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SPECIAL REPORT

Consensus-based recommendations for the diagnosis and treatment of anxiety and depression in children and adolescents with epilepsy: A report from the Psychiatric Pediatric Issues Task Force of the International League Against Epilepsy

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Abstract

The Psychiatric Pediatric Issues Task Force of the International League Against Epilepsy (ILAE) aimed to develop recommendations for the diagnosis and treatment of anxiety and depression in children and adolescents with epilepsy. The Task Force conducted a systematic review and identified two studies that assessed the accuracy of four screening measures for depression and anxiety symptoms compared with a psychiatric interview. Nine studies met the eligibility criteria for treatment of anxiety and depressive disorders or symptoms. The risk of bias and certainty of evidence were assessed. The evidence generated by this review followed by consensus where evidence was missing generated 47 recommendations. Those with a high level of agreement (≥80%) are summarized. *Diagnosis*: (1) Universal screening for anxiety and depression is recommended. Closer surveillance is recommended for children after 12 years, at higher risk (e.g., suicide-related behavior), with subthreshold symptoms, and experiencing seizure worsening or therapeutic modifications. (2) Multiple sources of ascertainment and a formal screening are recommended. Clinical interviews are recommended whenever possible. The healthcare provider must always explain that symptom recognition is essential to optimize treatment outcomes and reduce morbidity. (3) Questioning about the relationship between symptoms of anxiety or depression with seizure worsening/control and behavioral adverse

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effects of antiseizure medications is recommended. *Treatment*: (1) An individualized treatment plan is recommended. (2) For mild depression, active monitoring must be considered. (3) Referral to a mental health care provider must be considered for moderate to severe depression and anxiety. (4) Clinical care pathways must be developed. (5) Psychosocial interventions must be tailored and age-appropriate. (6) Healthcare providers must monitor children with epilepsy who are prescribed antidepressants, considering symptoms and functioning that may not improve simultaneously. (7) Caregiver education is essential to ensure treatment adherence. (8) A shared-care model involving all healthcare providers is recommended for children and adolescents with epilepsy and mental health disorders. We identified clinical decisions in the management of depression and anxiety that lack solid evidence and provide consensus-based guidance to address the care of children and adolescents with epilepsy.

KEYWORDS

anxiety, depression, diagnosis, epilepsy, treatment outcome

1 | INTRODUCTION

The World Health Organization (WHO) Comprehensive Mental Health Action Plan[1] emphasizes that "the early stages of life present a particularly important opportunity to promote mental health and prevent mental disorders, as up to 50% of mental disorders in adults begin before the age of 14 years."[2] Globally, in 2019, the reported mean prevalence of mental disorders in the age range of 5 to 24 years is 11.63%, that is, 293 million children and adolescents. There is a marked increase over the years, from 6.80% in childhood for those aged 5 to 9 years to 13.63% in late adolescence for those aged 20 to 24 years. Anxiety disorders have the overall highest prevalence (3.35%). Mood disorders have a stepped increase from childhood (1%) to early (2.7%) and late adolescence (3.9%).[2]

In children and adolescents with mental health disorders, early identification is key to early intervention.[1] The comorbidity between depression and anxiety is also substantial. For youth with depression, rates of anxiety disorder range from 15% to 75%, making anxiety the most common comorbid disorder. Among youth with anxiety disorders, comorbid depressive disorder occurs in 10% to 15%.[3]

Practice guidelines and recommendations provide guidance to clinicians, patients, and policymakers to improve access to quality mental health care.[4,5] Although guidelines have been developed for specialty care settings (e.g., the American Academy of Child and Adolescent Psychiatry),[6] there are differences in training and practices between the primary and specialty care settings, thereby limiting the simple transfer of guidelines from one setting to another.

Key points

- Universal and systematic screening for anxiety and depression is recommended.
- Children with symptoms of anxiety and depression must be closely monitored.
- For mild depression, active monitoring must be considered.
- Referral to a mental health care provider must be considered for moderate to severe depression and anxiety.
- Clinical care pathways must be developed and a shared-care model involving all health care providers is recommended.

In children with epilepsy, two epidemiologic studies have shown higher rates of mental health disorders in comparison to the general population and to children with non-neurological chronic disorders (e.g., diabetes).[7,8] A systematic review and meta-analysis indicated high overall pooled prevalence of anxiety disorders (18.9%) and depression (13.5%) in youth with epilepsy.[9]

Children and adolescents with epilepsy face many negative outcomes that are associated with depression and anxiety, including disrupted relationships, school

failure, increased risk of a lifelong persistent psychiatric disorder, worse quality of life, and suicide-related behaviors.[10–14] The high prevalence of these disorders, and their poor outcomes, contrasts with the shortage of mental health care services and providers.[15–20] In particular, pediatric neurologists often have insufficient training in the management of depression and anxiety, and yet are required to act as primary mental health care providers.[21–28]

The Psychiatric Pediatric Issues Task Force (TF), established in 2018, is a liaison between the Pediatric and the Psychiatry Commissions of the International League Against Epilepsy (ILAE). The TF involved experts from all ILAE world regions. Recognizing the shortage of mental health care, the ILAE entrusted the TF with developing clear, objective, and clinically meaningful recommendations for depression and anxiety, considering the diagnosis of these disorders, identification and rating of their symptoms, and treatment to provide guidance to all health care providers caring for children and adolescents with epilepsy.

2 | METHODS

The TF conducted a systematic review to identify the evidence for the diagnosis and treatment of depressive and anxiety symptoms and disorders in pediatric epilepsy. It was followed by a Delphi process to provide consensus-based recommendations in areas where the evidence was lacking or limited. This protocol, reviewed by the ILAE Standard and Best Practice Council and endorsed by the ILAE Executive Committee, followed the Guideline development standards and adhered to the ILAE handbook and toolkit for guideline development updated in 2022.[6,29]

2.1 | Clinical practice guideline working group

Following consultation with the ILAE's Executive Committee, a working group was formed comprising the chairs of the Psychiatry (M.K.) and Pediatric Commissions (S.A.) and nine TF members, including four child neurologists (K.V., E.W., J.M.W., and F.C.), one pediatric and adolescent psychiatrist (G.V.P.), one neuropsychiatrist (M.M.), one psychologist (C.R.), one nurse (S.K.), and one neuropsychologist (M.L.S.) with expertise in the field and representing all ILAE regions. In addition, one librarian with expertise in medical systematic reviews (V.C.), one psychiatrist with expertise in methodology and epidemiology (Y.W.P.), and three methodologists (F.B., N.J., and I.G.D.) were involved at different stages. Two postgraduate students (R.M.C. and S.V.) with expertise in systematic and scoping reviews were involved in the systematic review process.

2.2 | Evidence-based recommendations

2.2.1 | Priority questions

Two priority questions were formulated following the PICO (population, intervention[s], comparator[s], outcome[s]) format, addressing diagnostic test accuracy and efficacy of treatment of depression and anxiety disorder or symptoms in children with epilepsy (Figure 1).

Priority Question	Population	Intervention[s]	Comparator[s]	Outcome[s]
1. What is the accuracy of each of the index tests compared to an appropriate reference standard for the identification of anxiety and depressive symptoms?	Children and adolescents with epilepsy and depressive and/ or anxiety disorder assessed with a psychiatric interview	Index Test	Reference Test (Psychiatric Interview)	Diagnostic Accuracy
2. How effective are pharmacological and how efficacious are non-pharmacological interventions to reduce depression and anxiety symptoms and or disorders and adolescents in children with epilepsy?	Children and adolescents with epilepsy and depressive and/ or anxiety disorder or symptoms	Pharmacological or non-pharmacological treatment for depression and or anxiety disorder or symptoms	Other type of treatment or placebo or waiting list or usual care or before-and-after	Change in severity of anxiety and depression severity score or clinical improvement

FIGURE 1 Priority questions for diagnosis and treatment.

2.2.2 | Systematic review

The systematic review protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews; CRD42020202682 and CRD42020202702), and the results were reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards, except for the abstract, since the goal of this was to develop clinical practice standards rather than purely a systematic review.[30] PRISMA is shown in Figure 2.

2.2.3 | Eligibility criteria

Diagnosis

Included in the review were studies with original data involving children and adolescents who had been diagnosed with epilepsy of any type. Also included were articles that provided the diagnostic accuracy of depression and/or anxiety with screening tools for depression and anxiety in comparison to a gold-standard measure (clinical diagnostic interviews, structured and semi-structured psychiatric interviews). The timeframe was from database inception to the date of the last search (June 2024). Articles in all languages were eligible for consideration.

The exclusion criteria were as follows: reviews; studies that assessed psychiatric disorders with psychiatric interviews but without providing information about depression or anxiety; studies for which the diagnosis was based on chart review; studies that assessed the severity of depression and anxiety rather than validating screening tools for anxiety and/or depression; studies that assessed cognitive function but not psychiatric disorders; case series (≤10) and case report studies; studies with a mixed sample (e.g., adults and children) that precluded separate analysis of children's data; and studies for which it was not possible to separate children with depression and/or anxiety from other psychiatric disorders.

Studies that assessed the accuracy of measurement or tools (index test) compared to a psychiatric interview (reference test) were eligible for review. However, we excluded convergent validity studies, which aim to identify how closely a test is related to other tests that measure the same (or similar) construct.

Treatment

For treatment, the inclusion criteria were articles based on original data, randomized controlled trials, prospective non-randomized controlled and uncontrolled studies (with a control group including participants acting

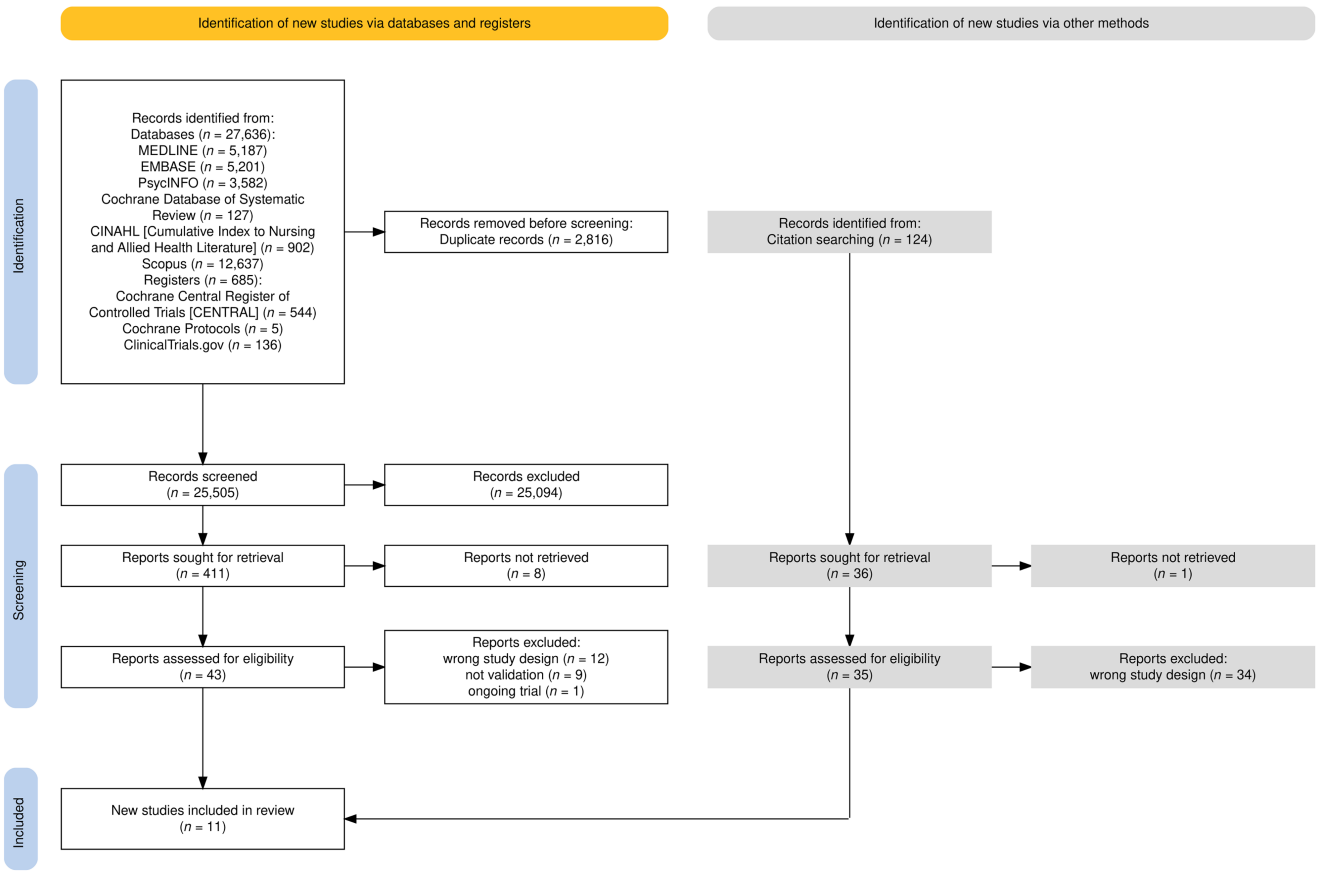

FIGURE 2 PRISMA.

as their own control group, i.e., before–after studies). In addition, we included studies reporting on pharmacological and non-pharmacological intervention, with children and adolescents with a confirmed diagnosis of epilepsy (any type), with rates of depression and anxiety before and after intervention, or clear data about clinical change. There was no restriction to date (from database inception to date) and language.

The exclusion criteria were case series and case reports, not possible to separate child data from a combined child and adult sample (mixed ages), and not possible to distinguish depression and anxiety from other psychiatric and behavioral disorders (e.g., internalizing symptoms, emotional symptoms). In addition, we excluded editorials, dissertations, abstracts, conference proceedings, letters to the editor, opinions, and studies that failed to report the data required for this review.

Review articles, systematic reviews, and meta-analyses were hand-searched to check references for other relevant articles.

2.2.4 | Search strategy

The search strategy (see Supplementary Material 1) was developed by a librarian with expertise in scoping and systematic review (V.C.) in collaboration with study investigators with knowledge in the field (systematic reviews, scoping reviews, pediatric neurology, epilepsy, and psychiatric disorders; G.P., Y.P.W., K.V., and N.J.). Electronic bibliographic databases (MEDLINE, Scopus, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials [CENTRAL], Cochrane Epilepsy Group Specialized Register, Cochrane Database of Systematic Reviews, and CINAHL [Cumulative Index to Nursing and Allied Health Literature]) were searched from their respective inception dates onward with no restrictions on date, country, or language of publication. The first search was performed on August 10, 2020, repeated on May 17, 2021, and updated on October 1, 2023 and June 2, 2024. The reference lists of previously published reviews and all studies included in this review were hand-searched (K.V. and R.M.) to ensure that no articles were missed. Systematic reviews and meta-analyses were not included; however, their reference lists were screened to identify relevant articles. Literature not formally published in sources such as books or journal articles and not submitted for peer review (e.g., government reports, conference proceedings, graduate dissertations, unpublished clinical trials) was not considered for the systematic review.[31]

2.2.5 | Study selection

All files were uploaded into RAYYAN,[31] an online tool that helps streamline the systematic review screening process. A two-step process was used to select studies for inclusion in this review. First, two authors (K.V. and R.M.C.) reviewed titles and abstracts to identify articles meeting the pre-determined eligibility criteria after duplicate studies were removed. Second, full text review of all abstracts identified in the first stage was undertaken. Two reviewers conducted all steps independently, and disagreements were resolved by discussion with a third reviewer (S.A.). Native speakers of the respective language screened non-English articles using the same process. When details were lacking in published papers, the authors attempted to contact study authors.

2.2.6 | Data extraction

For diagnosis, the following data were extracted: screening tool(s) under validation, cut points assessed, reference standard used for validation, the study-specific prevalence of depression and anxiety based on the reference standard, and measures of diagnostic accuracy. Sensitivity (Se) and specificity (Sp) needed to be available.

Whenever possible, other measures of accuracy were obtained (i.e., positive predictive value [PPV], negative predictive value [NPV], true positives [TPs], false positives [FPs], true negatives [TNs], false negatives [FNs], receiver-operating characteristic [ROC] and area under the curve [AUC], binomial regression coefficient, Cronbach's alpha, Kappa, likelihood ratios, and any effect modifiers/confounders assessed).

For treatment, the following data were extracted: assessment method for anxiety and depression, depression and anxiety intervention (e.g., cognitive behavioral therapy *vs* other measures), and assessment of psychopathology (criteria used and prevalence), time of intervention, and time of follow-up after intervention.

Additional methodological and clinical data extracted included journal/year, location of study (according to the ILAE region), recruitment setting, age (range, mean, and standard deviation, when available), sex, data regarding epilepsy, and antiseizure medication ([ASM]; as coded by original study authors).

2.2.7 | Risk of bias and certainty of evidence

Two reviewers (K.V. and R.M.) assessed the risk of bias and rated the certainty of evidence independently. A methodologist (I.G.D.) provided supervision, reviewed this assessment, and resolved discrepancies.

Risk of bias

Diagnosis. The risk of bias and applicability was assessed using the Quality Assessment of Diagnostic Accuracy Studies, version 2 (QUADAS-2).[32] Overall assessment of bias was based on responses to four domains: (1) patient selection, (2) index test, (3) reference standard, and (4) flow and timing (flow of patients through the study and timing of index tests) and reference standard, for which there were multiple signaling questions to guide the assessment of each domain. If one or more of the four domains were considered as having a high or unclear risk of bias, the overall classification was rated as having a high risk of bias. The overall risk of bias was considered low only if all domains were rated as having a low risk of bias. The level of applicability (applicability concern) was also assessed using a signaling question for the first three domains previously listed to identify if the domain of interest was consistent with the review question.

Treatment. For randomized controlled trials (RCTs), we assessed all domains of the Cochrane tool for assessing the risk of bias—RoB 2.[33] We rated each of the following six domains as low, high, or unclear risk of bias: method of generating random sequence, allocation concealment, blinding methods, incomplete outcome data, selective outcome reporting, and other sources of bias.

In addition, prospective cohort studies were considered due to scarce data on the treatment of anxiety and depression in the pediatric population with RCTs. The risk of bias for non-randomized controlled trials (NRCTs) was assessed using the ROBINS-I tool[34] to determine the risk of bias as low, moderate, serious, and critical. This tool considers seven domains of bias: (1) two domains of bias pre-intervention (bias due to confounding and bias in the selection of participants into the study); (2) one domain of bias at intervention (bias in the measurement of interventions); and (3) four domains of bias post-intervention (bias due to departures from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result).

Certainty of evidence

The certainty of evidence was graded using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to include judgments: very low, low, moderate or high level of evidence for diagnosis or identification of symptoms and treatment.[30] In addition, we used the American Academy of Neurology (AAN) Practice Guidelines grading system (comparison studies) for treatment.[35]

By assessing for risk of bias (QUADAS-2, RoB 2, and ROBINS-I) and certainty of evidence, the TF assessed studies and not measures or treatments. In the case of low or very low certainty of evidence, we opted for an expert opinion obtained by consensus, as explained below (2.3. Consensus-based recommendations).

2.3 | Consensus-based recommendations

2.3.1 | Delphi process

A Delphi process was followed to develop consensus-based recommendations. The expert consensus was sought to address relevant issues regarding diagnosis of disorders and/or identification of symptoms (e.g., time of assessment, source of information) and treatment (e.g., stage approach for treatment) not captured by the systematic review. The TF created a *Delphi Writing Group* to develop the initial Delphi questionnaire. Participants included the Chairs of the ILAE Psychiatry Commission (M.K.), Pediatric Commission (S.A.), Psychiatric Pediatric Issues TF (K.V. and C.R.), and a Delphi expert and the Chair of the ILAE Standards and Best Practice Council (N.J.).

2.3.2 | Delphi development and revision

The members of the Psychiatric Pediatric Issues TF—*Delphi Working Group*—participated in online and on-site meetings to discuss the scope of this study that led to the elements for the survey. The *Delphi Writing Group* then generated the first Delphi questionnaire including assessment and treatment of anxiety and depression in children. The statements were based on articles obtained during this review, current guidelines for identification and treatment of anxiety and depression in children and adolescents in general,[22,28,36–40] and based on the expertise of those involved in this process. The initial questionnaire was sent to all TF members. Revisions were made based on their feedback. The TF members were asked to base their responses related to preferred gold-standard care rather than the providers local capacity or on the resources available in their health care system. Each criterion was rated on a 5-point Likert scale. The final version was then revised by the whole group implementing additional suggestions to generate the recommendations for the Delphi process.

2.3.3 | Delphi panel

The Delphi panel of respondents was selected by the TF based on their expertise and credibility in the field. The panel was selected to achieve a broad representation of relevant clinical disciplines (pediatric epileptologists, child and adult neuropsychiatrists, neuropsychiatrists, child neurologists, psychologists, nurses, and neuropsychologists) and all ILAE regions.

2.3.4 | Formulating statements

The first-round Delphi survey contained 47 statements (Supplementary Material 2). All statements were based on a 5-point Likert response scale: 1. strongly agree, 2. agree, 3. neither agree nor disagree, 4. disagree, 5. strongly disagree. The initial survey was emailed to 104 participants. Three reminders were sent (one per month for every round). Forty-one participants responded to the initial survey. Eight of the 41 respondents provided demographic data but did not proceed to the core recommendations, as they indicated that "they were not involved in the care of children with epilepsy." The second round of the Delphi survey included 10 statements where 80% agreement still needed to be reached. Thirty-three respondents, who responded to the first round, were invited and all responded to the questionnaire. These 10 recommendations were modified based on the feedback from Round 1. Again, a total of three reminders were sent. The third round of the Delphi survey comprised one modified statement about psychiatric interviews that was sent to the 33 respondents. A total of three reminders were sent and 27 responded to this questionnaire. In the first and second rounds, participants were encouraged to elaborate on their answers if they "disagreed" or "strongly disagreed" with a comment and references, whenever appropriate. Based on comments and references, statements were rephrased, modified, removed, and added.

2.4 | Statistical analysis and consensus formulations

Results of the literature were summarized qualitatively reporting information as provided in the original included articles.

The level of agreement for consensus was set at ≥80% (agree/strongly agree).

2.5 | Evidence-based recommendations

After evaluating the certainty of the evidence for diagnosis and treatment, we provided evidence-based recommendations if the certainty of evidence, according to the GRADE, was moderate or strong.

If the certainty of evidence for a given diagnosis or treatment was judged to be "very low" or "low," we provided this information and complemented with consensus-based recommendations on this topic. We also emphasized the need for further research in this area.

2.6 | Expert recommendations

After the three rounds, the survey responses were converted into recommendations if consensus was reached, that is, ≥80% "agree/strongly agree." We adopted the following strategy. (1) A strong level of agreement (≥80% agree/strongly agree)—the recommendation was adopted and included. (2) A moderate level of agreement (<80% but ≥70% agree/strongly agree)—recommendations were revised by members of the Psychiatric Pediatric Issues TF if needed based on the feedback received in the previous round and were subjected to another round. (3) A low level of agreement (<70% agree/strongly agree) after the first round or rewording in the following rounds—recommendation was removed.

3 | RESULTS

3.1 | Systematic review

A total of 28 321 abstracts were identified of which 2816 were duplicates. Of these, 411 articles were reviewed in full text, 43 were assessed for eligibility, and 11 met all eligibility criteria for diagnosis or identification of symptoms and treatment of depression and anxiety.[41–49] The results were reported following PRISMA 2020 standards[30] (Figure 2).

3.1.1 | Diagnosis/identification of symptoms

The characteristics of the two studies that met the eligibility criteria for diagnosis[43,49] are presented in Table 1. Table 2 shows the sensitivity and specificity of assessment measures for anxiety and depression symptoms compared to a semi-structured psychiatric interview (Kiddie Schedule for Affective Disorders and Schizophrenia [K-SADS]).

These studies had an unclear risk of bias in at least one of the four QUADAS-2 rating system categories[32] (Figure 3). Using the GRADE system,[50] the certainty of evidence was very low (Supplementary Material 3A).

3.1.2 | Treatment

The nine studies (six RCTs and three NRCTs) met the eligibility criteria for treatment used K-SADS-PL to diagnose depression or anxiety disorder[41,42,44–48] (Table 3). The demographics and epilepsy characteristics are shown in Table 4. The outcome variables of depressive and anxious symptoms are shown in Table 5 (Supplementary Material 4). All studies, except for one,[48] used rating scales to assess symptoms severity before and after the intervention.

TABLE 1 Demographic and epilepsy characteristics of diagnostic studies.

Study	Psychiatric interview	Ascertainment source	Questionnaire under validation	*N*	*N* included for validation	Sex (%)	Age (years), age range mean [SD]	Age of epilepsy onset, (years) mean [SD]	Duration of epilepsy, (years) mean [SD]	Epilepsy type (%)		Antiseizure medication (%)	
Caplan. *Epilepsia*, 2005	KSADS-PL KSADS-E	Tertiary and community	CDI MASC CBCL Internalizing—Anxiety/ Depression	171	57	M: 47 F: 53	5–16 10.3 [2.7]	5.7 [3.21]	4.7 [3.21]	Focal Generalized[a]	58.5 41.5	0 01 ≥02	8 68 24
Wagner [b] *J of Child Neurol* 2013	KSADS Depression Module	Tertiary	NDDI-E-Y (11-item)	93	5	M: 53 F: 47	10–17 14 [2.0]	8 [5.01] Age range: 0–16 years	—	Focal Generalized Unknown	59.1 34.4 7.5	0 1 ≥2	2 65 34

Abbreviations: CBCL, Child Behavior Checklist; CDI, Children's Depression Inventory; F, female; K-SADS-E, Kiddie-Schedule for Affective Disorders and Schizophrenia—Epidemiological Version; K-SADS-PL, Kiddie-Schedule for Affective Disorders and Schizophrenia—Present and Lifetime Version; M, male; MASC, Multidimensional Anxiety Scale for Children; N, number of patients; NDDI-E-Y, Neurological Disorders Depression Inventory for Epilepsy in Youth; SD, standard deviation.

[a]Childhood Absence Epilepsy.

[b]Data available for the whole group (93).

TABLE 2 Diagnostic accuracy studies—validation studies using psychiatric interviews.

Study	*N*	Tool	Cut-point	Reference standard	Sensitivity	Specificity	PPV	NPV	AUC
Caplan *Epilepsia* 2005	57	CDI	≥50	KSADS-PL and E[a]	.583	.733	NR	NR	NR
		MASC	≥50		.867	.718	NR	NR	NR
		CBCL Internalizing	≥67		.627	.694	NR	NR	NR
		CBCL Anxiety + Depression	≥67		.38	.919	NR	NR	NR
Wagner *J Child Neurol* 2013	93	NDDI-E-Y 11 items	≥27	KSADS-PL[b]	.80	.71	.14	.98	.79 (.58–.99)

Abbreviations: AUC, area under the curve; CBCL, Child Behavior Checklist; CDI, Children's Depression Inventory; K-SADS-E, Kiddie-Schedule for Affective Disorders and Schizophrenia—Epidemiological Version; K-SADS-PL, Kiddie-Schedule for Affective Disorders and Schizophrenia—Present and Lifetime Version; MASC, Multidimensional Anxiety Scale for Children; NDDI-E-Y, Neurological Disorders Depression Inventory for Epilepsy in Youth; NPV, negative predictive value; NR, not reported by the authors; PPV, positive predictive value.

[a]The primary author or a trained research assistant administered the K-SADS to each child and parent. A consensus DSM-IV diagnosis was reached after reviewing videotapes of the child's interviews and audiotapes of the parent's interviews. A child was excluded from the study if a diagnostic consensus was not reached.

[b]KSADS-PL Module for Depression was applied by a phone.

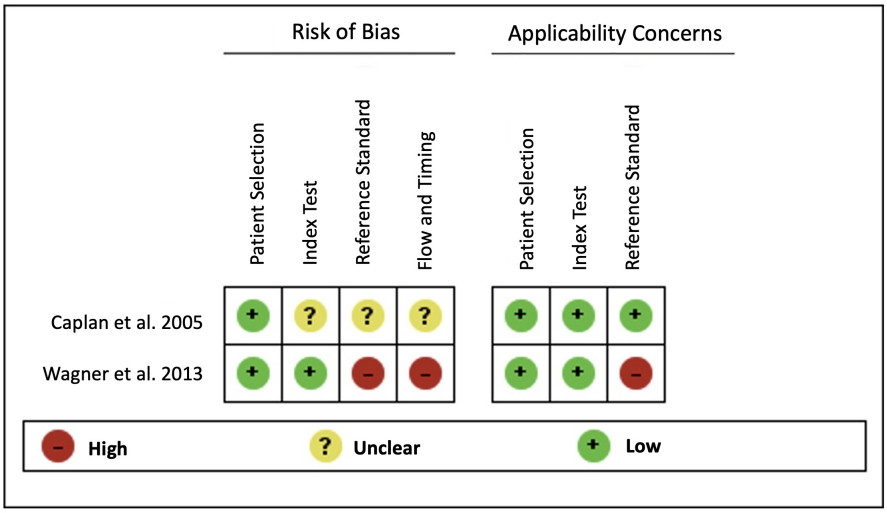

FIGURE 3 Summary of QUADAS-2 assessment of included studies. "Risk of bias" summary: Review authors' judgments about each "risk of bias" domain for each included study.

Eight studies assessed non-pharmacological interventions, including psychotherapy,[41,45,47,51,52] psychoeducational intervention,[44] and physical activity[42] (Figure 4).

The most frequent type of psychotherapy evaluated was cognitive behavioral therapy (CBT)[41,45,47,52,53] used in three RCTs and in two NRCTs for anxiety. One prospective NRCT used pharmacological treatment with selective serotonin reuptake inhibitor (SSRI; fluoxetine or sertraline) in 36 children and adolescents with epilepsy and depression followed for 1 year[48] (Figure 5).

Only one large and multi-center RCT[51] addressing a modified version of CBT had a low risk of bias, providing evidence for a modified and modular version of CBT (Supplementary Material 3B).

The categorization according to the AAN therapeutic classification of evidence scheme is shown in Table 6.

4 | RECOMMENDATIONS FOR DIAGNOSIS OF ANXIETY AND DEPRESSION IN CHILDREN AND ADOLESCENTS WITH EPILEPSY

In these recommendations, the word diagnosis is used in a broader sense to refer to disorders or symptoms. However, the TF makes clear if diagnosing disorders (e.g., psychiatric interview) or identifying symptoms (e.g., behavioral checklists and rating scales).

The assessment of anxiety and depression in pediatric epilepsy comprises different aspects such as the timing (when), the source of information (who), and the instrument used for evaluation (how). The TF acknowledges that physicians need support and training to identify and manage mental health disorders in this population.

4.1 | General recommendations for diagnosis of anxiety and depression in children with epilepsy

4.1.1 | Identification and surveillance

High-quality guidelines for non-specialists recommend universal screening for anxiety and depression with some differences in age group.[22,55]

Recommendation 1: Universal screening for anxiety and depression is recommended for all children and adolescents with new-onset epilepsy at age 7 years or older (baseline) and annually thereafter.[54]

Level of Agreement: Very Strong (97%).

Because there is a paucity of data on children with epilepsy, recommendations from the general population were adopted. The need for early screening and identification is further recommended in the following scenarios: psychiatric or behavioral disorders already present before the first seizure,[48,56] new-onset epilepsy,[57,58] or at the first appointment.[59,60] In chronic epilepsy, regardless of the severity, periodic screening is reinforced by the knowledge that children with chronic disorders have higher rates of psychopathology.[7–9]

TABLE 3 Characteristics of treatment studies.

Author	Year	Retrospective or prospective	Study design	Location Region	Type of intervention	Ascertainment	Sample size	Age range [mean (SD)]	Gender (%Girls)
Martinovic, *E&B*	2006	Prospective	Randomized controlled trial	Serbia Europe	Non-pharmacological Psychotherapy—CBT	Tertiary	Total:30 IG: 15 CG:15	13–19 [17.4 (±1.6)] IG (CBI): 17.2 (2.5) CG (TAU): 17.6 (2.2)	Total:60 IG: 60 CG:60
Tajrishi *Iran Red Crescent Med J.*	2015	Prospective	Randomized controlled trial	Iran Middle East	Non-pharmacological Psychotherapy—CBT	Community	Total: 30 IG: 15 CG: 15	14–18 [15.87 (+1.41)]	Total: 43.3 IG: 46.7 CG: 40
Li *Psychiatry Investig*	2016	Prospective	Randomized controlled trial	China Asia	Non-pharmacological Psychotherapy—SFT	Tertiary, single center	Total: 104 IG: 52 CG:52	13–20 IG: [17, 14 (±1.82)] CG:[16, 98 (±2.06)]	Total: 55,3 IG: 50 CG:51.9
Dorris *E&B*	2017	Prospective	Randomized controlled trial	United Kingdom Europe	Non-pharmacological Psychoeducational	Tertiary, multicentric	Total: 83 IG: 40 CG:43	12–17 IG: 14.4 (±1.5) CG:14.3 (±1.4)	Total: 60.2 IG: 65.4 CG:66.7
Brown *E&B*	2019	Prospective Longitudinal	Randomized controlled trial	Canada North America	Non-pharmacological Behavioral Counseling + Physical Activity	Secondary, multicentric	Total: 115 IG: 56 CG:59	08–14 [11.37 (±1.91)] IG: 11.54 (±1.93) CG: 11.20 (±1.86)	Total: 50.8 IG: 50 CG:50.8
Bennett *The Lancet*	2024	Prospective	Randomized controlled trial	England and Northern Ireland Europe	Non-pharmacological Psychotherapy—CBT	Tertiary, multicentric	Total: 334 IG:166 CG:168	03–18 [10.4 (±3.8)] IG: 10.5 (±3.6) GC: 10.3 (±4.0)	Total: 50 IG: 49 CG:52
Thomé-Souza *E&B*	2007	Prospective	Non-randomized	Brazil Latin America	Pharmacological SSRIs (Fluoxetine and Sertraline) Psychotherapy	Tertiary single center	Total:36	5–18 [12.78 (±3.04)][a]	52.8
Blocher *E&B*	2013	Prospective	Non-randomized	United States of America North America	Non-pharmacological Psychotherapy	Secondary and tertiary centers	Total:15	8–13 [11 (±1.51)]	T53.3
Jones *E&B*	2014	Prospective	Non-randomized	United States of America North America	Non-pharmacological Psychotherapy	Secondary and tertiary centers	Total:15	8–13 [11 (±1.51)]	57.14

Abbreviations: CBT, Cognitive Behavioral Therapy; CG, control group; F, female; IG, intervention group; SD, standard deviation; SFT, Systemic family Therpay; SSRIs, selective serotonine reuptake inhibitors.

[a]Provided by the authors.

TABLE 4 Demographic and epilepsy characteristics of treatment studies.

Study	Sample	Age (years) mean [SD]		Sex (F%)	Mean age of epilepsy onset (years) [±standard deviation]		Duration of epilepsy (years)		Type of epilepsy (%)			Antiseizure medication (%)		
		IG	CG		IG [SD]	CG [SD]	IG	CG		IG	CG		CG	IG
Martinovic *E&B* 2006	30 children with subthreshold depression IG: 15 CG: 15	17.2 [2.5]	17.6 [2.2]	Total: 60[a]	UD	UD	.7 [.4]	.8 [.3]	Focal (Partial) Generalized	9[60] 6[40]	9[66.7] 5[33.3]	0 1 ≥2	0 46.7 53.3	0 60 40
Tajrishi *Iran Red Crescent Med J* 2015	30 children with epilepsy IG: 15 CG: 15	NA	NA	43,33 IG: 46,66 CG:40.0	—	—	—	—	—	—	—		—	—
Li *Psychiatry Investig*, 2016	104 children with anxiety and depression IG: 52 CG: 52	17.14 [1.82]	16.98 [2.06]	IG: 50 CG: 51.9	—	—	5.38 [5.0]	6.59 [5.20]	Focal (Partial) Generalized Others	NR 33[63.5] 19[36.5]	NR 34[65.4] 18[34.6]	1 ≥2	50 50	51.92 48.1
Dorris *E&B*, 2017	83 children without psychiatric comorbidity IG:40 CG:43	14.4 [1.5]	14.3 [1.4]	IG: 65.4 GC: 66.7	—	—	7.4 [3.9]	5.6 [3.5]	Genetic Generalized Focal Unspecified Benign Rolandic Epilepsy Unknown	20 [50] 15 [37.5] 03 [7.5] 02 [5]	21 [48.8] 18 [41.9] 03 [7] 01 [2.2]	1 2 3	52.3 32.5 10	69.8 25.6 4.6
Brown *E&B* 2019	115 children without psychiatric comorbidity IG: 56 GC: 59	11.54 [1.93]	11.20 [1.86]	Total: 62[a]	7.74 [3.32]	7.04 [3.0]	3.8 [3.2]	4.22 [2.79]	Partial (Simple + Complex) Generalized[c]	23[41.7] 48[85.7]	20[33.9] [89.8]	0 1 2 3	8.9 64.3 17.8 5.3	11.9 55.9 25.4 5.1
Bennett *The Lancet* 2024	334 children with psychiatric comorbidity	10.5 (±3.6)	10.3 (±4.0)	IG:49 CG:52	NA	NA	5.5 [3.7]	5.3 [3.7]	NA	NA			NA	NA
Thome-Souza *E&B* 2007	36 children with major depressive disorder	6–16 11.97 [3.04]		47.22	6.1 [6.8] Age range: .1–16years		6.4 [5.1] Age Range: .25–16years		Focal Generalized	100 0		1 2 3	66.7 19.4 13.9	
Blocher *E&B* 2013	15 children with anxiety disorders	8–13 11.0 [1.51]		53.3	7.0 [3.0]		4.12 [2.82]		Focal Generalized	73.3 27.7		0 1	20 80	
Jones *Seizure* 2014	15 children with anxiety disorders	8–13 11.0 [1.51]		53.3	7.0 [3.0]		4.12 [2.82]		Focal Generalized	73.3 27.7		0 1	20 80	

Abbreviations: CG, control group; IG, intervention group; NA, not available data; NR, not reported by the authors; NRCT, non-randomized controlled trials; RCT, randomized controlled trials.

[a]There was no difference in biological sex among the groups, only in the total group.

[b]Terminology used for epilepsy type is the same used in the original article where data was extracted.

[c]Generalized includes generalized tonic-clonic, absence, myoclonic, atonic.

TABLE 5 Characterization of outcome variables of depressive and anxious symptoms.

Study	Type of intervention	Treatment method	Primary outcome	Secondary outcome	AAN class	COE
Martinovic *E&B* 2006	Psychotherapy	Cognitive-Behavioral Intervention vs TAU	**BDI** **CES-D** **HAMD**	**QOLIE-31** **Total Score** **Cognitive risk factors**	I	Low
Li *Psychiatry Investig* 2016	Psychotherapy	Systemic Family Therapy + ASM vs ASM	**Seizure Frequency** **HAMA** **HAMD** **SSRS** **FAD** **SSFD** **(Family Atmosphere)** **Total Family** **Function Score**		III	Low
Tajrishi *Iran Red Crescent Med J* 2015	Psychotherapy	Cognitive-Behavioral Interventions CBI vs Routine Program (Communication training, anger management, life-skills training)	**GHQ** Depression Subscale	-	III	Low
Brown *E&B* 2019	Psychoeducational	Behavioral counseling to increase physical activity	CDI-S CHEQOL KIDSCREEN-27 Mood Physical activity		III	Low
Bennett *The Lancet* 2024	Psychotherapy	Personalized Modular CBI vs Usual care for mental health	**SDQ Total** **(at 6 months)**	**SDQ Total** **(at 12 months)** **SDQ Impact Scale** **RCADS** **total anxiety and depression** **Depression** **Total anxiety** **PedsQL** **(mood/behavior)** **PHQ-9** **GAD-7**	I	High
Thome-Souza *E&B* 2007	Pharmacological	SSRIs (Fluoxetine and Sertraline)	Worsening of Seizures (Seizure Diary)	Adverse effects **KSADS-PL** **(MDD)**	IV	Low

TABLE 5 (Continued)

Study	Type of intervention	Treatment method	Primary outcome	Secondary outcome	AAN class	COE
Blocher *E&B* 2013	Psychotherapy	Computer-assisted CBT	**MASC (C)** **SCARED (C)** **SCARED (P)** **CBCL Total (P)** **CBCL internalizing**	**CDI**	IV	Low
Jones *Seizure* 2014	Psychotherapy	Computer-assisted CBT	**SCARED- Social Anxiety**		IV	Low

Note: Bold indicates improvement that was clinically improvement or statistical significance.

Abbreviations: B-IPQ, Brief—Illness Representations Questionnaire; C, children; CA-SUS, Child and Adolescent Service Use Schedule; CBCL, Child Behavior Checklist; CBI, cognitive behavioral intervention, CBT, cognitive behavioral therapy; EKP-G, The Epilepsy Knowledge Profile-General; FAD, family assessment device; GAD, Generalized Anxiety Disorder; GEOS-YP, Glasgow Epilepsy Outcome Scale for Young Persons; GHQ, General Health Questionnaire; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale; K-SADS-PL, Kiddie-Schedule for Affective Disorders and Schizophrenia—Present and Lifetime Version; MICE:, Mental Health Intervention for Children with Epilepsy; MASC, Multidimensional Anxiety Scale for Children; MDD, major depressive disorder; NA, not applicable; P, parents; PedsQ, Pediatric Quality of Life Inventory; PedsQL, Pediatric Quality of Life Epilepsy Module; PHQ-9, Patient Health Questionnaire; PI-ED, Pediatric Index of Emotional Distress; RCADS, Revised Child Anxiety and Depression Scale; SCARED, Screen for Child Anxiety Related Disorders; SQD: Strengths and Difficulties Questionnaire; SSEC-C, Seizure Self Efficacy Scale for Children; SSFD, Scale of Systemic Family Dynamics; SSRIs, selective serotonin reuptake inhibitors; SSRS, Social Support Rating Scale; TAU, therapy as usual; UD, unavailable data.

4.1.2 | Closer surveillance

Recommendation 2: In line with the Guidelines of the American Academy of Pediatrics,[28] closer surveillance with more frequent screening or clinical evaluation for anxiety and/or depression in children and adolescents with epilepsy is recommended:

1. For children, after 12 years of age;
2. For children and adolescents with risk factors such as previous history or family history of psychiatric disorder (e.g., depression, anxiety, bipolar disorder, suicide-related behaviors, substance use, and other psychiatric illness);
3. For children and adolescents exposed to significant psychosocial stressors (e.g., family crises, physical and sexual abuse, neglect, and other trauma histories, foster care, adoption); and
4. For those with frequent somatic complaints.

Level of Agreement: Very Strong (97%).

Recommendation 3: Closer surveillance is also recommended for children and adolescents with epilepsy experiencing seizure worsening or therapeutic modifications (e.g., introducing antiseizure medication with negative psychotropic effects or withdrawing antiseizure medication with positive psychotropic effects).

Level of Agreement: Very Strong (97%).

In the general population, risk factors mentioned in Recommendation 2 indicate that children at higher risk require closer surveillance.[28,39,61–68] In addition, in children with epilepsy, modifications of therapeutic strategies and epilepsy aggravation are additional concerns and demand attention.[69–72] Health care providers must consider that vigilant recognition and active monitoring for psychiatric morbidity in children and adolescents with epilepsy represent the cornerstone of management, since earlier interventions may decrease symptoms of depression and anxiety[59,60] and prevent disorders in children with milder symptoms.[47]

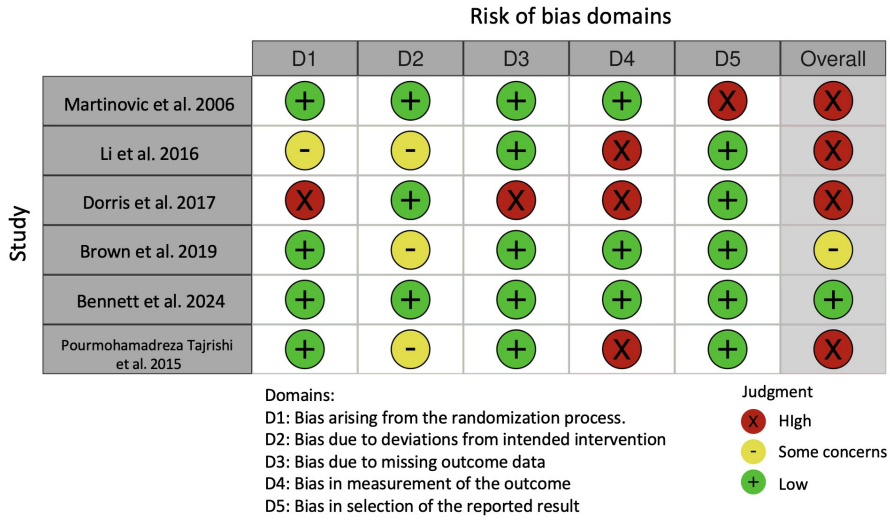

FIGURE 4 Summary of RoB 2 assessment of included randomized controlled trials (RCTs). "Risk of bias" summary: Review authors' judgments about each "risk of bias" domain for each included RCT.

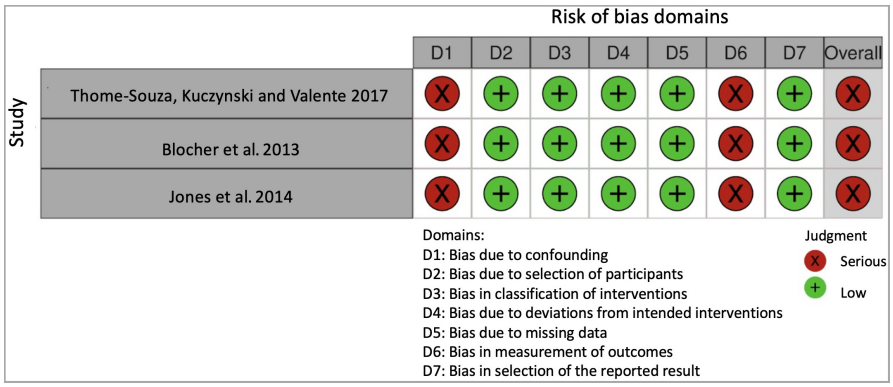

FIGURE 5 Summary of ROBINS-I assessment of included non-randomized clinical trials. "Risk of bias" summary: Review authors' judgments about each "risk of bias" domain.

4.1.3 | Source of ascertainment of depression and anxiety

Recommendation 4: When interviewing a child/adolescent with epilepsy about depression and anxiety, it is recommended that both the child/adolescent and their parents be interviewed, whenever possible.

Level of Agreement: Very Strong (97%).

The child's interview is desirable but cannot be considered in isolation, since the child's abilities to report symptoms may be limited. Age and intellectual level must be considered. Young children may need their parents, especially at the first contact. On the other hand, adolescents may need an explanation about the relevance of their parent's information. The assessment of children and adolescents with moderate to severe/profound intellectual disability is beyond the scope of this work.

Obtaining a diagnostic picture of the child requires multisource information, including the family, and whenever possible, the school.[39] Therefore, this TF, in line with previous clinical practice guidelines (CPGs)[28,37–39] and evidence from children with epilepsy,[73,74] recommends that the caregiver must be involved in the process of diagnosis or identification of symptoms. When family/caregiver are involved in the assessment providing information, attention should be given to the limits of adolescents' confidentiality. Parents and adolescents must be aware of the information that can be disclosed or not.

4.1.4 | Recommendations for choice of instruments for formal assessment of depressive and anxiety symptoms

Clinicians and researchers aiming to assess either depression or anxiety face the difficult task of choosing from many symptom checklists and rating scales or interviews. These checklists or rating scales are used widely because they are a time-effective method of obtaining clinical information with a small burden to respondents. In addition, they can be administered in almost any setting to multiple informants (e.g., parents, teachers, and youth) using various

TABLE 6 American Academy of Neurology Level of Evidence Class (AAN LOE Class).

Intervention		Study	Comparison (control) group	Treatment allocation	Completeness of follow-up	Masking	Number of primary outcome	Secondary outcome	AAN LOE class
Psychological Treatment	CBT	Martinovic, 2006	↑ CBT vs TAU	↑	↑	↑	**↑ ≤2**	↑	I
		Tajrishi, 2015	↓	N/A	N/A	↓	↑	N/A	III
		Jones, 2014	↓	N/A	N/A	N/A	N/A	N/A	IV
		Blocher, 2013	↓	N/A	N/A	N/A	N/A	N/A	IV
		Bennett, 2024	↑ CBT vs TAU	↑	↑	↑	↑	↑	I
	STF	Li, 2016	↑ SFT vs inactive control	?	?	↓	↑ ≤2	↑	III
Physical Treatment	Fitbit	Brown, 2019	↑ Fitbit + counseling vs Fitbit	↑	?	↓	**↑ ≤2**	↑	III
Psychoeducational (self-management)		Dorris, 2017	↑ Psychosocial intervention vs waiting list	↑	**↓ (>20% drop out)**	↓	**↓ ≥3**	↑	III
Pharmacological	SSRIs	Thomé-Souza, 2017	↓	N/A	N/A	N/A	N/A	N/A	IV

Note: ↓: ↑:?: unclear.

Abbreviations: CBT: cognitive behavioral therapy: N/A, not applicable; SSRIs, Selective Serotonin Reuptake Inhibitors; SFT, systemic family therapy; TAU, therapy as usual.

strategies of administration (e.g., on-site, online, by mail, computer).[75,76]

Health care providers must be aware that checklists and scales represent a first-level screening for mental health disorders. All have limitations and are not designed to diagnose disorders, but rather to assess and score symptoms identifying those who need more in-depth evaluation.

The two studies[43,49] that met the eligibility criteria for diagnosis provided a very low certainty of evidence. Rating screening measures as methodologically sound or adequate for their internal consistency is beyond the scope of this study. Considering this scenario, health care providers may base the selection on their own expertise and clinical supports in their practices.

4.1.5 | Behavioral checklist

Broadband behavioral checklists/questionnaires—longer and shorter—are measures of behavior across age groups and have been used in children with epilepsy. The Psychiatric Pediatric Issues TF identified the Child Behavioral Checklist (CBCL)[77,78] followed by the Behavior Assessment System for Children (BASC)[78–80] as the most frequently used longer broadband behavioral checklists.

Recommendation 5: A formal screening questionnaire, either paper-and-pencil or electronic, is recommended as a first-level screen to assess symptoms of depression and anxiety in children and adolescents with epilepsy.

Level of Agreement: Very Strong (93.9%).

Recommendation 6: In busy clinical settings, it is recommended that a staged approach be used, beginning with a shorter behavioral checklist (e.g., Strengths and Difficulties Questionnaire). If the screen is positive, it must be followed by a more comprehensive checklist (e.g., Child Behavior Checklist, Behavior Assessment System for Children) or specific rating scales for depression and anxiety, with additional questions on suicidal ideation for children and adolescents with epilepsy who screen positive.

Level of Agreement: Strong (87.9%).

Recommendation 7: Health care providers must choose the most appropriate checklist based on feasibility (e.g., time required to complete it); availability in the interviewee's language, cost, assessment (parents [young children]; or parents and children [older children and adolescents]) with epilepsy and familiarity with the questionnaire.

Level of Agreement: Very Strong (97%).

Caplan et al.[43] assessed the diagnostic accuracy of CBCL subfactors internalizing scale and anxiety/affective against a gold-standard reference (the semi-structured diagnostic interview [K-SADS])[43] designed to assess current and past episodes of psychopathology in children and adolescents according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) administered in a face-to-face meeting.[43] The CBCL Anxiety/Affective factor score showed the best specificity (.92%) to predict mood (affective) and anxiety disorder diagnosis. The CBCL Anxiety/Affective factor showed a sensitivity of .38%. The CBCL internalizing scores presented a sensitivity of .63% and a specificity of .69%. Due to the very low level of certainty of the evidence provided, expert consensus was needed. The expert panel recommends the use of broadband checklists in the clinical setting.

The analysis of the validity of the CBCL for children with new-onset[81] and chronic epilepsy[82] showed that the difference between scores was evident mainly for the narrowband scales (Attention Problems, Withdrawal, and Thought Problems), but negligible for the broadband scales (Internalizing Problems and Total Problems). In the broadband checklists, the health care provider must be aware that symptoms of anxiety and depression are aggregated under one subfactor or subdomain (e.g., internalizing symptoms).

The TF acknowledges that longer broadband checklists/questionnaires are useful yet may not be feasible in under-resourced clinical settings. For the non-specialist, a staged approach beginning with a shorter behavioral checklist followed by a more comprehensive checklist, specific rating scales, or, whenever possible, a clinical interview may be helpful.

4.1.6 | Rating scales

More narrowly focused depression or anxiety symptom rating scales have been developed to permit valid and reliable quantitative assessment of specific symptoms. The Psychiatric Pediatric Issues TF acknowledges the undeniable importance of these scales to identify, to assess symptoms over time, and after intervention.

Recommendation 8: Depression and anxiety symptom scales are recommended to assess the presence and severity of symptoms in children and adolescents with epilepsy in order to establish a baseline against which response to therapeutic interventions can then be compared.

Level of Agreement: Very Strong (97%).

Recommendation 9: In the clinical and research setting, it is recommended to use an instrument of choice to quantify self-reported symptoms of depression and anxiety in children and adolescents with epilepsy. The instrument of choice must be translated and validated for the interviewees' or respondents' language.

Level of Agreement: Very Strong (90.6%).

Recommendation 10: The choice of the assessment instrument of symptoms of depression and anxiety in children and adolescents with epilepsy must consider the expertise of each health care provider, the available resources, and the feasibility in every setting.

Level of Agreement: Very Strong (96.9%).

Recommendation 11: The health care provider involved in the care of children and adolescents with epilepsy must always explain that the diagnosis of symptoms is essential to optimize treatment outcome and reduce morbidity using language understandable to lay people.

Level of Agreement: Very Strong (100%).

Recommendation 12: Children and adolescents with epilepsy and subthreshold symptoms who do not meet the criteria for a diagnosis of depression or anxiety, are at higher risk for developing these disorders and need be assessed more frequently.

Level of Agreement: Strong (84.8%).

The Psychiatric Pediatric Issues TF identified that the most frequently used were Children Depression Inventory (CDI) and Beck Depression Inventory (BDI I and II). The Neurological Disorders Depression Inventory for Epilepsy in Youth (NDDI-E-Y) Level is the only instrument developed for adolescents (12–17 years) with epilepsy.

The Psychiatric Pediatric Issues TF identified eight self-administered questionnaires for anxiety symptoms in children with epilepsy. The most frequently used instruments for anxiety symptoms are the following: STAI-CH (State and Trait Anxiety Inventory for Children), RCMAS (Revised Children's Manifest Anxiety Scale), SCARED (Screen for Child Anxiety Related Disorders), and MASC (Multidimensional Anxiety Scale for Children).

Caplan et al.[43] assessed the diagnostic accuracy of two rating scales—CDI for depressive symptoms and MASC for anxiety symptoms against K-SADS. The MASC provided the best sensitivity (.87%), and the CDI had a sensitivity of .58% and a specificity of .73%. Wagner et al.[49] assessed the diagnostic accuracy of the NDDI-E-Y 11 items (not the revised version) Eighty-seven patients responded to the K-SADS (reference standard), and five scored as having a mild or severe major depressive disorder or depressive disorder not otherwise specified. This rating scale provided a sensitivity of .80% and a specificity of .71% with a cutoff of 27. Due to the very low level of certainty of the evidence provided, expert consensus was needed for rating scales. The expert panel recommends the use of rating scales in the clinical setting.

Based on the current evidence and expert opinion, the TF cannot recommend one checklist or one rating scale over the others. In this context, physicians must consider feasibility, their expertise with the instrument, and translation for the language of the respondent.

4.1.7 | Special considerations regarding seizure control and antiseizure medication

Recommendation 13: Interictal and peri-ictal symptoms require distinct therapeutic strategies. The health care provider must actively ask if symptoms of anxiety or depression are related to seizure worsening in children and adolescents with epilepsy.

Level of Agreement: Very Strong (100%).

Recommendation 14: It is recommended when assessing for symptoms of anxiety and depression that the health care provider investigate the presence of seizures in the past hours, as this could reflect an adjustment reaction rather than an anxiety or depressive disorder.

Level of Agreement: Strong (84.4%).

Recommendation 15: Direct questioning of parents/caregivers and adolescents with epilepsy about new behavioral adverse effects of antiseizure medications, pre-existing symptoms aggravated by ASMs, and interictal depressive/anxious symptoms is recommended.

Level of Agreement: Very Strong (100%).

Recommendation 16: Parents and adolescents must be informed about the psychotropic properties of an antiseizure medications and possible behavioral adverse effects before it is prescribed to a child or adolescent with epilepsy.

Level of Agreement: Very Strong (97%).

Once the presence of anxiety and depressive symptoms is recognized, the next step is to identify whether the symptoms are exclusively peri-ictal, since these symptoms may not reflect the child's current state. Peri-ictal symptoms are not rare and clinicians need to specifically inquire about them because parents and children may not report them spontaneously.[83]

In addition, the negative effect of ASMs on mood is widely documented (e.g., levetiracetam, phenobarbital, perampanel, and vigabatrin) and should be considered.[84] On the other hand, valproate and lamotrigine may have a positive effect on mood.[84] Depressive disorders have been identified in children with epilepsy treated with phenobarbital,[85] but not in those with carbamazepine. Similar findings were reported with phenytoin but not with carbamazepine.[86]

The TF acknowledges and reinforces that transient worsening that is seizure related and ASM-behavioral adverse effects must be evaluated. However, it is advisable to inform the caregiver that seizure symptoms and ASM mood and behavioral adverse effects should not be included in the rating.[70,83]

In a clinical setting, when the examiner utilizes interviews and scales, the health care provider has the opportunity to not only assess but also, more importantly, to clarify and interpret the significance of the critical items that may be overrated due to seizures (e.g., withdrawal) and ASM (e.g., attention).[82]

The TF recognizes the relevance of not overlooking symptoms of anxiety and depression. Furthermore, we are aware of the challenges in distinguishing between interictal and peri-ictal symptoms in pediatric epilepsy, particularly in cases of pharmacoresistant epilepsy with frequent seizures. Therefore, we recommend that children who exhibit scores above the designated threshold be closely monitored.

4.1.8 | Psychiatric interviews

Recommendation 17: Specialized clinical evaluation by a provider with expertise in mental health (e.g., psychiatrist or psychologist) is strongly recommended, if possible, when clinical concerns for anxiety and depression are noted in the history or screening of a child or adolescent with epilepsy.

Level of Agreement: Very Strong (90.6%).

Recommendation 18: A structured and semi-structured psychiatric interview remains advisable for some research settings (e.g., screening tool validation studies) in children and adolescents with epilepsy.

Level of Agreement: Very Strong (100%).

Use of structured or semi-structured interviews is infrequent in non-research settings, since they demand training, time, cost, and thus can be a burden to patients and caregivers. The Psychiatric Pediatric Issues TF acknowledges that although standardized screening instruments are helpful for diagnosis, they do not replace a direct interview by a specialist. A comprehensive clinical evaluation and assessment of diagnostic criteria according to DSM or International Classification of Diseases (ICD) criteria is recommended.

4.2 | Treatment of depression and anxiety in children and adolescents with epilepsy

4.2.1 | General principles of treatment

Recommendation 19: Health care providers must develop a pragmatic treatment plan for anxiety and/or depression in children and adolescents with epilepsy and their caregivers. The treatment plan depends on the treatment setting and on the type of treatment—pharmacological and/or psychological.

Level of Agreement: Very Strong (100%).

Recommendation 20: The treatment plan for anxiety and/or depression must be feasible and practical, addressing the needs, fears, beliefs, religion, cultural background, and resources of children and adolescents with epilepsy and primary caregivers.

Level of Agreement: Very Strong (100%).

Mental health disorders in youth with epilepsy may add an extra burden to the patient and their family, due to stigma

Recommendation 21: A health care provider must monitor children and adolescents with epilepsy who have been prescribed antidepressants for adverse events, self-harm, and risk of suicidality. Onsite or online interviews with children and family members are recommended.

Level of Agreement: Very Strong (93.8%).*

as well as practical aspects, such as additional medication, appointments, and new health care providers (e.g., psychologist, psychiatrist).[87,88] There was consensus that patients with epilepsy and their families need a treatment plan for anxiety and/or depression that includes treatment type and setting based on patient and family's preferences and beliefs. In addition, providing information about the severity, the impact, and the risks must be part of this individualized plan.[89–93]

It is well known that treatment plans considering all aspects involved with the child and family and providing education lead to greater adherence and better outcomes in chronic disorders.[28,94–97] Panelists were unanimous that the treatment plan must be child and family centered, and that cultural beliefs must be respected to enhance the alliance between the patient/family and health care providers.

The TF recognizes that any treatment plan must consider age, resource, literacy, education, culture, religion, and specific cognitive impairments in persons with epilepsy.

Assessment during any treatment is mandatory. According to the American Academy of Child and Adolescent Psychiatry (AACAP),[39,40] standardized symptom rating scales can supplement clinical interviews, since these scales optimize therapists' abilities to assess treatment response and remission.[98]

4.2.2 | Monitoring and treatment initiation

Mild depression and anxiety

According to current CPGs for non-specialists in children and adolescents with mild depressive or anxiety disorder without additional burdens, active monitoring for 4–6 weeks is usually sufficient—provided that patients can manage their daily lives.[22,28,36,101,102] Active monitoring includes consultation and mental health education based on behavioral therapy to improve the understanding and management of depression and anxiety.[101,103]

Measures to improve mental health should be offered and reinforced, such as regular exercise, sleep hygiene, mindfulness, relaxation techniques, a balanced diet, everyday activities, and social interaction.[104]

Recommendation 22: In line with previous Guidelines National Institute for Health and Care Excellence,[38] American Academy of Pediatrics,[22,28,99] and American Psychological Association,[22,28,100] a period of watchful and active monitoring (4–6 weeks) for mild depression or anxiety must be considered in children and adolescents with epilepsy. (This recommendation does not apply for moderate to severe symptoms.)

Level of agreement: Very Strong (96.9%).

Recommendation 23: If possible, psychological support or programs to increase resilience and coping skills must be offered during the period of monitoring for children with mild symptoms of depression and anxiety.

Level of Agreement: Strong (96.9%).*

Recommendation 24: It is recommended that the watchful "active" monitoring in children and adolescents with epilepsy and mild symptoms of depression or anxiety, provided by a team member (e.g., nurses, social workers, junior fellows, residents) with basic training, include:

1. Weekly or biweekly visits (onsite, by phone, or online) with regular symptom checking,
2. Behavioral activation techniques (the prescription of exercise and leisure activities),
3. Sleep monitoring (sleep deterioration can aggravate depression and anxiety),
4. A peer support group (whenever possible),
5. Self-management goals for depression/anxiety and epilepsy, and
6. Educational materials (paper/website) for families and patients.

Level of Agreement: Strong (80.6%).

Two RCTs testing non-pharmacological treatment included psychoeducation[44] and behavioral counseling to improve physical activity.[42] The RCT with manual-based

psychosocial group intervention[44] showed improvement in self-management skills and knowledge about epilepsy. Participants with more severe mental health problems were excluded, reducing the range of possible improvement, although a decrease in the average scores of scales used for depressive symptoms (Beck Depression Inventory for Youth) and anxiety symptoms (Beck Anxiety Inventory for Youth) was observed. The RCT with behavioral counseling to increase physical therapy aiming to decrease depressive symptoms and improve quality of life was not beneficial because there was no increase in physical activity.[42] These Class III studies provided a low certainty level to guide recommendations, but according to expert opinion obtained through consensus, the TF recommends psychosocial interventions, such as psychoeducation, to increase epilepsy knowledge, coping strategies, self-efficacy, and quality of life, benefiting children and adolescents with epilepsy as well as their caregivers.[105]

During the monitoring period, patient must be reassessed with a formal screening (onsite, online, or by phone). Active monitoring with education and support must be always offered according to the stepped-care model.[36] The TF acknowledges the shortage of mental health professionals to assist these patients by providing proper support.[106,107] For this reason, we stress the importance of basic mental health training for health care providers caring for children if psychological support is unavailable or if there is a lengthy waiting list for milder cases.

According to the AACAP,[39,40] therapeutic task-sharing with a primary care provider, particularly for mild cases, expands access and conserves the time of the child psychiatrist for managing complex and severe presentations.

4.2.3 | Moderate to severe depression and anxiety

Recommendation 25: In moderate to severe depression, anxiety, and/or comorbid psychiatric conditions (e.g., substance abuse) in children and adolescents with epilepsy, the health care provider must refer to a mental health specialist (e.g., psychiatrist, psychologist) whenever possible.

Level of Agreement: Very Strong (90.6%).

There was uniform agreement for both the referral of severe cases to the specialist and the need to develop paths to mental health care. It is recommended to establish a collaboration with mental health care specialists to refer children and adolescents in advance. The collaborative care model with interdisciplinary team-based care including a consultant psychiatrist for advice or consultation in the primary care clinic may be helpful in high-, middle-, and low-income countries.[108–110] The TF acknowledges that integrated health care approaches are resource intensive to implement and maintain. Therefore, it may not be feasible to adopt such a model fully.

Recommendation 26: In the case of a lengthy wait time for mental health services for children and adolescents with epilepsy, the health care provider in charge must support active monitoring (onsite, online, by phone).

Level of Agreement: Very Strong (90.6%).

Recommendation 27: Epilepsy clinics/centers must develop clinical care pathways to facilitate access to mental health services for children and adolescents with epilepsy.

Level of Agreement: Very Strong (100%).

4.2.4 | Psychotherapy

Recommendation 28. Due to the limited evidence about the benefits of psychotherapy in children and adolescents with epilepsy, mental health providers are encouraged to base their treatment on trials conducted in children with depression and anxiety without epilepsy.

Level of Agreement: Strong (87.1%).

In children with depression and anxiety without epilepsy, psychotherapy is recommended as first-line treatment.[27,41] According to current AACAP guidelines for children with depression or anxiety without epilepsy, there is stronger evidence for CBT compared to other forms of therapy, including interpersonal therapy and familial therapy.[39,40]

In children and adolescents with epilepsy, CBT is the most frequent psychotherapy used to treat children with

Recommendation 29. The psychosocial intervention in children and adolescents with epilepsy should be tailored to the person's needs and severity of the depressive/anxious episode. Where available and indicated, cognitive behavioral therapy should be offered after assessing its suitability (e.g., personality characteristics, coping skills, family support, intellectual level, and social environment).

Level of Agreement: Very Strong (93.8%).

Recommendation 30 (Added after revision [June 2024]): Cognitive behavioral therapy may be beneficial for children and adolescents with epilepsy with anxiety and depressive symptoms and disorders.

Evidence-Based Certainty: Moderate.

anxiety and depressive symptoms and disorders. The MICE (Mental Health Intervention for Children with Epilepsy) trial, a large, multisite trial in the UK evaluating a personalized mental health intervention for children with epilepsy based on principles of CBT, showed that MICE plus usual care was superior to assessment-enhanced usual care in improving the primary outcome of emotional and behavioral difficulties, assessed via the SDQ, at 6 months post-randomization. In addition, it improved depression and anxiety on the RCADS according to parent report. (Class I study; Low Risk of Bias [RoB 2]; Certainty of Evidence for CBT: Moderate.)[51]

In adolescents with epilepsy and subthreshold depressive symptoms, one RCT[47] demonstrated that CBT was superior at improving depressive symptoms and preventing depressive disorder compared with psychotherapy as usual (Class I study; High Risk of Bias [RoB 2]; Certainty of Evidence for CBT: Low [GRADE]).

In children with epilepsy and anxiety disorder (generalized anxiety disorder, separation anxiety, and social anxiety/phobia), two NRCT studies[41,45] using a manual-based, computer-assisted CBT intervention (*Camp-Cope-A-Lot*) for 12 weeks showed significant reductions in symptoms of anxiety and depression, reported by children at completion of the intervention and at the 3-month follow-up. Similarly, parents reported fewer symptoms of anxiety and a reduction in behavioral problems. This intervention was safe, efficacious, and feasible. This finding has a low certainty of evidence due to the limited sample and high risk of bias. There was a significant reduction in symptoms of anxiety and depression (Class IV, High Risk of Bias [ROBINS-I], Low Certainty of Evidence [GRADE]).[41,45]

RCTs with large samples may help to determine the clinical and cost-effectiveness of adding a modular psychological intervention to usual care for the mental health disorders in comparison to assessment-enhanced usual care alone in children and adolescents with epilepsy.

Recommendation 31: Psychotherapy must be age appropriate. For younger children with epilepsy, the family must be involved directly or via family therapy with counseling.

Level of Agreement: Very Strong (93.8%).

The TF acknowledges that family involvement in the treatment of children with depression and anxiety is highly important. Treatment is characterized by a collaboration between patient, family, and therapist.[39,40] Strategies that promote the relationship, communication, parenting style, and parent modeling of mood dysregulation may provide additional benefits to the child's treatment.[39,40]

In children without epilepsy, there are some inconsistencies regarding the importance of family therapy in isolation. NICE[36] guidelines recommend family therapy as a first-line option, but other CPGs for primary care physicians do not comment on this modality.[22,28,37,38] According to the AACAP,[39,40] family-based interpersonal therapy (*vs* active control) improved clinician, parent, and self-reported symptoms of depression in children with major depressive disorder (MDD) and/or any depressive disorder. For adolescents or children with MDD, persistent depressive disorder, or any depressive disorder, family therapy improved depression response when compared with active control. However, the certainty of evidence for family therapy benefit in isolation is low.

In adolescents with epilepsy, one RCT with systemic family therapy that included 104 adolescents (52 intervention and 52 controls [receiving ASM only]) was identified. The primary aim was to document if systemic family therapy decreases symptoms of anxiety (Hamilton Anxiety Scale score ≥14 points) and depression (Hamilton Depression Scale score ≥20 points). Anxiety and depression symptoms were decreased significantly with systemic family therapy; meanwhile, the family dynamics and family functions were significantly improved, and the social support also increased.[46] This Class III study had a

high risk of bias and provided low certainty of evidence. Therefore, the current evidence is insufficient to provide recommendations regarding family therapy as an isolated form of treatment.

Recommendation 32: Peri-ictal symptoms in children and adolescents with epilepsy respond poorly to antidepressant medication, and psychological support for the child and family is advisable when symptoms are related to loss of control associated with seizure unpredictability.

Level of Agreement: Strong (81.3%).*

Current treatment strategy for peri-ictal anxiety and depression must aim to improve seizure control.

4.2.5 | Pharmacological treatment

Recommendation 33: Health care providers (neurologists and epileptologists with training/skills for mental health disorders) faced with treating interictal depression/anxiety in children and adolescents with epilepsy should use principles established for patients without epilepsy, considering the possible interaction with antiseizure medications and risk of seizure exacerbation.

Level of Agreement: Strong (96.8%).

The Psychiatric Pediatric Issues TF systematic review identified one open-label study (Class IV) using fluoxetine and sertraline for 36 children and adolescents with epilepsy and major depressive disorder diagnosed with K-SADS.[48] In this limited sample with a long follow-up of 12 months, the efficacy was high (97.2% reported clinical improvement) and seizure worsening was rare (two patients).[48] (Class IV; Risk of Bias: High [ROBINS-I]; Certainty of the Evidence: Low [GRADE]).

The TF acknowledges that medical education, training, and experience are necessary to prescribe antidepressant medications safely and effectively. In addition, an emergency risk plan and referral pathways must exist for patients at risk of suicide and self-harm. By including

Recommendation 34: Selective serotonin reuptake inhibitors are the first-line pharmacologic treatment of anxiety and/or depression in children/adolescents with epilepsy as they have a low seizure propensity and favorable side-effect profile.

Level of Agreement: Strong (86.7%).

Recommendation 35: Slow titration of selective serotonin reuptake inhibitors associated with careful and appropriate follow-up and monitoring is recommended for the treatment of anxiety and/or depression in children and adolescents with epilepsy.

Level of Agreement: Strong (83.9%).

recommendations for pharmacological treatment, the TF does not rule out the need for mental health care providers but recognizes the shortage of mental health services in high, middle, and low-income settings.[106,107,111] Current high-quality CPGs for children and adolescents without epilepsy recommend SSRIs (except paroxetine), preferably fluoxetine, as a first-line medication for major depressive disorder.[22,28,36–40] For anxiety, SSRIs are recommended for children and adolescents from 6 to 18 years with social anxiety, generalized anxiety disorder (GAD), separation anxiety, and panic disorders.[36,39,40]

In line with current recommendations, the TF strongly suggests increased monitoring for increases in suicidal ideation in the weeks following medication initiation.[22,28,36–40]

Complete symptom remission of depression and anxiety is the major goal of treatment. Clinicians should be aware that residual symptoms of depression and anxiety such as low mood, guilt, insomnia, anxiety, loss of interest, irritability, fatigue, and a range of somatic or physical symptoms may persist, despite adequate treatment. Residual symptoms are associated with higher rates of recurrence and/or development of MDD.[112–115]

Recommendation 36: Tricyclic antidepressants and monoamine oxidase inhibitors are not recommended as first-line treatment for the treatment of anxiety and/or depression in children and adolescents with epilepsy.

Level of Agreement: Strong (87.5%).*

The TF acknowledges that the availability of SSRIs may be limited in low-resource settings. Some local CPGs actively recommend against TCAs use,[36–38] and others do not provide any comment about it.

4.2.6 | Combination therapy

Recommendation 37: Psychotherapy should be associated with pharmacotherapy if considered appropriate for the treatment of anxiety and/or depression in children and adolescents with epilepsy.

Level of Agreement: Strong (87.1%).

The combination treatment (Combined Therapy) of SSRIs and CBT should be offered for MDD, GAD, social anxiety disorder, social anxiety, separation anxiety, or panic disorder whenever possible. In one RCT with adolescents with MDD without epilepsy, fluoxetine combined with CBT improved depressive symptoms (low certainty of evidence).[116]

In anxiety, two RCTs showed that combination therapy, compared with therapy alone and sertraline alone, improved primary anxiety and global function.[117] Combination therapy may represent a more effective short-term treatment than either treatment alone. The TF acknowledges the major difficulties that healthcare providers face in accessing combined therapy but understand that such recommendation may be useful for policymaking.

Recommendation 38: Epileptologists and/or pediatric neurologists should communicate with other health care providers, especially mental health providers, if they are prescribing a new antiseizure medication with negative psychotropic effect.

Level of Agreement: Strong (81.3%).

Appropriate management of ASMs is another component in the management of children and adolescents with epilepsy with symptoms of depression or anxiety. Health care providers should aim for the cautious selection of ASMs with a lower likelihood of psychiatric/behavioral adverse effects.[70,101,118–122] The TF acknowledges the importance of balancing such considerations relative to the primary objective of seizure control. Consideration must also be given to the cumulative impact of polytherapy in this context and polytherapy should be avoided where possible.

4.2.7 | Ongoing management

Recommendation 39: A health care provider must monitor children and adolescents with epilepsy prescribed with antidepressants for adverse effects, self-harm, and risk of suicide. Onsite or online interviews with children and family members are recommended.

Level of Agreement: Very Strong (93.8%).

Recommendation 40: In busy clinical settings, a checklist with the most common medication adverse effects is recommended in children and adolescents with epilepsy.

Level of Agreement: Strong (80.7%).

Recommendation 41: Education of family/primary caregivers is essential to guarantee adherence to treatment and adequate monitoring of psychiatric symptoms and adverse effects in children and adolescents with epilepsy.

Level of Agreement: Very Strong (96.8%).

In the ideal scenario, a mental health care provider with expertise must monitor for adverse effects, especially at the beginning of treatment. However, patients and families may report adverse effects or worsening symptoms during their appointment with the epileptologist, pediatric neurologist, pediatrician, or other health care providers. Therefore, health care providers who are providing care

Recommendation 42: Clinical trials have shown that symptoms and functioning do not improve at the same time. Therefore, the assessment of treatment strategy in children and adolescents with epilepsy and depression or anxiety must consider several domains, including:

1. Reduction of symptoms
2. Global functioning (social and academic)
3. Risk of suicide
4. Possible adverse effects from treatment with adverse-effect scales
5. Treatment adherence
6. New or ongoing environmental stressors (e.g., family conflict/dysfunction, academic issues, bullying)

Level of Agreement: Very Strong (100%).

to these children and adolescents must be aware of the treatment and its risks. In collaborative care or a shared-care model of care, the role of every care provider must be established, including monitoring.[18,27,123–125] There is no evidence to support that in-person monitoring is more effective than virtual monitoring after treatment initiation. More importantly, a regular and frequent schedule should be developed to obtain input from the adolescents and families to ensure adherence with the monitoring strategy.[126–129] This may include monitoring depressive symptoms, risky behaviors, and global functioning (e.g., school setting, interaction with peers). The contact with the family will ensure appropriate monitoring and enhance adherence.[28]

Recommendation 43: In line with the American Academy of Child and Adolescent Psychiatry (2022) and the American Academy of Pediatrics (2018) guidelines, it is recommended that children and adolescents with epilepsy treated for 12 months for anxiety and/or depression should be monitored every month for 6 to 12 months after full resolution of psychiatric symptoms.

Level of Agreement: Strong (80.6%).

Recommendation 44: In case of recurrence of anxiety and/or depressive symptoms, health care providers must treat and monitor children and adolescents with epilepsy monthly for up to 2 years, given the high recurrence rates. In case of recurrence, referral to a mental health provider is recommended.

Level of Agreement: Strong (87.1%).

Recommendation 45: If failure (i.e., symptoms, functioning) or partial efficacy to antidepressant/anxiolytic treatment is noted over a period of 6 to 8 weeks in a child or adolescent with epilepsy, referral to a mental health provider (e.g., psychiatrist, psychologist) is recommended.

Level of Agreement: Strong (90%).

Recommendation 46: The presence of new psychiatric conditions not previously identified (i.e., anxiety, mania, substance abuse) or imminent suicidal risk in children and adolescents with epilepsy requires immediate referral or treatment in a specialized setting (e.g., inpatient treatment).

Level of Agreement: Strong (83.9%).

In a systematic review and meta-analysis on anxiety disorder in children and adolescents (age range from 5 to 17 years) without epilepsy, improvement was observed within 2 weeks of treatment initiation, clinically significant improvement by week 6, and maximal improvement by 12 weeks or later.[130] For depression, a significant improvement in depression symptoms is expected within the first month of treatment initiation, with two-thirds of SSRI benefits by week 2 and maximal benefit by weeks 4–6.[39,131] The optimal duration of treatment with an initial depressive disorder is uncertain, but it is generally

accepted to continue therapy for 6–12 months after remission to reduce relapse. Depression with severe symptoms, longer duration, and relapses may benefit of longer treatment.[132] Referral to a mental health provider or, at least, consultant with an expert is recommended for cases of inefficacy, recurrence/relapses, the emergence of a new psychiatric condition (namely, those with moderate to severe symptoms), self-harm, or suicidal ideation/planning.

4.2.8 | Shared-care model

Recommendation 47: The ongoing involvement of the managing epilepsy team in the treatment of depression and anxiety is recommended to ensure acceptance, adherence to treatment, counseling, and support. A shared-care model is recommended in children and adolescents with epilepsy and mental health disorders.

Level of Agreement: Very Strong (96.8%).

According to expert consensus, health care professionals must be trained, educated, and prepared to refer to mental health care providers, when necessary or preferred. The primary health care provider also plays a substantial role in informing children and their families properly about the diagnosis and treatment choices mitigating the stigma of mental disorders. Integrated behavioral health care is defined as "the care a patient experiences as a result of a team of primary care and behavioral health clinicians, working together with patients and families, using a systematic and cost-effective approach to provide patient-centered care for a defined population."[133] In this context, the epileptologist introduces the patient to the behavioral health provider, and the behavioral health provider then engages the patient and begins the assessment and treatment process. The team follows a "stepped care" approach, allowing immediate and appropriate treatment without referral to mental health services. Higher levels of care are reserved for patients who are not improving or who have a more complicated presentation.[134] The team refines the diagnosis throughout treatment and provides medication adjustments, brief behavioral interventions, and education. Adjusting treatment, including referral to specialty mental health care, if needed, continues until treatment targets are accomplished. The process allows a sophisticated application of mental health skills, in short supply, to be leveraged across larger populations of patients.

5 | CONCLUSION

The recommendations address common and important aspects of the diagnosis and treatment of anxiety and depression in children and adolescents with epilepsy.

The Task Force of Psychiatric Pediatric Issues in Epilepsy of the ILAE aimed to provide scientific evidence and input from clinical experts adhering to the ILAE Recommendations for Guidelines.[29] This systematic approach aims at identifying studies with high certainty of evidence to inform recommendations.

Although depression and anxiety disorders and symptoms are common in children and adolescents with epilepsy, our systematic review showed that certainty of evidence is limited to put forward clinical guidelines. Regarding diagnosis, validation studies are scarce. Considering that one of the most important aspects in the design of a reliability study is the sample size,[135] the TF acknowledges that the process of validation is resource-intensive, time-consuming, and perhaps unfeasible in children with epilepsy. It does not imply that current checklist and rating studies must not be used in children with epilepsy, since the reliability was not assessed. The TF members and experts from ILAE regions, consulted in the Delphi process, agree that the assessment of depression and anxiety symptoms is strongly recommended.

Considering treatment, additional controlled, randomized, double-masked trials with large samples and follow-up are urgently needed. Adherence to the guidelines (e.g., CONSORT guidelines) and a thorough description of intervention protocols and standard inventories are necessary to ensure reproducibility. As stated by others,[136] adequate randomization with allocation concealment and blinded outcome assessment are mandatory to increase the overall quality of RCT study designs. Because attrition is often high in research that requires active participation, an intention-to-treat analysis should be carried out. Attention to these critical methodological aspects minimizes the risk of bias in these studies and may inform future evidence-based recommendations on pharmacological treatment.

The Delphi method, used to generate recommendations, provides expert consensus in a structured process. It offers several strengths that make it a valuable tool for decision-making, such as anonymity and iterative process, minimizing the impact of personal biases, and allowing geographical representation. An overreliance on expert opinions and limited group dynamics is a common weakness of the Delphi process. We adopted measures to

minimize the bias introduced by expert selection (e.g., experts from the same group) and facilitators. We considered experts from all ILAE regions and revised recommendations based on their opinions during three rounds.

Children and adolescents with epilepsy are at a higher risk of experiencing mental health disorders, such as depression and anxiety, compared to children without epilepsy and those with non-neurological chronic disorders.[4,5] Therefore, they must be routinely and systematically screened for these conditions. The treatment for these disorders should follow the same guidelines used to treat children and adolescents without epilepsy. However, due to the unpredictability of seizures and the potential adverse effects of ASMs on behavior, special care is required if seizures worsen or if the therapy requires modification.

The TF acknowledges the shortage of mental health providers, which often makes it necessary to adopt an integrated model of care with shared responsibilities. Education is needed for primary and secondary care centers and pathways of referral for severe cases.

This study has identified gaps in the management of depression and anxiety of children and adolescents with epilepsy. Future trials providing more robust data may represent the basis for future clinical practice guidelines and support public policies.

Aligned with the ILAE mission and IGAP (Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders) objectives to deliver effective and timely diagnosis and treatment,[137] these recommendations provided a guide for addressing challenging areas in the care of children and adolescents with epilepsy who are at a higher risk of developing depression and anxiety in the clinical setting of high, middle, and low-resource settings.

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DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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ENDNOTES

*Comment added (modified) based on the Delphi panel comments (2nd round of Delphi).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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