Supplementary Material 1

Eligibility Criteria – Diagnosis

Inclusion Criteria
1. Articles included original data (i.e., not a review)
2. Studies with children and adolescents with a confirmed diagnosis of epilepsy (any type)
3. Psychiatric interviews reporting rates of depressive and/ or anxiety disorder
4. Validation studies on the diagnostic accuracy (at least, specificity and sensitivity) of depression and/or anxiety screening tools relative to a gold-standard comparison measure (clinical diagnostic interviews and/or psychiatric interviews)
5. From inception to date
6. All languages

Exclusion Criteria
1. Assessed psychiatric disorders with psychiatric interviews but did not provide information about depression or anxiety disorder
2. Diagnosis based on chart review
3. Assessed the severity of the depression and anxiety rather than validating screening tools for anxiety and/or depression
4. Assessed cognitive function but not psychiatric disorders
5. Case series and case report studies
6. Mixed sample (e.g., adults and children) that precluded separate analysis of children's data
7. Not possible to separate children with psychiatric disorders from children with other disorders
8. Not possible to separate children with depression and/or anxiety from other psychiatric disorders
9. Studies including children and adolescent with intellectual disability
10. Animal studies
11. Editorials, dissertations, abstracts, conference proceedings, letters to editor, opinions and studies that failed to report the data required for this review
12. Review articles, systematic reviews, and meta-analyses were hand searched to check references for other relevant articles

Eligibility Criteria – Treatment

Inclusion Criteria
1. Articles included original data (i.e. not a review)
2. Randomized controlled trials
3. Prospective non-randomized controlled and uncontrolled studies (with a control group including participants acting as their own control group (i.e., before-after studies)
4. Studies with pharmacological and non-pharmacological intervention
5. Studies with children and adolescents with a confirmed diagnosis of epilepsy (any type)
6. Studies with rates of depression and anxiety before and after intervention
7. From inception to date
8. All languages

Exclusion Criteria

1. Case series and case reports
2. Not possible to separate children data from a total child and adult sample (mixed ages)
3. Not possible to separate children with depression and/or anxiety from other psychiatric disorders
4. Not possible to distinguish depression and anxiety from other psychiatric and behavioral disorders (e.g., internalizing symptoms, emotional symptoms)
5. Studies including children and adolescent with intellectual disability.
7. Animal studies
8. Editorials, dissertations, abstracts, conference proceedings, letters to the editor, opinions, and studies that fail to report the information required for this review.
9. Studies that fail to report the information required for this review.
10. Review articles, systematic reviews, and meta-analysis (the reference lists will be screened for other relevant
11. Articles will be considered as a source of possible articles not previously detected by our search.

Supplementary Material 2

Supplementary Table 1. Search terms and yields

Database (searched until Oct 01, 2023)	**Search terms used**	**Yield**
Medline via PubMed (1946 to present)	1. Epilepsy[mh] 2. Seizures[mh] 3. Seizure*[tw] 4. Convuls*[tw] 5. Epilep*[tw] 6. 1 OR 2 OR 3 OR 4 OR 5 7. Depressive Disorder[mh] 8. Depression[mh] 9. Mood Disorders[mh] 10. Anxiety Disorders[mh] 11. Anxiety[mh] 12. Depress*[tw] 13. Mood Disorder*[tw] 14. Affective Disorder*[tw] 15. Cyclothym*[tw] 16. Dysthym*[tw] 17. Anxiet*[tw] 18. Anxious[tw] 19. Panic*[tw] 20. Agoraphobia*[tw] 21. Phobia*[tw] 22. Phobic[tw] 23. Obsess*[tw] 24. Compuls*[tw] 25. Hoarding[tw] 26. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 27. Child[mh] 28. Adolescent[mh] 29. Young Adult[mh] 30. Child[tw] 31. Children[tw] 32. Childhood[tw] 33. Adolescen*[tw] 34. Paediatric*[tw] 35. Pediatric*[tw] 36. Teen*[tw] 37. Young adult*[tw] 38. 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 39. 6 AND 26 AND 38	5,016

PsycInfo via APA (1887 to present)	1. IndexTerms: "Epilepsy" 2. IndexTerms: "Audiogenic Seizures" 3. IndexTerms: "Grand Mal Seizures" 4. IndexTerms: "Petit Mal Seizures" 5. IndexTerms: "Status Epilepticus" 6. IndexTerms: "Seizures" 7. Title, Abstract, Keywords: seizure* 8. Title, Abstract, Keywords: convuls* 9. Title, Abstract, Keywords: epilep* 10. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 11. IndexTerms: "Disruptive Mood Dysregulation Disorder" 12. IndexTerms: "Seasonal Affective Disorder" 13. IndexTerms: "Affective Disorders" 14. IndexTerms: "Major Depression" 15. IndexTerms: "Depression Emotion" 16. IndexTerms: "Dysthymic Disorder" 17. IndexTerms: "Endogenous Depression" 18. IndexTerms: "Reactive Depression" 19. IndexTerms: "Recurrent Depression" 20. IndexTerms: "Treatment Resistant Depression" 21. IndexTerms: "Anxiety" 22. IndexTerms: "Anxiety Sensitivity" 23. IndexTerms: "Computer Anxiety" 24. IndexTerms: "Death Anxiety" 25. IndexTerms: "Health Anxiety" 26. IndexTerms: "Mathematics Anxiety" 27. IndexTerms: "Performance Anxiety" 28. IndexTerms: "Social Anxiety" 29. IndexTerms: "Speech Anxiety" 30. IndexTerms: "Test Anxiety" 31. IndexTerms: "Anxiety Management" 32. IndexTerms: "Panic Disorder" 33. IndexTerms: "Panic Attack" 34. IndexTerms: "Panic" 35. IndexTerms: "Phobias" 36. IndexTerms: "Anxiety Disorders" 37. Title, Abstract, Keywords: Depress* 38. Title, Abstract, Keywords: "Mood Disorder*" 39. Title, Abstract, Keywords: "Affective Disorder*" 40. Title, Abstract, Keywords: Cyclothym* 41. Title, Abstract, Keywords: Dysthym* 42. Title, Abstract, Keywords: Anxiet* 43. Title, Abstract, Keywords: Anxious 44. Title, Abstract, Keywords: Panic* 45. Title, Abstract, Keywords: Agoraphobia* 46. Title, Abstract, Keywords: Phobia*	3,582

	47. 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 48. Any Field: Child 49. Any Field: Children 50. Any Field: Childhood 51. Any Field: Adolescen* 52. Any Field: Paediatric* 53. Any Field: Pediatric* 54. Any Field: Teen* 55. Any Field: "Young adult*" 56. 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 57. 10 AND 47 AND 56	
Embase via Elsevier (1947 to present)	1. 'Epilepsy'/exp OR 2. 'Seizure'/de OR 3. 'Seizure*':ti,ab,kw OR 4. 'Convuls*':ti,ab,kw OR 5. 'Epilep*':ti,ab,kw 6. 1 OR 2 OR 3 OR 4 OR 5 7. 'Mood disorder'/exp OR 8. 'Anxiety disorder'/exp OR 9. 'Anxiety'/exp OR 10. 'Depress*':ti,ab,kw OR 11. 'Mood Disorder*':ti,ab,kw OR 12. 'Affective Disorder*':ti,ab,kw OR 13. 'Cyclothym*':ti,ab,kw OR 14. 'Dysthym*':ti,ab,kw OR 15. 'Anxiet*':ti,ab,kw OR 16. 'Anxious':ti,ab,kw OR 17. 'Panic*':ti,ab,kw OR 18. 'Agoraphobia*':ti,ab,kw OR 19. 'Phobia*':ti,ab,kw OR 20. 'Phobic':ti,ab,kw OR 21. 'Obsess*':ti,ab,kw OR 22. 'Compuls*':ti,ab,kw OR 23. 'Hoarding':ti,ab,kw 24. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 25. 'Child'/exp 26. 'Juvenile'/exp OR 27. 'Young adult'/exp OR 28. 'Child':ti,ab,kw OR 29. 'Children':ti,ab,kw OR 30. 'Childhood':ti,ab,kw OR	4,871

	31. 'Adolescen*':ti,ab,kw OR 32. 'Paediatric*':ti,ab,kw OR 33. 'Pediatric*':ti,ab,kw OR 34. 'Teen*':ti,ab,kw OR 35. 'Young adult*':ti,ab,kw 36. 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 37. 6 AND 24 AND 36 38. [embase]/lim NOT ([embase]/lim AND [medline]/lim) 39. 37 AND 38	
CINAHL via EBSCOhost (1937 to present)	1. MH Epilepsy 2. MH Seizures 3. TI,AB seizure* 4. TI,AB convuls* 5. TI,AB epilep* 6. 1 OR 2 OR 3 OR 4 OR 5 7. MH "Depressive Disorder" 8. MH Depression 9. MH "Mood Disorders" 10. MH "Anxiety Disorders" 11. MH Anxiety 12. TI,AB Depress* 13. TI,AB "Mood Disorder*" 14. TI,AB "Affective Disorder*" 15. TI,AB Cyclothym* 16. TI,AB Dysthym* 17. TI,AB Anxiet* 18. TI,AB Anxious 19. TI,AB Panic* 20. TI,AB Agoraphobia* 21. TI,AB Phobia* 22. TI,AB Phobic 23. TI,AB Obsess* 24. TI,AB Compuls* 25. TI,AB Hoarding 26. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 27. MH Child 28. MH Adolescent 29. MH "Young Adult" 30. TI,AB child 31. TI,AB children 32. TI,AB childhood 33. TI,AB adolescen* 34. TI,AB paediatric* 35. TI,AB pediatric* 36. TI,AB teen*	895

	37. TI,AB "young adult*" 38. 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 39. 6 AND 26 AND 38	
Scopus (1823 to present)	1. TITLE-ABS-KEY(seizure*) 2. TITLE-ABS-KEY(convuls*) 3. TITLE-ABS-KEY(epilep*) 4. 1 OR 2 OR 3 5. TITLE-ABS-KEY(depress*) 6. TITLE-ABS-KEY("Mood Disorder*") 7. TITLE-ABS-KEY("Affective Disorder*") 8. TITLE-ABS-KEY(Cyclothym*) 9. TITLE-ABS-KEY(dysthym*) 10. TITLE-ABS-KEY(anxiet*) 11. TITLE-ABS-KEY(anxious) 12. TITLE-ABS-KEY(panic*) 13. TITLE-ABS-KEY(Agoraphobia*) 14. TITLE-ABS-KEY(Phobia*) 15. TITLE-ABS-KEY(Phobic) 16. TITLE-ABS-KEY(obsess*) 17. TITLE-ABS-KEY(compuls*) 18. TITLE-ABS-KEY(hoarding) 19. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 20. TITLE-ABS-KEY(child) 21. TITLE-ABS-KEY(children) 22. TITLE-ABS-KEY(childhood) 23. TITLE-ABS-KEY(adolescen*) 24. TITLE-ABS-KEY(paediatric*) 25. TITLE-ABS-KEY(pediatric*) 26. TITLE-ABS-KEY(teen*) 27. TITLE-ABS-KEY("young adult*") 28. 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 29. 4 AND 19 AND 28	11,852
Cochrane Database of Systematic Reviews (Issue 8, August 2020)	1. Seizure* 2. Convuls* 3. Epilep* 4. 1 OR 2 OR 3 5. Depress* 6. "Mood Disorder*" 7. "Affective Disorder*" 8. Cyclothym* 9. Dysthym* 10. Anxiet* 11. Anxious 12. Panic* 13. Agoraphobia*	111

	14. Phobia* 15. Phobic 16. Obsess* 17. Compuls* 18. Hoarding 19. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 20. Child 21. Children 22. Childhood 23. Adolescen* 24. Paediatric* 25. Pediatric* 26. Teen* 27. "Young adult*" 28. 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 29. 4 AND 19 AND 28	
Cochrane Central Register of Controlled Trials (Issue 8, August 2020)	1. Seizure* 2. Convuls* 3. Epilep* 4. 1 OR 2 OR 3 5. Depress* 6. "Mood Disorder*" 7. "Affective Disorder*" 8. Cyclothym* 9. Dysthym* 10. Anxiet* 11. Anxious 12. Panic* 13. Agoraphobia* 14. Phobia* 15. Phobic 16. Obsess* 17. Compuls* 18. Hoarding 19. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 20. Child 21. Children 22. Childhood 23. Adolescen* 24. Paediatric* 25. Pediatric* 26. Teen* 27. "Young adult*" 28. 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 29. 4 AND 19 AND 28	508

ClinicalTrials.gov	1. Seizure* 2. Convuls* 3. Epilep* 4. 1 OR 2 OR 3 5. Depress* 6. "Mood Disorder*" 7. "Affective Disorder*" 8. Cyclothym* 9. Dysthym* 10. Anxiet* 11. Anxious 12. Panic* 13. Agoraphobia* 14. Phobia* 15. Phobic 16. Obsess* 17. Compuls* 18. Hoarding 19. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 20. 4 AND 19 21. AppliedFilter: Child (birth-17)	136

Supplementary Material 3: Level of agreement of rounds 1, 2 and 3 of the Delphi survey

Recommendation	Round 1	Round 2	Round 3
Universal screening for anxiety and depression is recommended in all children and adolescents with new-onset epilepsy age seven or older (baseline) and annually thereafter (adapted from Kerr et al., 2011).	96.97%	N/A	N/A
In line with the Guidelines of the American Academy of Pediatrics (Zuckerbrot et al., 2018), closer surveillance with more frequent screening or clinical evaluation for anxiety and/or depression in children and adolescents with epilepsy is recommended: 1. In adolescents, specifically after the age of 12 years; 2. In those 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. In the setting of significant psychosocial stressors (e.g., family crises, physical and sexual abuse, neglect, and other trauma histories, foster care, adoption); and 4. In those with frequent somatic complaints.	96.97%	N/A	N/A
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).	96.97%	N/A	N/A
When interviewing a child/adolescent with epilepsy about depression and anxiety, it is recommended that both the child/adolescent with epilepsy and their parents be interviewed, whenever possible.	96.97%	N/A	N/A
A formal screening questionnaire, either on paper or electronically, is recommended as a first-level screen to assess for symptoms of depression and anxiety in children and adolescents with epilepsy.	93.94%	N/A	N/A
In busy clinical settings, it is recommended to follow a staged approach beginning with a shorter behavioral checklist (e.g., SDQ). If the screen is positive, it must be followed by a more comprehensive checklist (e.g., CBCL, BASC) or specific rating scales for depression and anxiety, with additional questions on suicidal ideation for children and adolescents with epilepsy who screen positive.	87.88%	N/A	N/A
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.	96.97%	N/A	N/A
Depression and anxiety symptom scales are recommended to quantify the presence and severity of a symptom in children and adolescents with epilepsy; this serves to establish a baseline against which response to therapeutic intervention, such as medication, can then be compared.	96.97%	N/A	N/A
In the clinical and research settings, the CDI/CDI-2 is recommended as the instrument of choice to quantify self-reported depressive symptoms in children and adolescents with epilepsy if translated and validated for the interviewee's language. [#]	71.88%	N/A	N/A

The NDDI-E-Y is also recommended as a reliable and easy-to-apply self-report questionnaire for adolescents (12-17 years) with epilepsy and depressive symptoms. Its use may be limited by the number of available translated versions and the narrow age range. #	71.88%	N/A	N/A
The choice of one questionnaire over the other must consider the expertise of every health care provider and the feasibility in every setting. If the MASC is available, it is recommended as a suitable choice for children and adolescents with epilepsy. *	66.67%	N/A	N/A
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 interviewee's language. *Validation against a structured or semi-structured psychiatric interview	N/A	90.63%	N/A
The choice of questionnaire for the assessment of symptoms of depression and anxiety must consider the expertise of every health care provider, the available resources, and the feasibility in every setting.	N/A	96.88%	N/A
The health care provider involved in the care of children and adolescents with epilepsy must always explain that identifying symptoms is essential to optimize treatment outcome and reduce morbidity using language understandable to laypeople.	100%	N/A	N/A
When assessing symptoms of anxiety and depression with questionnaires that address suicidal behavior, the health care provider must have the consent of the families and the adolescents with epilepsy.*	67.74%	N/A	N/A
Children and adolescents with epilepsy and subthreshold symptoms that do not meet the criteria for a diagnosis of depression or anxiety, are at higher risk to develop these disorders and must be assessed more often.	84.84%	N/A	N/A
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/control in children and adolescents with epilepsy.	100%	N/A	N/A
It is recommended when assessing for symptoms of anxiety and depression that the health care provider ask whether the child or adolescent with epilepsy had a seizure in the past 24 hours as this could reflect an adjustment reaction rather than an anxiety or depressive disorder.	84.38%	N/A	N/A
The direct questioning of parents/caregivers and adolescents with epilepsy about new behavioral adverse effects of ASMs, pre-existing symptoms aggravated by ASMs, and interictal depressive/anxious symptoms is recommended.	100%	N/A	N/A
Parents and adolescents must be informed about the psychotropic properties of an ASM and possible behavioral adverse effects before it is prescribed to a child or adolescent with epilepsy.	96.97%	N/A	N/A
Specialized clinical evaluation by a provider with expertise in mental health (e.g., psychiatrist or psychologist) is highly advisable when possible if clinical concerns for anxiety and depression are noted on history or screening in a child or adolescent with epilepsy.	90.63%	N/A	N/A

A structured and semi-structured psychiatric Interview (e.g., K-SADS) is not feasible in most clinical settings; however, it remains advisable for research purposes (e.g., validation studies) in children and adolescents with epilepsy.	75%	N/A	N/A
A structured and semi-structured psychiatric Interview (e.g., K-SADS) is not feasible in most clinical settings; however, it remains advisable for some research settings (e.g., screening tool validation studies) in children and adolescents with epilepsy.	N/A	74.95%	N/A
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.	N/A	N/A	100%
In clinical settings, the Development and Well-Being Assessment (DABWA) may represent a feasible option to identify mental health disorders in children and adolescents with epilepsy.#*	N/A	62.51%	N/A
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 consists of deciding the treatment setting and determining the type of treatment - pharmacological and/or psychological.	100%	N/A	N/A
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.	100%	N/A	N/A
As treatment is an ongoing process, the treatment plan for anxiety and/or depression in children and adolescents with epilepsy must be reassessed monthly to determine the need for and phase of the treatment.	78.13%	N/A	N/A
The treatment plan for anxiety and/or depression in children and adolescents with epilepsy must be regularly reassessed to determine the need for and phase of the treatment.	N/A	100%	N/A
In line with previous Guidelines (National Institute for Health and Care Excellence [NICE], American Academy of Pediatrics [AAP], American Psychological Association [APA]), a period of watchful monitoring (from 6 to 8 weeks) for mild depression or anxiety must be considered in children and adolescents with epilepsy**.**	77.42%	N/A	N/A
In line with previous Guidelines (National Institute for Health and Care Excellence [NICE], American Academy of Pediatrics [AAP], American Psychological Association [APA]), a period of watchful 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)	N/A	96.88%	N/A
If possible, psychological support or programs to increase resilience and coping must be offered must be offered during the period of monitoring for children with mild depression and anxiety.#	N/A	96.88%	N/A
It is recommended that the watchful monitoring in children and adolescents with epilepsy and mild depression or anxiety, provided by a team member (e.g., nurses, social workers, junior fellows, residents) with	80.64%	N/A	N/A

basic training, include:1. weekly or biweekly visits (onsite, by phone, or online) with regular symptom checking2. 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, and6. educational materials (paper/ website) for families and patients.			
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.	90.63%	N/A	N/A
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).	90.63%	N/A	N/A
Epilepsy clinics/centers must develop clinical care pathways to facilitate access to mental health services for children and adolescents with epilepsy.	100%	N/A	N/A
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.	87.10%	N/A	N/A
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).	93.75%	N/A	N/A
The psychotherapy must be age-appropriate, and for younger children with epilepsy, the family must be involved directly or via family therapy and counseling.	93.75%	N/A	N/A
Periictal symptoms in children and adolescents with epilepsy respond poorly to antidepressant medication, and psychotherapy is advisable when symptoms are related to loss of control associated with seizure unpredictability.	71.88%	N/A	N/A
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.	N/A	81.26%	N/A
Health care providers (neurologists, epileptologists with training/ skills) 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.	96.77%	N/A	N/A
SSRIs must be regarded as 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.	86.67%	N/A	N/A

Tricyclic antidepressants and monoamine oxidase inhibitors are not recommended for the treatment of anxiety and/or depression in children and adolescents with epilepsy.	74.19%	N/A	N/A
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.	N/A	87.5%	N/A
Slow titration of SSRIs 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.	83.87%	N/A	N/A
Psychotherapy should be associated with pharmacotherapy if considered appropriate for the treatment of anxiety and/or depression in children and adolescents with epilepsy.	87.10%	N/A	N/A
Epileptologists and/or pediatric neurologists should communicate with other healthcare providers, especially mental health providers, if they are prescribing a new antiseizure medication with psychotropic effect.	81.25%	N/A	N/A
Epileptologists and pediatric neurologists prescribing antidepressants to children and adolescents with epilepsy must provide monthly monitoring to assess adverse effects, self-harm, and suicide risk. On site or online interviews with children and family members is recommended.	79.31%	N/A	N/A
A health care provider must monitor children and adolescents with epilepsy prescribed with antidepressants for adverse effects, self-harm, and suicide risk. Onsite or online interviews with children and family members is recommended.	N/A	93.75%	N/A
In busy clinical settings, a checklist with the most common antidepressant/anxiolytic adverse effects is recommended in children and adolescents with epilepsy.	80.65%	N/A	N/A
Education of family/primary caregiver is essential to guarantee adherence to antidepressant/anxiolytic and adequate monitoring of psychiatric symptoms and adverse-effects in children and adolescents with epilepsy.	96.77%	N/A	N/A
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 take into account several domains, including: 1. Efficacy 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).	100%	N/A	N/A
In line with the American Academy of Child (2007) and Adolescent Psychiatry 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.	80.64%	N/A	N/A

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.	87.10%	N/A	N/A
If antidepressant/anxiolytic treatment inefficacy (i.e., symptoms, functioning) or partial efficacy is detected over a period of six to eight weeks in a child or adolescent with epilepsy, referral to a mental health provider (e.g., psychiatrist, psychologist) is recommended.	90%	N/A	N/A
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 require immediate referral or treatment in a specialized setting (e.g., inpatient treatment).	83.87%	N/A	N/A
The ongoing involvement of the managing epilepsy 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.	96.78%	N/A	N/A

N/A: non-applicable

*Removed due to the level of agreement (<70%)

#Included or modified due to comments from the Delphi Panel

Supplementary Material 4A: GRADE for Validation Studies

Question: Should [index test CDI] be used to diagnose [Depressive Symptoms] in [pediatric epilepsy population]?

Question: Should [index test CDI] be used to diagnose [Depressive Symptoms] in [pediatric epilepsy population]?

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 100 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 58%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with [Depressive/ Symptoms])	1 studies 21 patients	cohort & case-control type studies	serious [a]	not serious	not serious	serious [b,c]	publication bias strongly suspected [d]	34 (21 to 44)	0 (0 to 0)	0 (0 to 0)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [Depressive Symptoms])								24 (14 to 37)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without [Depressive Symptoms])	1 studies 11 patients	case-control type accuracy study	serious [a]	not serious	not serious	serious [b,c]	publication bias strongly suspected [d]	31 (18 to 38)	73 (43 to 90)	73 (43 to 90)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [Depressive Symptoms])								11 (4 to 24)	27 (10 to 57)	27 (10 to 57)	

Sensitivity	0.58 (95% CI: 0.37 to 0.76)
Specificity	0.73 (95% CI: 0.43 to 0.90)

Prevalences	58%	0%	0%

Explanations

a. Unclear risk of bias in index, reference, and flow and timing domains.

b. The best specificity to predict an affective and anxiety disorder diagnosis in the patients compared with the CDI compared to KSADS.

c. CI95% imprecise, since the review authors calculated its value.

d. A single study.

Question: Should [index test CBCL] be used to diagnose [Anxiety and Depressive Symptoms] in [pediatric epilepsy population]?

Sensitivity	0.38 (95% CI: 0.27 to 0.51)
Specificity	0.92 (95% CI: 0.87 to 0.95)

Prevalences	21%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 100 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 21%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with [Anxiety and Depressive Symptoms])	1 studies 57 patients	cohort & case-control type studies	serious [a]	serious [b]	not serious	serious [c]	publication bias strongly suspected [d]	8 (6 to 11)	0 (0 to 0)	0 (0 to 0)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [Anxiety and Depressive Symptoms])								13 (10 to 15)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without [Anxiety and Depressive Symptoms])	1 studies 114 patients	cohort & case-control type studies	serious [a]	serious [b]	not serious	serious [c]	publication bias strongly suspected [d]	73 (69 to 75)	92 (87 to 95)	92 (87 to 95)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [Anxiety and Depressive Symptoms])								6 (4 to 10)	8 (5 to 13)	8 (5 to 13)	

Explanations

a. Unclear risk of bias in index, reference, and flow and timing domains.

b. Anxiety and depression were pooled.

c. CI95% imprecise, since the review authors calculated its value.

d. A single study.

Question: Should [index test MASC] be used to diagnose [Anxiety Symptoms] in [pediatric epilepsy population]?

Sensitivity	0.87 (95% CI: 0.71 to 0.94)
Specificity	0.72 (95% CI: 0.49 to 0.86)

Prevalences	15%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 100 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 15%	
True positives (patients with [Anxiety Symptoms])	1 studies 36 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	publication bias strongly suspected [b]	13 (11 to 14)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [Anxiety Symptoms])								2 (1 to 4)	
True negatives (patients without [Anxiety Symptoms])	1 studies 21 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	publication bias strongly suspected [b]	61 (42 to 73)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [Anxiety Symptoms])								24 (12 to 43)	

Explanations

a. Unclear risk of bias in index, reference, and flow and timing domains.

b. Single study. CI Specificity large.

Question: Should [index tes NDDI 11 items] be used to diagnose [Depressive Symptoms] in [Youth with Epilepsy population]?

Sensitivity	0.80 (95% CI: 0.58 to 0.99)
Specificity	0.71 (95% CI: 0.50 to 0.80)

Prevalences	34%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 100 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 34%	pre-test probability of 0%	pre-test probability of 0%	
True positives (patients with [Depressive Symptoms])	1 studies 5 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	publication bias strongly suspected [c]	27 (20 to 34)	0 (0 to 0)	0 (0 to 0)	⨁◯◯◯ VERY LOW
False negatives (patients incorrectly classified as not having [Depressive Symptoms])								7 (0 to 14)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without [Depressive Symptoms])	1 studies 82 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	publication bias strongly suspected [c]	47 (33 to 53)	71 (50 to 80)	71 (50 to 80)	⨁◯◯◯ VERY LOW
False positives (patients incorrectly classified as having [Depressive Symptoms])								19 (13 to 33)	29 (20 to 50)	29 (20 to 50)	

Explanations

a. Unclear risk of bias in index, reference, and flow and timing domains.

b. Only one study and wide confidence intervals.

c. Single study.

Supplementary Material 4B: GRADE for primary outcomes (treatment).

Certainty assessment							Certainty assessment
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Efficacy of non-pharmacological treatment (non-CBT) for depressive symptoms							
3	RCT	Serious[a]	Serious[b]	Not serious[c]	Not serious[d]	None	⊕⊕◯◯ LOW
Efficacy of non-pharmacological treatment (CBT) for depressive symptoms (Prevention of depressive disorder)							
1	RCT	Serious[e]	Not serious	Not serious	Not serious	Publication bias strongly suspected[f]	⊕⊕◯◯ LOW
Efficacy of non-pharmacological treatment (CBT) for anxiety disorder							
2	Observational studies	Serious[g]	Not serious	Not serious	Serious[h]	Publication bias strongly suspected all plausible residual confounding would reduce the demonstrated[f]	⊕⊕◯◯ LOW
Efficacy of pharmacological treatment (SSRI) for depressive disorder (MDD)							
1	Observational studies	Serious[h]	Not serious	Not serious	Serious[i]	Publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect[f]	⊕⊕◯◯ LOW

Explanations

a. 2/3 studies with a high risk of bias and 1/3 unclear. Limitation: allocation, blinding of participants and staff measurements. Significant limitations some criteria sufficient to lower confidence in the estimate of effect.

b. Inconsistency can be explained by differences in populations, interventions, or outcomes, mainly in intervention and outcomes.

c. The available studies may have measured the impact of the intervention of interest on outcomes related to, but different from, those of primary importance to patients.

d. Very few events. IC as expected.

e. High risk of bias in selection of the reporting results.

f. Small sample sizes. There is no “negative” study.

g. 2/2 high risk of bias: confounding and measurements of outcomes.

h. Reasons: 1. same sample in both studies; 2. low number of patients; 3. well-controlled epilepsy (not representative); 4. not controlled for confounding factors.

i. High risk of bias: confounding and measurements of outcomes.

j. CI not available.