patient well-being. Psychometrically sound and free epilepsy-specific HRQOL tools include the Quality of Life in Epilepsy (QOLIE) adult (QOLIE-10, QOLIE-31, QOLIE-89) and adolescent (QOLIE-48) measures\textsuperscript{31,32} and the newer PedsQL Epilepsy Modules.\textsuperscript{33,34} Parent-proxy report of their child’s HRQOL can also be obtained via the Quality of Life in Childhood Epilepsy Questionnaire (4-18 years old).\textsuperscript{35,36} Additionally, the assessment of psychiatric/psychological symptoms at baseline can inform the choice of an AED, given that a history of psychological symptoms increases the vulnerability to subsequent behavioral/emotional side effects.\textsuperscript{37,38} Subsequently, this baseline information can help determine whether psychological symptoms arising during the course of treatment could be an AED side effect or an exacerbation of a premorbid or comorbid psychological disorder. Continued assessment of AED side effects over the course of epilepsy can inform changes to medications and/or alternative treatments (eg, diet) and is important to consider at each epilepsy visit given the relationship between side effects, adherence, and HRQOL.\textsuperscript{39} Standardized evaluation of side effects is available through use of the Pediatric Epilepsy Side Effects Questionnaire\textsuperscript{40} and the Liverpool Adverse Event Profile.\textsuperscript{41,42}

### 3.1.2 | Considerations for pediatric populations

Multi-informant screening is ideal for pediatric populations. Although children are often better reporters of their own internalizing symptoms,\textsuperscript{43} caregivers can provide a unique and beneficial perspective for some behaviors/deficits, such as executive functioning and oppositional or hyperactive behaviors.\textsuperscript{44} Caregivers are also critical reporters when children have cognitive impairment developmental delays or are too young to provide valid responses.

### 3.1.3 | Recommendations for psychological screening

Psychological screening is indicated, given the high prevalence of mental health disorders in individuals with epilepsy. According to the AAN practice guideline, patients with epilepsy should complete mental health screenings as part of routine epilepsy care.\textsuperscript{27} Specific clinical recommendations include:

1. Each epilepsy visit should include, at a minimum, a clinical question regarding mental health and quality of life. Screening is encouraged at epilepsy diagnosis, prior to and following AED initiation or changes, and at routine time intervals (eg, yearly).
2. Practitioners should consider multi-informant screenings for children and also for adults, when indicated and available.
3. A measure of psychological functioning should be administered prior to AED initiation and over the course of AED treatment.
4. Practitioners should consider including a standardized evaluation of AED side effects.
5. Practitioners are encouraged to consider a measure of HRQOL.
6. If screening identifies significant symptoms or a problem, patients should undergo a formal mental health assessment to inform the selection of the appropriate treatment elements based on individual needs. Family members may provide key details of past events during this evaluation.

### 3.2 | Psychoeducation for patients, parents, and caregivers

Psychoeducational interventions involve the dissemination of knowledge and education regarding seizures, treatments, comorbid conditions, and lifestyle challenges. Most psychological interventions involve an aspect of education; this next section is reserved solely for interventions that focus primarily on education and not on the development of behavioral, cognitive, or meditation skills.

### 3.2.1 | Evaluation of the evidence for psychoeducational interventions

According to several national guidelines (eg, Scottish Intercollegiate Guidelines Network; National Institute of \ldots
Clinical Health and Care Excellence, United Kingdom; American Epilepsy Society), additional personalized information on treatment, possible outcomes, and specific risks must be provided to patients and families following an epilepsy diagnosis. Patients may experience challenges with adjustment to and worries about the epilepsy diagnosis after learning about potential legal, psychosocial, and health ramifications. Additionally, research indicates that individuals with epilepsy and/or their caregivers frequently misunderstand basic information about epilepsy, including knowledge about their diagnosis, seizure precipitants or triggers, purpose and potential side effects of AEDs, safety concerns, and the risks of seizures. A large amount of the variance in HRQOL is explained by individuals’ perceptions of their illness, and educational interventions may modify illness perceptions and improve an individual’s HRQOL. Therefore, it is prudent to follow up the initial communication of an epilepsy diagnosis with (psycho)education about seizures, treatments and their side effects, comorbid conditions, and self-management and quality of life issues. The AAN recommends providing personalized epilepsy safety information and education on a yearly basis.

Of the 15 RCTs investigating educational interventions, 4 studies were LOE II, 4 studies were LOE III, and 7 studies were LOE IV. All 4 LOE II studies reported improvements in their various primary outcomes: medication adherence, epilepsy knowledge and satisfaction with information and support, and HRQOL. The LOE II studies investigated psychoeducational interventions that were delivered by specialized epilepsy nurses or trained medical doctors to individuals and included personalized information during routine visits or a general information package during a series of scheduled sessions.

### 3.2.2 | Psychoeducational interventions for epilepsy receive a GRADE recommendation of STRONG

There is moderate- to high-quality evidence that psychoeducational interventions produce a clinically meaningful improvement in health-related outcomes in individuals with epilepsy, including medication adherence, satisfaction with information and support, and HRQOL (Table 3).

### 3.2.3 | Considerations for pediatric populations

Clinicians are encouraged to take into consideration the developmental abilities of children and level of understanding when discussing an epilepsy diagnosis with children and their families. Material should be presented in child-friendly terms, with pictorial representations when possible or game-based formats. Depending on the child’s developmental level and chronological age, clinicians may wish to discuss some aspects of epilepsy with caregivers only (eg, sudden unexpected death in epilepsy).

### 3.2.4 | Specific clinical recommendations for epilepsy psychoeducation

Specific clinical recommendations for epilepsy psychoeducation include:

1. Each patient with epilepsy should receive psychoeducation.
2. Because a diagnosis of epilepsy may create fear and shock in individuals and/or families, a follow-up to the initial diagnosis is recommended to provide specific details regarding psychoeducation for a particular patient’s epilepsy symptoms, characteristics, and needs.
3. Psychoeducation may focus on seizure knowledge and treatments, information needs and support, and/or comorbid conditions.
4. Psychoeducation may be provided individually or in a group setting.
5. Psychoeducation should be provided to patients with consideration for their developmental level, health literacy, and information and support needs.
6. Clinicians are encouraged to select an evidence-based educational intervention that suits the needs of their patients (adult vs child, group vs individual) and to assess before and after outcomes (eg, knowledge) to monitor whether their patients are learning from the intervention.
7. Clinicians are encouraged to continue to routinely assess their patient’s needs for psychoeducation about epilepsy, its treatments, and comorbid conditions across the lifespan.

### 3.3 | Depressive symptoms

There is substantial evidence supporting the idea of a bidirectional relationship between epilepsy and depression. Shared neurobiological mechanisms, for example, lesion of mesial temporal structures and hippocampus volume loss, shed light on the reasons for their coexistence and interlinking relationship. Depression may predate the onset of epilepsy; a history of depression is associated with a two- to fourfold increase in the risk for an unprovoked seizure. Depression can also be a psychological reaction to epilepsy, and it is a significant predictor of seizure outcomes with pharmacological and surgical treatments. There is newer evidence for specific clusters of depressive symptoms in persons with epilepsy, with the
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Study</th>
<th>Treatment method</th>
<th>Primary outcomes</th>
<th>Secondary outcomes</th>
<th>Blinding</th>
<th>Randomization</th>
<th>Concealed allocation</th>
<th>Masked assessment</th>
<th>Attrition</th>
<th>AAN LOE class</th>
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<tbody>
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<td>Educational interventions</td>
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<td></td>
<td>↑</td>
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<td></td>
<td>Dash 2015&lt;sup&gt;53&lt;/sup&gt;</td>
<td>MMAS ↑</td>
<td></td>
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<td>↑</td>
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<tr>
<td></td>
<td>Helgeson 1990&lt;sup&gt;64&lt;/sup&gt;</td>
<td>Misinformation about epilepsy ↓</td>
<td>Fear of seizures</td>
<td>↓</td>
<td>↑</td>
<td>?</td>
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<td>?</td>
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<tr>
<td></td>
<td>Jantzen 2009&lt;sup&gt;57&lt;/sup&gt;</td>
<td>DISABKIDS ↑</td>
<td>Disclosure of epilepsy ↑</td>
<td>↑</td>
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<td>III</td>
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<td>Lua 2013&lt;sup&gt;61&lt;/sup&gt;</td>
<td>MQOLIE-30 ↑</td>
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<td>IV</td>
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<td></td>
<td>May 2002&lt;sup&gt;58&lt;/sup&gt;</td>
<td>SF-36 ↔</td>
<td>D-S’ ↔</td>
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<td>III</td>
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<tr>
<td></td>
<td>Olley 2001&lt;sup&gt;65&lt;/sup&gt;</td>
<td>Knowledge about illness ↑</td>
<td>BDI ↓</td>
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<td>↑</td>
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<td>?</td>
<td>IV</td>
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<td>Rau 2006&lt;sup&gt;59&lt;/sup&gt;</td>
<td>KINDL ↔</td>
<td>Seizure frequency ↔</td>
<td>↑</td>
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<td>↑</td>
<td>III</td>
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<td>Ridsdale 2006&lt;sup&gt;66&lt;/sup&gt;</td>
<td>Satisfaction with advice ↑</td>
<td>Knowledge of epilepsy ↔</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>IV</td>
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<tr>
<td></td>
<td>Präflin 2016&lt;sup&gt;55&lt;/sup&gt;</td>
<td>Counseling</td>
<td>Satisfaction with information and support ↑</td>
<td>QOLIE-31 ↔, HADS-D ↔, HADS-A ↔</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
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<tr>
<td></td>
<td>Beretta 2014&lt;sup&gt;54&lt;/sup&gt;</td>
<td>Patient-tailored medication education</td>
<td>Drug-related problems ↓</td>
<td>QOLIE-31 ↔</td>
<td>↑</td>
<td>↓</td>
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<tr>
<td></td>
<td>Mixed</td>
<td>Helde 2005&lt;sup&gt;56&lt;/sup&gt;</td>
<td>QOLIE-89 ↑</td>
<td></td>
<td>↑</td>
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↑, significant increase/high risk of bias; ↓, significant decrease/low risk of bias; ↔, result was not significant/unclear risk of bias; AAN, American Academy of Neurology; BDI, Beck Depression Inventory; DISABKIDS, Quality of Life in Children and Adolescents with Disabilities and Their Families; D-S’, Depressive Mood Scale; ESMS, Epilepsy Self-Management Scale; HADS-A, Hospital Anxiety Depression Scale—Anxiety; HADS-D, Hospital Anxiety Depression Scale—Depression; KINDL, Gesundheitsbezogene Lebensqualität und psychosoziale Auswirkungen der Epilepsie (Health-Related Quality of Life and Psychosocial Consequences of Epilepsy); LOE, Level of Evidence; MMAS, modified Morisky Medication Adherence Scale; MQOLIE-30, Malay Quality of Life Inventory in Epilepsy-30; QOLIE, Quality of Life Inventory in Epilepsy; SF-36, Short-Form 36.
more common cluster consisting of a cognitive phenotype (eg, self-critical cognitions, such as ineffectiveness).74

3.3.1 Evaluation of the evidence for interventions for depressive symptoms

Nine RCTs investigated psychological interventions for individuals with epilepsy with depression symptoms75–83 or as a preventative intervention for clinical depression in patients with subthreshold depressive symptoms.84 The following 7 studies measured depressive symptoms as secondary outcome: 4 RCTs investigated psychological interventions,85–88 1 RCT investigated a self-management program,89 and 2 RCTs investigated educational programs.55,65

Of these 16 studies, 1 study was LOE I,84 5 studies were LOE II,55,75,76,79,86,89 2 studies were LOE III,78,85 and the remaining 8 studies were LOE IV.53,65,77,81–83,87,88 Most LOE I and II studies reported significant reduction in depressive symptoms; exceptions were 1 depression-specific intervention LOE II study that reported a reduction in suicidal ideation but no other significant changes on a generic depression scale75,76 and the educational program55 that did not find any significant changes in depressive symptoms. The highest level of evidence pertains to skill-based training and behavioral interventions. Techniques comprised behavioral and social activation, problem solving and goal setting skills, training of social competencies, and identifying social support. These were particularly effective in addressing behavioral symptoms of depression and its associated limitations, such as social withdrawal, hypersomnia, physical inactivity, and unemployment (Table 4).75,76,84

3.3.2 Interventions for depressive symptoms in epilepsy receive a GRADE recommendation of STRONG

There is moderate-to-high quality evidence that skill-based and behavioral psychological interventions produce a clinically meaningful effect on depressive symptoms, including suicidal ideation in individuals with epilepsy.

3.3.3 Considerations for pediatric populations

There are limited data for the treatment of depression or depressive symptoms in pediatric epilepsy populations84; thus, clinicians are encouraged to base treatment on the results of treatment trials conducted with children with depression in nonepilepsy populations.90 Treatment may include psychoeducation to children and family as well as cognitive-behavioral therapy for children,90 and most child-focused depression protocols include strong family involvement in treatment (eg, encouragement of mastery of skills).

Notably, similar to adults, negative cognitions (ineffectiveness) may be more relevant than mood symptoms in youth with epilepsy, and interventions should target such symptoms.91 Those who have risk factors for depression (eg, family history of mood disorders, coexisting medical condition, psychosocial adversities) should be evaluated by clinicians at regular intervals92 for the prevention of clinical depression, early diagnosis, and treatment.

3.3.4 Specific clinical recommendations for depressive symptoms

Specific clinical recommendations for depressive symptoms include:

1. Depression should be assessed in routine epilepsy care following epilepsy diagnosis regardless of drug responsiveness.
2. Psychological interventions can be provided individually or in a group format.
3. Treatment components may include behavioral intervention (eg, social activation) and skill-based interventions (eg, problem solving, social skills training).
4. Treatment outcomes should be monitored using standardized inventories/rating scales.

3.4 Treatment nonadherence and self-management

Adherence is defined as the extent to which a person’s behavior coincides with medical or health advice.93 In contrast, self-management is defined as the interaction of health behaviors and related processes that patients and families engage in to care for a chronic condition.94 AED nonadherence ranges from 25% to 50%,95,96 in adults and 43%-58%39,97 in children with epilepsy. The consequences of nonadherence can be severe, including continued seizures,39,98 poor HRQOL,99 higher health care costs and utilization,100 pharmacoresistance,101 and even death.102

3.4.1 Evaluation of the evidence for interventions for adherence and self-management

Three RCTs investigated psychological interventions specifically aiming at increasing medication adherence.103–105 Two studies investigated self-management interventions that measured medication adherence as a secondary outcome.106,107 Two studies104,107 were LOE II, and the 3 remaining studies were LOE IV.103,105,106 Significant results were reported for the LOE II pediatric adherence intervention, whereas no significant changes were reported for the self-management program. Thus, the highest level
<table>
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<tr>
<th>Intervention</th>
<th>Study</th>
<th>Treatment method</th>
<th>Primary outcomes</th>
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</table>

↑, significant increase/high risk of bias; ↓, significant decrease/low risk of bias; ↔, result was not significant/unclear risk of bias; AAN, American Academy of Neurology; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; CBT, cognitive behavioral therapy; CES-D, Center for Epidemiological Study on Depression Scale; DACL, Depression Adjustment Checklist; GHQ, General Health Questionnaire; HADS, Hospital Anxiety Depression Scale; MDI, Mini International Neuropsychiatric Interview; MMPI, Minnesota Multiphasic Personality Inventory; MT, mindfulness therapy; NDDI-E, Neurological Depressive Disorders Inventory–Epilepsy; PHQ-9, Patient Health Questionnaire-9; SFT, systemic family therapy.
of evidence pertains to education and teaching families of children with epilepsy about problem solving strategies.

### 3.4.2 Adherence/self-management interventions for epilepsy receive a GRADE recommendation of STRONG

There is moderate- to high-quality evidence that multicomponent interventions that include education and problem solving produce a clinically meaningful effect on medication adherence in children with epilepsy (Table 5).

### 3.4.3 Considerations for pediatric populations

Parents are encouraged to partner with children and adolescents to manage the treatment regimen, including supervision regarding taking AEDs and avoidance of seizure triggers. Parental involvement can aid in ensuring that adherence does not decline in adolescents, a vulnerable developmental period. Technology-focused adherence solutions may be particularly salient for adolescents.\(^{108}\)

### 3.4.4 Specific clinical recommendations for adherence/self-management

Specific clinical recommendations for adherence/self-management include:

1. Adherence should be assessed during routine clinical practice in a nonjudgmental and open dialogue.
2. Clinicians are encouraged to assess barriers to adherence and problem-solve ways to improve adherence.
3. Technology-focused solutions should be used that enhance reminders and that may be well received and beneficial in establishing good adherence behaviors.

### 3.5 Seizures

The aim of nonpharmacological seizure management techniques is to increase life quality as well as decrease seizure frequency and/or duration. Seizure management techniques could pragmatically be divided into 3 different approaches: (1) interventions to influence the consequences of seizures, for example, mindfulness training on awareness and non-judgmental acceptance of seizure-related physical symptoms; (2) interventions to affect the onset of seizures, for example, discrimination of seizure triggers through a functional analysis of individual seizure development and lifestyle recommendations for stress coping; and (3) techniques to abort ongoing seizures, for example, aura interruption techniques, that is, countermeasures to stop seizures from developing.\(^{109–112}\)
3.5.1 | Evaluation of the evidence for interventions for seizure-related outcomes

Four RCTs investigated psychological interventions aiming primarily to decrease seizure frequency.\textsuperscript{88,113–116} Five studies investigated psychological interventions,\textsuperscript{75,76,82,86,109,110} and 2 studies\textsuperscript{58,59} investigated an educational program that targeted nonseizure outcomes and included seizure frequency as a secondary outcome. Two studies\textsuperscript{75,76,86} were LOE II, 3 studies were LOE III,\textsuperscript{58,59,113} and the remaining 6 studies were LOE IV.\textsuperscript{82,88,109,110,114–116} A significant decrease in seizure frequency was reported in 1 LOE II study\textsuperscript{86} that focused on mindfulness training together with a set of lifestyle recommendations that facilitated coping with seizure-related disturbances and stressful situations, and in 1 of the 2 educational programs\textsuperscript{58} that were both rated LOE III. Therefore, the highest level of evidence pertains to mindfulness-based therapies as well as lifestyle recommendations that facilitated stress coping. These allow patients to notice and acknowledge their emotional processes and physical symptoms related to their seizures, so as to facilitate acceptance and coping.

3.5.2 | Psychological interventions for seizure-related outcomes receive a GRADE recommendation of WEAK

The evidence is inconclusive, suggesting an important area for future research. Whereas there is moderate- to high-quality evidence that mindfulness-based therapies and lifestyle modifications that focus on improving HRQOL produce a clinically meaningful effect on seizure frequency in individuals with epilepsy, there is also evidence that cognitive behavioral therapy–based interventions focused on improving depressive symptoms do not have a clinically meaningful effect on seizure-related outcomes in individuals with epilepsy (Table 6).

3.5.3 | Considerations for pediatric populations

The development of psychological seizure management techniques may have to involve an assessment of the child’s family background and family dynamics.\textsuperscript{99} Because parents and teachers may observe preseizure events, they may be taught to reinforce stress reduction and other healthy behaviors.\textsuperscript{114,115}

3.5.4 | Specific clinical recommendations for seizure-related outcomes

Specific clinical recommendations for seizure-related outcomes include:

1. Clinicians are encouraged to inquire about their patients’ interest in learning mindfulness training on awareness and nonjudgmental acceptance of seizure-related physical symptoms.
2. Clinicians should provide education to patients and family members on the interlinking relationship between psychological factors and seizures, and therefore psychological treatments could be included as part of epilepsy care.
3. Clinicians are encouraged to investigate details of seizure development (eg, seizure precipitants, coping) and to make lifestyle recommendations relevant to individual patients.
4. Mindfulness training designed for patients with epilepsy should be an adjunctive treatment option where resources allow.

3.6 | Anxiety

Panic and generalized anxiety are more frequent in adults and older adolescents with epilepsy than in the corresponding general population and may have a marked negative impact on HRQOL.\textsuperscript{117} In the assessment of anxiety disorders, clinicians need to consider the temporal relationship of anxiety symptoms and seizures. This subsection focuses on interictal anxiety symptoms that may be related to a fear of future seizures as well as fears of epilepsy-related consequences (psychosocial worries) and complications (such as injury, brain damage, memory impairment). The anticipatory anxiety about seizures may also take the form of seizure phobia, which may lead to maladaptive avoidance and isolation. It is, however, important to note that equally disabling anxiety symptoms (eg, social phobia, generalized anxiety) may also occur separately from seizure-related worries and are also important to address.\textsuperscript{118} Perceived stigma is a risk factor for increased anxiety, which again illustrates the interrelatedness of psychological issues.\textsuperscript{119,120}

3.6.1 | Evaluation of the evidence for interventions for anxiety symptoms

Only 1 RCT investigated a psychological intervention specifically aiming to decrease anxiety symptoms.\textsuperscript{82} Four studies investigating psychological interventions,\textsuperscript{77,78,86,87} 1 study investigating a self-management program,\textsuperscript{89} and 1 study investigating an educational program\textsuperscript{55} measured anxiety symptoms as a secondary outcome. Three studies\textsuperscript{55,86,89} were LOE II, and 1 study\textsuperscript{78} was LOE III, whereas the remaining 3 studies were LOE IV.\textsuperscript{77,82,87} Of all LOE II studies, only the psychological intervention that measured anxiety symptoms as a secondary outcome reported a significant decrease in anxiety symptoms.\textsuperscript{86} Hence, the highest level of evidence pertains to the
<table>
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<tr>
<th>Intervention</th>
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Seizure index = seizure frequency × 9 × seizure duration in seconds.

↑, significant increase/high risk of bias; ↓, significant decrease/low risk of bias; ↔, result was not significant/unclear risk of bias; AAN, American Academy of Neurology; ACT, acceptance and commitment therapy; CBT, cognitive behavioral therapy; LOE, Level of Evidence; MT, mindfulness therapy; SFT, systemic family therapy; SSI, Seizure Severity Index.
implementation of mindfulness exercises that may facilitate the process of awareness, experience, and finally acceptance of feelings of anxiety.

3.6.2 | Interventions for anxiety symptoms in epilepsy receive a GRADE recommendation of WEAK

The evidence is somewhat inconclusive, suggesting this is an important area for future research. Although there is moderate- to high-quality evidence that mindfulness-based interventions produce a clinically meaningful effect on anxiety symptoms in individuals with epilepsy, several other moderate- to high-quality studies did not demonstrate a meaningful effect. Notably, in many of these interventions, anxiety was a secondary outcome (Table 4).

3.6.3 | Considerations for pediatric populations

Many parents refer to the experience of their child’s first seizure as traumatic, which may lead to anxieties concerning the condition.57 As a consequence, children may develop a fear of seizures by observing anxious parental reactions.121 Psychological interventions that aim at alleviating anxiety in children may also have a secondary goal of addressing parents’ fear of seizures.114,115 Similar to depression, caregiver involvement in encouragement of skill rehearsal is important for skill mastery in children.

3.6.4 | Specific clinical recommendations for anxiety symptoms

Specific clinical recommendations for anxiety symptoms include:

1. Clinicians are encouraged to assess interictal anxiety symptoms that may be related to a fear of future seizures and fear of epilepsy-related complications.
2. Complex psychosocial worries, such as perceived stigma, may exacerbate symptoms of anxiety, and should be evaluated and addressed.
3. The highest level of evidence pertains to the implementation of mindfulness exercises that may facilitate the process of awareness, experience, and finally acceptance of feelings of anxiety. Therefore, health care providers are encouraged to refer patients with anxiety symptoms for mindfulness-based interventions to alleviate their anxiety symptoms.

3.7 | Neurocognitive disturbances

Cognitive impairment can be associated with epilepsy and adds to disability beyond seizures alone, particularly in those with temporal lobe epilepsy and drug-resistant epilepsy.122,123 The details of cognitive assessment and training in epilepsy were thoroughly discussed in separate recommendation statements.124 Instead of providing rehabilitation or training that targets objective cognitive deficits, psychological treatments may aim at managing the relationship between mood, anxiety, and subjective cognitive complaints, which may not be reflected in objective evidence of cognitive impairment.125

3.7.1 | Evaluation of the evidence for interventions for neurocognitive disturbances

Only 1 RCT investigated a psychological intervention specifically focused on cognitive symptoms (LOE III),85 and 1 other study86 measured cognitive functions as secondary outcome (LOE II). The highest level of evidence pertains to a mindfulness-based training for individuals with epilepsy, aiming to cultivate patients’ self-awareness and focused attention. The completion of this treatment was associated with significant improvements in objective measures of delayed verbal memory in patients with drug-resistant epilepsy compared to controls86; however, no changes were reported in other cognitive measures, including attention, nonverbal memory, and executive functions. A home-based self-management program (HOBSCOTCH) incorporating psychoeducation, self-awareness training, compensatory strategies, and cognitive training has been developed and has been shown to be associated with significant improvement in objective cognitive performance.85

Using acceptance and commitment therapy tailored for individuals with epilepsy, Lundgren et al109,110 guided individuals to develop a nonjudgmental acceptance of their memory functions and refocused patients on the achievement of valued life goals despite the preconceived obstacle of impaired cognitive functioning. In a controlled study (LOE IV), this intervention was found to be associated with significantly improved HRQOL.109,110

3.7.2 | Interventions for neurocognitive disturbances in epilepsy receive a GRADE recommendation of STRONG

There is moderate- to high-quality evidence that mindfulness-based interventions produce a clinically meaningful effect on neurocognitive disturbances in individuals with epilepsy.

3.7.3 | Considerations for pediatric populations

The prevalence of attention-deficit/hyperactivity disorder (ADHD) is higher in pediatric epilepsy than in the general
population, with rates of 30%-40% in children with epilepsy. There are very few studies examining the benefit of psychological interventions for children with epilepsy and comorbid ADHD, and our search did not yield RCTs of psychotherapy for epilepsy and ADHD. Expert reviews on treatment of ADHD in individuals with epilepsy emphasize the need to address cognition. Moreover, the general child literature has a strong evidence base for the efficacy of behavioral interventions in reducing ADHD symptoms in children. Given the comorbid learning disabilities and the neurocognitive deficits common in children with epilepsy, it is also important to discuss potential learning problems, provide access to resources (eg, educational interventions), communicate with school personnel, and facilitate referrals for neuropsychological evaluations. Commercially available products have also recently been tested in epilepsy and may prove to be beneficial. A new Web-based executive functioning intervention for adolescents is currently being tested and may be one way to help youth with epilepsy overcome cognitive skill deficits.

### 3.7.4 Specific clinical recommendations for neurocognitive disturbances

Specific clinical recommendations for neurocognitive disturbances include:

1. Clinicians are encouraged to be aware of the interrelationship between mood, anxiety, and subjective cognitive complaints, which may not be reflected in objective evidence of cognitive impairment.
2. Cognitive assessment and training may complement mindfulness-based training aiming to increase patients’ self-awareness and focused attention.
3. Several strategies can be built into psychological interventions for individuals with epilepsy with subjective neurocognitive disturbances to enhance a sense of self-reliance. These techniques include incorporating written handouts, joint reviews of the preceding sessions to reinforce memory for session content, shortening treatment sessions, and audio-recording sessions to enable the individuals to review the content between sessions. Such techniques have been found to be beneficial.
4. In the absence of data to support the efficacy of behavioral interventions tailored to children with epilepsy and ADHD, clinicians are encouraged to apply the evidence-based behavioral techniques supported in the general child literature.

### 3.8 Social and family problems and stigma

Having epilepsy may be associated with vocational, educational, social, and personal difficulties. Individuals with epilepsy are less likely to be well educated, to be employed, and/or to have a romantic partner. They also experience social difficulties, including social isolation, social competence, and other social skills deficits. Family functioning, including communication, social support, adaptation, mastery, and conflict, is often impacted by epilepsy. Personal experiences with epilepsy may involve perceived stigma, defined as a set of negative and often unfair beliefs about something. Perceptions of stigma can lead to concealment to avoid the anticipated negative consequences of epilepsy disclosure in societies at all stages of economic development. Although the strength of the perception of stigma may be associated with internal factors, such as low self-esteem, there are also external factors, including cultural and religious differences contributing to stigma. The extent to which independence and autonomy are encouraged also varies considerably between cultures. Regardless of these cultural differences, epilepsy may result in significant restrictions in an individual’s social functioning and independence, which may be self-imposed or imposed by others.
targeted toward pediatric patients and their caregivers, and none of the identified studies measured outcomes relating explicitly to stigma.

3.8.2 | Interventions for social and family problems and stigma in epilepsy receive a GRADE recommendation of STRONG

There is moderate- to high-quality evidence that psychological, adherence, and self-management interventions produce a clinically meaningful effect on symptoms related to social and family problems and stigma.

3.8.3 | Considerations for pediatric populations

Children and adolescents with epilepsy are at greater than average risk of having increased dependence on parents. Parents are often overly restrictive and overprotective of their children with epilepsy, which can influence social growth and independence.

3.8.4 | Specific clinical recommendations for social problems and stigma

Specific clinical recommendations for social problems and stigma include:

1. Clinicians should inquire about the extent to which individuals with epilepsy feel affected by interpersonal and social problems, including problems affecting individuals with epilepsy at their workplace, in school, or in their private lives.
2. This assessment may include evaluation of barriers to open communication about epilepsy to avoid anticipated negative consequences of disclosure.
3. Treatment components should be incorporated that address internal factors contributing to social and family problems and stigma such as social and communication skills (eg, assertion training, training of epilepsy-related communication), social activation (eg, community integration, identification of social support), and parenting skills.

4 | TREATMENT DELIVERY AND SERVICE CONSIDERATIONS

The described treatment elements may be delivered face to face or via telehealth technology (eg, computer, smartphone, tablet, telephone) in an individual or group setting or in a combination of these modalities.

4.1 | Evaluation of the treatment delivery and implementation modalities

A group setting used by itself or as an adjunct to individual sessions not only may be more cost-effective than individual sessions, it also offers some unique advantages such as group role modeling to practice skills and the solicitation and exchange of individual experiences, perspectives, and self-management strategies. Group interventions were investigated by 1 LOE I psychological intervention study, 1 LOE II psychological intervention study, and 1 LOE II self-management intervention study. All of these studies reported significant improvements in their primary outcome measures. More than half of all investigated educational interventions were delivered in a group setting.

In addition to face-to-face delivery by trained health professionals, telehealth options have been explored in 1 LOE II psychological intervention study investigating a Web-based treatment aiming to decrease depressive symptoms (Deprexis), 1 LOE IV Web-based self-management program (WebEase), and 1 LOE IV Short Message Service–based educational program (Mobile Epilepsy Educational System). Interactive engagement can be promoted by questions and quizzes or the opportunity to send personal inquiries that are answered by program providers, which allows for the personalized delivery of educational materials (eg, tailoring). One LOE IV study investigated the telephone-based delivery of a psychological intervention in a group setting. All of the aforementioned studies reported significant results regarding their primary outcome measures. Because limited access to psychological treatments that are specifically designed to address the needs and concerns of people with epilepsy seems be the rule rather than the exception, telehealth modalities may help break down barriers to delivering psychological treatments in some resource-poor settings and help facilitate treatment for individuals with active seizures who live in areas with poor public transportation. Some studies in pediatric epilepsy suggest that telehealth modalities have similar outcomes and therapeutic alliance as face-to-face interventions. A meta-analysis found no differences between face to face and telehealth in the general population. Similarly, home-based delivery of multimodal interventions may eliminate barriers and promote collaboration between community/public health care professionals and epilepsy specialists. One LOE II study and 1 LOE III study reported significant improvements in primary outcomes.

Optimal treatment implementation remains an ongoing area of development. Because the development of new skills and the formation of new habits require time and regular practice, most interventions aim to increase
participants’ practice of relevant skills by embedding knowledge into treatment sessions spread out over time. Education protocols can, for example, either be delivered en bloc as a 2-day course or in a weekly format. Half of all 14 studies investigating educational programs had chosen to deliver their interventions using at least 2 sessions that were at least 1 month apart. LOE I and II studies of psychological interventions and 1 self-management intervention reporting significant primary outcome results were implemented in at least 4 sessions that were delivered with a maximum frequency of weekly sessions and a minimum frequency of 2-3 weeks between sessions. Depending on their primary treatment method, these interventions included practice assignments between sessions. Booster sessions following a more intense treatment period may increase skill retention.

4.2 | Home-based, group-based, and telehealth intervention delivery in epilepsy receive a GRADE recommendation of STRONG

There is moderate- to high-quality evidence that home-based, group-based, and telehealth-based treatments produce a clinically meaningful effect on a broad range of symptoms in individuals with epilepsy, including suicidal ideation and depressive symptoms, as well as HRQOL.

4.3 | Considerations for pediatric populations

Electronic and telehealth treatment modalities (eg, telephone, computer, mobile health, electronic health) may be particularly beneficial to families of children with epilepsy, who must consider balancing the needs of the child with epilepsy and other children, difficulty taking time off from work/school, et cetera to engage in psychological treatment. Adolescents have a strong preference for technology and are thus also more likely to be amenable to telehealth treatment modalities.

4.4 | Specific clinical recommendations for treatment delivery and implementation

Specific clinical recommendations for treatment delivery and implementation include:

1. The described treatment elements may be delivered face-to-face in clinical settings or home-based, via telehealth technology.
2. Psychological interventions can be provided individually or in a group format.
3. Clinicians are encouraged to choose treatment delivery modalities based on local treatment resources (eg, community/public health care professionals) and barriers (eg, poor public transportation).
4. A group setting may be more cost-effective than individual sessions and offer unique advantages (eg, exchange of individual experiences, elicitation of group support and encouragement).
5. Although it is beyond the scope of this paper to discuss the differences in treatment implementation and delivery across cultures, we encourage the implementation of basic elements of psychological interventions, including education and self-help resources (including, eg, relaxation CDs, seizure tracking devices).
6. Although providers and patients may wish to compress intervention content, they are encouraged to consider the dose(s) of treatments suggested by the empirical literature to permit sufficient scope for consolidating change by including practice by participants between sessions.
7. To decrease anxieties in nonmedical mental health care professionals over treating patients with seizures, a protocol should be generated for individual patients, detailing how seizures that may occur during treatment sessions should be managed.

5 | TRAINING RECOMMENDATIONS

Mental health providers who have had extensive professional training in the delivery of psychological interventions may have greater capacity to deliver psychological treatment for people with epilepsy than epilepsy-specific providers who have had very limited (if any) training in providing noneducational psychological interventions. Medical professionals such as epilepsy nurses are equipped to provide educational and basic self-management interventions and can be equipped for other psychological interventions (cognitive behavioral, mindfulness) with specific training (eg, psychiatric nursing degree, completed training on a specific treatment protocol). Thus, we would recommend the following:

1. It is important to acknowledge that the required training for specific interventions depends on the professional background and expertise of the person delivering the intervention, the nature of the treatment package, and how well the treatment has been described and manualized.
2. A mental health professional delivering the intervention elements should have basic knowledge regarding epilepsy, including etiology and classification of seizures, treatment options, and psychopathology.
3. Conversely, a medical professional delivering any psychological intervention elements should receive training
in the administration of psychological interventions in general as well as specific, detailed training in the implementation of the specific intervention protocol being administered.

4. Epilepsy-specific psychological interventions should ideally be implemented by professionals in direct contact with the diagnostician and the treating medical epilepsy specialist.

5. Some interventions, such as PEARLS, UPLIFT, and MOSES/FAMOSES, offer and require the completion of program-specific training prior to implementation, with variability in the extent and mode of training\(^58–60,75,76,80,83,148–150\) to ensure the treatment is delivered as intended.

6 | CONCLUSION

All patients should be screened for mental health comorbidities, and patients with psychological symptoms should be referred for further evaluation and treatment of indicated or at-risk psychological symptoms. Evidence supports that psychological therapies that target comorbid mental health symptoms and HRQOL should be considered in the comprehensive treatment of individuals with epilepsy. The strongest evidence was identified for the most common mental health problems, including depression, as well as health behaviors, such as adherence. Treatments for these disorders and challenges received STRONG recommendations. Treatment protocols and training on the intervention techniques and delivery are available for many of the interventions discussed. Few treatments have been evaluated with the same rigor in children and adolescents compared to adults, and we lack studies focusing on anxiety as an intervention target and primary outcome. In addition, RCTs investigating psychological interventions in other common comorbidities, such as ADHD and substance abuse in adults and children with epilepsy, are absent. However, there is a strong evidence base for the benefit of psychological interventions in treating these disorders in the general population, which can be used to inform the development of epilepsy-specific intervention protocols and RCT designs to evaluate the efficacy of these interventions in the epilepsy population. Epilepsy health care providers are encouraged to promote psychological treatments as an integral part of epilepsy care and to know the resources available in their area.

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DISCLOSURE OF CONFLICT OF INTEREST

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ORCID

Rosa Michaelis  
https://orcid.org/0000-0002-2577-0824

Laura H. Goldstein  
http://orcid.org/0000-0001-9387-3035

Markus Reuber  
http://orcid.org/0000-0002-4104-6705

William Curt LaFrance Jr.  
http://orcid.org/0000-0002-4901-3852

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