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Review

Psychosocial factors associated with anxiety and depression in adolescents with epilepsy: A systematic review

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ABSTRACT

Anxiety and depression are common in adolescents with epilepsy. Identifying psychosocial risk factors for anxiety and depression is essential for adolescents with epilepsy to receive appropriate support. This systematic review synthesised findings of studies examining the relationship between psychosocial factors and anxiety and/or depression in adolescents with epilepsy. Outcomes were anxiety, depression, and mixed anxiety & depression. Six electronic databases were searched for studies which: used cross-sectional or prospective designs; quantitatively evaluated the relationship between psychosocial factors and anxiety and/or depression; presented results for adolescents with epilepsy aged 9–18 years; and used validated measures of anxiety and/or depression. Psychosocial factors were categorised as intrapersonal, interpersonal, or parent-specific factors. Sixteen studies (23 articles) were included. All but one were cross-sectional. Regarding intrapersonal factors, alternative mental health difficulties were consistently positively associated with all three outcomes. Negative attitude towards epilepsy, lower seizure self-efficacy, lower self-esteem and stigma were consistently positively associated with depression. Interpersonal factors (i.e., lower family functioning assessed from an adolescent's perspective) and parent-specific factors (i.e., parental stigma, stress, anxiety and psychopathology) were positively associated with at least one outcome. Adolescent epilepsy management should exceed assessment of biological/biomedical factors and incorporate assessment of psychosocial risk factors. Prospective studies examining the interplay between biological/biomedical factors and the psychosocial factors underpinning anxiety and depression in adolescents with epilepsy are needed.

1. Introduction

Epilepsy is one of the most common neurological conditions in childhood [1], affecting around 22 million youth worldwide [2]. Epilepsy accounts for approximately 13 million disability adjusted life years each year [3] and is responsible for approximately 0.5 % of the global burden of disease [4]. Around 19 % and 14 % of youth with epilepsy[1] meet diagnostic criteria for anxiety and depressive disorders, respectively [5], 3 to 5 times higher than in the general youth population [6]. In comparison to healthy control samples, youth with epilepsy also experience significantly higher anxiety ($d = 0.57$) and depressive ($d = 0.42$) symptoms [5]. Anxiety and/or depression in youth with epilepsy is associated with poorer academic achievement, increased suicidal ideation, reduced quality of life (QoL), and higher health resource utilization [7–10]. It is therefore imperative that youth with epilepsy have access to appropriate interventions to reduce anxiety and depression. To inform the development and implementation of appropriate interventions, identifying risk factors associated with anxiety and depression in youth with epilepsy is essential.

Potential risk factors associated with anxiety and depression in epilepsy have been categorised into four main areas: sociodemographic (e.g., age, gender), antiseizure medications (ASMs; e.g., ASM type, mono- *vs.* poly-therapy), epilepsy-specific characteristics (e.g., seizure type and frequency, age of epilepsy onset), and psychosocial variables [11].

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[1] Cited studies defined 'youth with epilepsy' across slightly different age ranges. We have used the term 'youth with epilepsy' as a general term encompassing children and adolescents aged 0–18.

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Research has primarily focused on identifying sociodemographic, ASM and epilepsy-specific risk factors [11,12] and has thus far produced mixed findings [13–15]. While efforts to identify psychosocial risk factors has received less attention than the other three areas [12], there is growing evidence that psychosocial factors have a greater impact on anxiety and depression in people with epilepsy than risk factors across the other three areas [16–20]. As all ASMs can trigger anxiety and depressive symptoms [21], switching to an alternative ASM following occurrence of anxiety and/or depressive symptoms is appropriate clinically. However, ASM side-effects alone do not explain the high rates of anxiety and depression experienced by youth with epilepsy [22,23]. Moreover, as many sociodemographic and epilepsy-specific variables are not readily modifiable (e.g., age, seizure type) the clinical utility of identifying risk factors across these areas is questionable. Therefore, identifying psychosocial risk factors associated with anxiety and depression in youth with epilepsy appears a more clinically useful path [12,24].

Despite limited understanding of the psychosocial risk factors associated with anxiety and depression in youth with epilepsy, 10 trials have evaluated the efficacy of psychological interventions for anxiety and/or depression in youth with epilepsy [25–34]. The psychological interventions evaluated in these trials aimed to modify a range of psychosocial factors including attitude toward having epilepsy, coping skills, illness appraisals, and family dynamics. Eight of the 10 trials were primarily designed to evaluate the feasibility and acceptability of interventions (i.e., phase I trials) [25–27,30–34]; while only two were full-scale trials primarily designed to test intervention efficacy (i.e., phase II trials) [28,29]. Findings are mixed; seven trials reported a significant reduction in anxiety and/or depression from pre- to post-intervention [26,28–31,33,35] and three reported a significant reduction from pre-intervention to 3- or 6-month follow-up [26,29,31]. Alternatively, three reported no significant reduction in anxiety and/or depression from pre- to post-intervention [27,32,34] and one reported no significant reduction from pre-intervention to 3-month follow-up [27]. These findings indicate that psychological interventions may reduce anxiety and/or depression in youth with epilepsy. However, as most of these trials were phase I intervention trials with underpowered samples, confidence in such findings is limited. Moreover, as none of the trials explored which psychosocial variables mediated treatment effects, it is unclear which psychosocial variables targeted for modification in these interventions were influential (or not) in the reduction of anxiety and/or depression.

Prior to conducting large-scale high-quality psychological intervention trials for youth with epilepsy, it is important to develop a better understanding of the psychosocial variables associated with anxiety and depression in youth with epilepsy, as this could help inform the development of theoretically-driven psychological interventions, considered best practice in intervention development [36,37]. The psychosocial variables associated with anxiety and depression in youth with epilepsy can differ depending on the life stage of a young person (e.g., young childhood *vs.* adolescence) [38]. As adolescence is a time of physical, social, and psychological change, developing an understanding of the psychosocial variables associated with anxiety and depression in youth with epilepsy during adolescence is a prerequisite to developing effective and age-appropriate psychological interventions for this group. While several studies have examined whether psychosocial variables are associated with anxiety and/or depression in adolescents with epilepsy [14,15,39], no systematic review has been conducted. The aim of the current review, therefore, is to systematically identify, appraise and synthesise the findings of studies examining the relationship between psychosocial variables (i.e., subjective psychological and/or social variables) and anxiety and/or depression in adolescents with epilepsy.

2. Method

This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [40]. The protocol is registered in the PROSPERO database (CRD42021293698).

2.1. Eligibility

Studies were included if they: 1) used a cross-sectional or prospective design; 2) conducted and reported findings of a quantitative analysis exploring the relationship between anxiety and/or depression and a psychosocial variable (multivariate analyses were included if anxiety and/or depression was the outcome variable); 3) reported findings specifically for adolescents with epilepsy aged 9–18; 4) assessed anxiety and/or depression using a validated self-report questionnaire (or subscale of a validated self-report questionnaire) or a validated structured diagnostic interview; and 5) were published in English in a peer-reviewed journal.

Prospective studies were included if relevant analyses were conducted at baseline or if anxiety and/or depression was measured at follow-up. Intervention studies were included if relevant analyses were conducted pre-intervention (post-intervention data was excluded). Studies were excluded if all participants were specifically recruited based on a medical or neurological comorbidity (e.g., if having an intellectual disability or non-epileptic seizure disorder were part of the inclusion criteria for the whole sample). Commentaries, conference abstracts, case-studies, editorials, and review articles were excluded.

Outcome variables were anxiety, depression, and mixed anxiety & depression. Psychosocial variables were grouped into three categories based on the following definitions: 'intrapersonal factors' (subjective psychological and/or social characteristics located directly within the adolescent with epilepsy); 'interpersonal factors' (involving the relationship between the adolescent with epilepsy and another); and 'parent-specific factors' (subjective psychological and/or social characteristics located directly within the parent of the adolescent with epilepsy).

2.2. Search strategy

Medline, Web of Science, PsycINFO, CINAHL, psycARTICLE, and AMED were searched from their inception to July 2022 using a combination of terms related to epilepsy, emotional distress, and youth (see Appendix A for search terms). Search terms were limited to titles and abstracts and filtered by language (English) and document type (journal articles). Reference lists of included studies and relevant reviews [14,15,39,41] were hand-searched to ensure relevant articles were not missed. Searches were updated in March 2023 to identify additional relevant studies.

2.3. Screening and selection

Study screening was shared by three reviewers (JT, CD, & CM). One reviewer (JT) independently assessed all titles and abstracts; while two reviewers (CD & CM) each independently assessed approximately half of all titles and abstracts. At this stage, agreement between JT and the other reviewers (CD & CM) was high (91 %). Next, the full-text of all potentially relevant articles were retrieved and assessed for inclusion by one reviewer (JT). To check for consistency in selection, the other reviewers (CD & CM) each independently assessed a random 10 % of full-text articles. At both stages, discrepancies were resolved through discussion between two reviewers (i.e., JT & CD; JT & CM). Any unsolved discrepancies were resolved through discussion with a fourth reviewer (PF or MGC).

2.4. Data extraction and synthesis

Using a specially-devised data extraction form (see Appendix B), data were extracted and tabulated from all eligible studies by one reviewer

(JT). When studies recruited a broader sample, which included relevant analyses for a sub-group of participants meeting our eligibility criteria (i.e., adolescents with epilepsy aged 9–18), only data for the population meeting our eligibility criteria were extracted.

Extracted data included general study details, participant details, design and methodology details, and a summary of reported findings (including were possible relevant *p*, *t*, and *F* values, correlation coefficient values, standardized beta coefficients or odds ratios, and percentage of individual variance explained; R^2 values for overall models and unstandardized beta coefficients were not extracted). Articles that reported data from the same study were interpreted and referred to as a single study with all relevant articles listed. Each outcome variable (anxiety, depression, and mixed anxiety & depression) was examined separately.

Due to heterogeneity across studies, meta-analysis was considered inappropriate. Therefore, data were synthesised narratively. Correlation coefficient values of $\leq$ 0.3, 0.4 to 0.6, and $\geq$ 0.7, and OR values of $\leq$ 1.68, 1.69 to 3.47, and $\geq$ 6.7 were interpreted as weak, moderate and strong, respectively [42,43].

2.5. Risk of bias

Risk of bias of included studies was assessed using a modified version of a quality assessment tool for observational studies developed by the

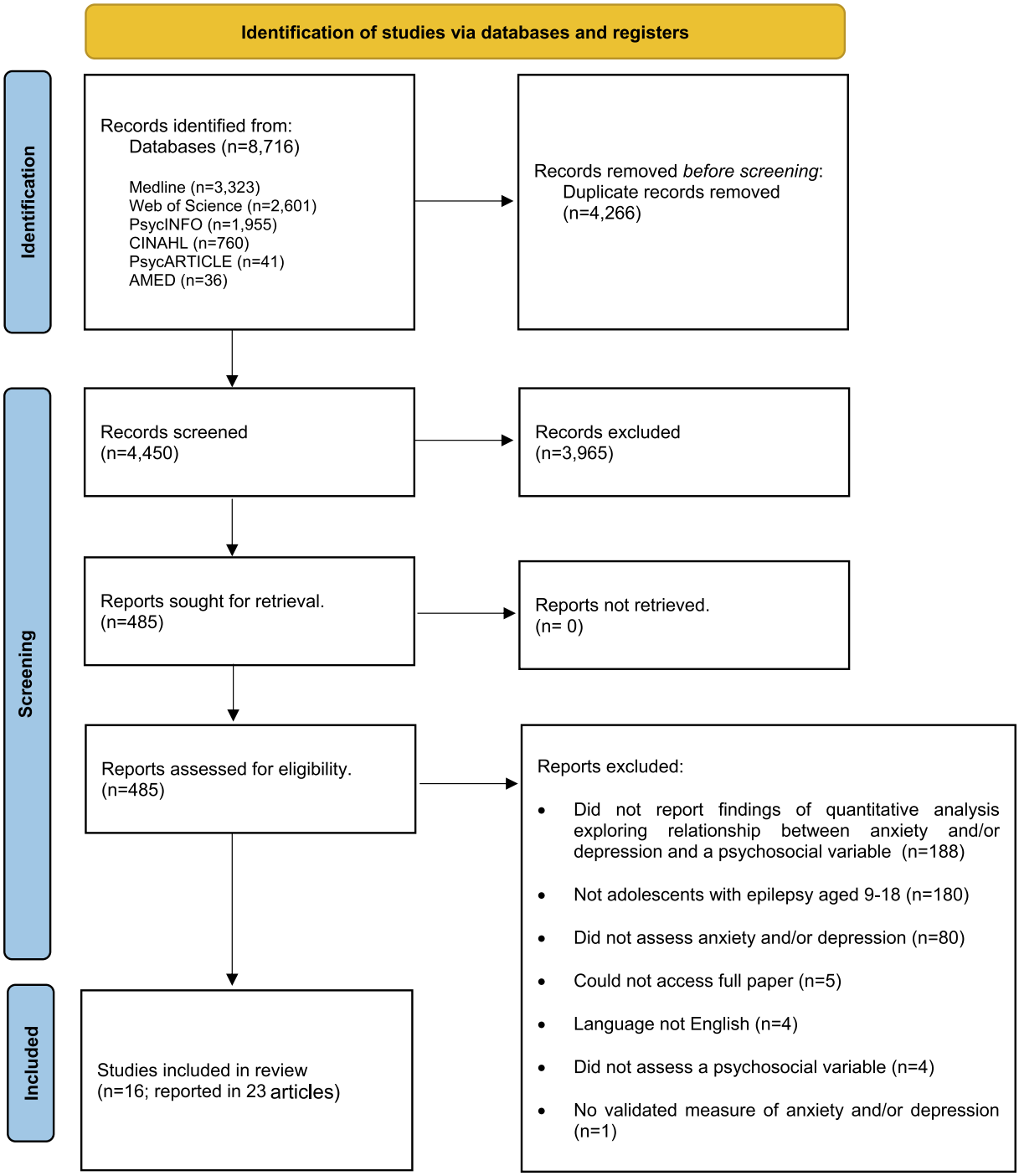

Fig. 1. PRISMA diagram summarising the screening process for included studies.

Agency for Healthcare Research and Quality [44] (see Appendix C). One reviewer (JT) independently assessed the quality of all included studies, while two reviewers (CD & CM) each independently assessed approximately half of included studies. Discrepancies were resolved through discussion between reviewers (i.e., JT & CD; JT & CM). Unresolved discrepancies were resolved through discussion with a fourth reviewer (PF or MGC). When assessing the risk of bias of analysis methods, we only assessed the risk of bias for the analyses included in this review (i.e., analyses evaluating the relationship between psychosocial variables and anxiety and/or depression).

3. Results

The electronic database search retrieved 8,716 articles. After removal of duplicates, 4,450 remained for screening based on title and abstract. Of these, 3,965 clearly did not meet inclusion criteria. The full-text of the remaining 485 articles were assessed for eligibility. Overall, 23 articles corresponding to 16 studies were eligible and included (Fig. 1; see Appendix D for reference list of included articles).

Study characteristics are displayed in Table 1. Seven studies were conducted in North America and all but one study was cross-sectional. Nine studies (14 articles) measured one outcome (e.g., anxiety, depression, or mixed anxiety & depression), six studies (eight articles) measured two outcomes, and one study (one article) measured all three outcomes. Depression was the most frequently assessed outcome (13 studies, 20 articles); followed by anxiety (six studies, eight articles); and mixed anxiety & depression (five studies, five articles). Of the 13 studies measuring depression, 10 used self-report measures, two used self-report and parent-proxy measures, and one used a structured clinical interview. Of the six studies measuring anxiety, four used self-report measures; one used a parent-proxy measure, and one used a structured clinical interview. Of the five studies measuring mixed anxiety & depression, three used self-report measures and two used parent-proxy measures. The most used depression outcome measure was the Child Depression Index (CDI) [45], used in seven studies (10 articles); and the most used mixed anxiety & depression outcome measure was the anxiety/depression subscale of the Child Behavior Checklist (CBCL) [46,47], used in four studies (four articles). No anxiety outcome measure was used in more than one study. A glossary of the outcome measures used are shown in Table 2. Only six studies included multivariate analysis.

Participant characteristics are displayed in Table 3. Sample sizes ranged from 23 to 289. Mean sample age ranged from 11.8 to 15.6 years. Mean duration of epilepsy was reported in eight studies and ranged from 5 to 7.5 years. The proportion of participants taking ASMs was reported in 14 studies and ranged from 75 % to 100 %.

Only six studies (eight articles) included multivariate analysis investigating whether psychosocial variables are associated with anxiety and/or depression (in which anxiety and/or depression was the outcome variable). Of those six studies, there was considerable variation in entry method, and it was often unclear which variables were included in the final model. There was also considerable variability in the statistics reported for multivariate analysis. While only standardized beta coefficients are included in the narrative write-up, additional statistics (e.g., R^2 values) are included in Table 5, were possible.

3.1. Risk of bias

Risk of bias for the 16 included studies is presented in Table 4. The main limitations related to sample size calculation and control of potential confounders. Only one study [48] justified the sample size solely based on sample size recommendations and no study conducted a power analysis. Most studies did not control for confounders (as most conducted only univariate analyses).

Of the six studies (eight articles) conducting multivariate analyses, only three studies (across three articles) [19,38,49] controlled for all relevant confounders (i.e., variables significantly associated with anxiety and/or depression from univariate analyses and clinical/demographic variables associated with anxiety and/or depression in youth with epilepsy in prior reviews, i.e., age, gender, seizure frequency, number of ASMs, duration of epilepsy) [14,39]. The other three studies (across five articles) [50–54] only partially controlled for relevant confounders. All studies recruited participants through neurology or paediatric clinics or epilepsy centres, increasing the likelihood participants had a confirmed epilepsy diagnosis. However, only three studies (four articles) [49,52,55,56] sampled patients consecutively, a method which reduces likelihood of selection bias. As no study conducted power analysis, general rules of thumb were used to decide if studies were adequately powered (i.e., $n \geq 50$ for univariate analysis; $n \geq 104 +$ the number of IVs entered in the model for multivariate analysis) [57,58]. Nine studies (across 12 articles) [19,48,56,59–67] had an adequately powered sample to conduct their analyses; while seven studies (across 11 articles) [38,49–55,68–70] conducted some or all of their analyses with an underpowered sample. Most studies used validated measures to assess psychosocial variables.

Table 1
Study characteristics.

Author	Sampling method	Recruitment setting	Design	Country
Adewuya & Ola, 2005 [49]; Adewuya & Oseni, 2005 [55]	Consecutive	Neuropsychiatric outpatient clinics	Cross-sectional	Nigeria
Austin et al. 2004 [59]; Caplin et al. 2002 [60]; Dunn et al. 2009 [61]	Purposive	Paediatric neurology outpatient clinics, schools (via school nurses), paediatric neurologist private practices	Cross-sectional	USA
Çengel-Kültür et al. 2009 [68]	Purposive	Paediatric clinic	Cross-sectional	Turkey
Dunn et al. 1999 [50]; Haber et al. 2003 [51]	Purposive	Paediatric neurology outpatient clinics, neurologist private practices	Cross-sectional	USA
Eddy et al. 2010 [56]	Consecutive	Paediatric neuropsychiatry clinic	Cross-sectional	UK
Güven et al. 2015 [48]	Purposive	Paediatric neurology clinics	Cross-sectional	Turkey
Kellerman et al. 2017 [62]	Purposive	Epilepsy clinic	Cross-sectional	USA
Kwong et al. 2016 [19]; 2016 [63]	Purposive	Neurology outpatient clinics	Cross-sectional	Hong Kong
Lai et al. 2015 [64]	Purposive	Paediatric hospital, hospitals, medical centre	Prospective (6-month follow-up)	USA
Miniksar et al. 2022 [65]	Purposive	Paediatric neurology outpatient clinics	Cross-sectional	Turkey
Puka et al. 2017 [38]	Purposive	Epilepsy centres	Cross-sectional	Canada
Rizou et al. 2015 [52]	Consecutive	Paediatric epilepsy clinic	Cross-sectional	Greece
Shatla et al. 2011 [69]	Prospective	Paediatric epilepsy clinic	Cross-sectional	Egypt
Wagner et al. 2009 [54], 2012 [70], 2012 [53]	Purposive	Paediatric epilepsy clinic	Cross-sectional	USA
Wagner et al. 2013 [66]	Purposive	Epilepsy centre	Cross-sectional	USA
Young et al. 2023 [67]	Purposive	Paediatric outpatient clinics	Cross-sectional	South Korea

Table 2
Glossary of anxiety and depression measures used in included studies.

Validated outcome measure/structured clinical interview	Abbreviation	Assessment method	Outcome	Studies used (n)	Articles used (n)
Children's Depression Inventory[a]	CDI	Self-report	Depression	7	10
Child Behaviour Checklist (anxiety/depression subscale)[b,c]	CBCL	Parent-proxy; self-report	Mixed anxiety & depression	4	4
Neurological Disorders Depression Inventory-Epilepsy for Youth	NDDI-E-Y	Self-report	Depression	2	2
16-item Quick Inventory of Depressive Symptomatology- Self-Report	QIDS-SR16	Self-report	Depression	1	1
Adolescent Symptom Inventory/ Child Symptom Inventory-4 (anxiety & depressive disorder items)	ASI-4	Parent-proxy	Anxiety (anxiety disorders), depression (depressive disorders)	1	1
Behavior Assessment System for Children – 2nd edition (depression subscale)	BASC-II	Parent-proxy	Depression	1	1
Diagnostic Interview Schedule for Children – version 4 (anxiety & depressive disorder modules)[d]	DISC-IV	Structured clinical interview	Anxiety (anxiety disorders), depression (depressive disorders)	1	2
Generalized Anxiety Disorder-7	GAD-7	Self-report	Anxiety	1	1
Hospital Anxiety & Depression Scale	HADS	Self-report	Anxiety, depression	1	2
Multidimensional Anxiety Scale for Children	MASC	Self-report	Anxiety	1	1
Neurology Quality of Life Measurement System – anxiety & depression subscales	NeuroQol	Self-report	Anxiety, depression	1	1
Revised Children's Anxiety & Depression Scale	RCADS	Self-report	Mixed anxiety & depression	1	1

Note. [a]Five studies used the original 27-item version of the CDI & two used the 27-item Turkish version of the CDI; [b]two studies used the CBCL parent-proxy version & two used the youth self-report (YSR) version; [c]one study used the adapted Turkish version of the CBCL; [d]Adewuya & Ola (2005) [49] and Adewuya & Oseni, (2005) [55] administered the youth and parent-proxy version of the DISC-IV. The authors combined the information from the two versions. If either respondent (youth or parent) reported information that met criteria for the relevant psychiatric diagnoses within the last 12 months, the authors concluded that the relevant psychiatric diagnosis was currently present.

3.2. Psychosocial factors associated with anxiety

3.2.1. Intrapersonal factors

3.2.1.1. Epilepsy-specific beliefs and attitudes. One study (two articles) [49,55] assessed attitude towards having epilepsy, perceived epilepsy-related stigma, and the impact of epilepsy on adjustment and development. When entered in a multiple regression model with clinical, demographic and other psychosocial variables, none of these variables were significantly associated with anxiety.

3.2.1.2. General beliefs and attitudes. One study [63] measured self-esteem and one [56] measured sense of self (a similar construct to self-esteem). Anxiety was significantly associated with both global and specific aspects of self-esteem (ρ = -0.22 to -0.48; *OR* = 1.13 to 1.29) but was not significantly associated with sense of self.

3.2.1.3. Alternative mental health difficulties. Four studies [19,38,61,64] assessed the relationship between anxiety and alternative mental health difficulties. Anxiety was significantly associated with depression (r = 0.66; *OR* = 1.21) [19,38], even after controlling for clinical and demographic variables (*OR* = 1.22) [19]. Anxiety was also significantly associated with mixed anxiety & depression (r = 0.48 for those aged 9–12; r = 0.62 for those aged 13–14) [61]. When assessed cross-sectionally, anxiety was significantly associated with mental wellbeing (defined as 'emotional functioning' and 'general mental health'; ρ = -0.51 to -0.60) [64]. However, when assessed prospectively, mean change in anxiety from baseline to 6-month follow-up was not significantly associated with mean change in mental wellbeing [64].

3.2.1.4. Other intrapersonal factors. Two studies [56,64] assessed QoL. Eddy et al. (2010) found that QoL was significantly associated with anxiety (ρ = -0.40) [56]. However, after correcting for multiple comparisons, this association was no longer significant. Lai et al. (2015) found that, when assessed cross-sectionally, QoL was significantly associated with anxiety (ρ = -0.29) [64]. However, when assessed prospectively, Lai et al. (2015) found that mean change in QoL from baseline to 6-month follow-up was not significantly associated with mean change in anxiety [64]. General life satisfaction was assessed in one study [56] and was not significantly associated with anxiety.

3.2.2. Interpersonal factors

3.2.2.1. Family factors. Two studies [38,49] assessed adaptive family resources (i.e., family mastery, family esteem & communication, family social support, financial well-being). After accounting for sex, number of ASMs and/or parental anxiety, adaptive family resources were not significantly associated with anxiety. Two studies [38,55] assessed family functioning (both from a parental perspective). Findings were mixed. Adewuya & Oseni (2005) found a significant association with anxiety (*t*-test only) [55]; while Puka et al. (2017) found no significant association [38].

3.2.2.2. Other interpersonal factors. Single studies assessed other interpersonal factors. Anxiety was significantly associated with social functioning (ρ = -0.37) [64]. Anxiety was also significantly associated with quality of family and peer relationships (ρ = -0.29) but after correcting for multiple comparisons, this association was no longer significant [56]. Anxiety was not significantly associated with satisfaction with one's broader social and cultural environment [56].

3.2.3. Parent-specific factors

3.2.3.1. Parental epilepsy-specific beliefs and attitudes. Parental perceived stigma towards epilepsy (i.e., parent's perception of their child being stigmatised) was assessed in one study [49]. When entered in a multiple regression model with clinical, demographic, and other psychosocial variables, parental perceived stigma was not significantly associated with anxiety.

3.2.3.2. Parental mental health difficulties. Two studies [38,49] assessed parental mental health difficulties and reported contradictory findings. When entered in a multiple regression model with clinical, demographic and/or other psychosocial variables, anxiety was significantly associated with parental anxiety (β = 0.35) [38] but was not significantly associated with parental psychopathology [49] or parental depression [38].

Table 3
Participant characteristics from included studies.

Author	N	Mean age (years) (SD) [range]	Ethnicity or race (%)	Female (%)	Mean age at seizure onset (years) (SD)	Mean epilepsy duration (years) (SD)	Seizure type(s) (%)	Seizure frequency (%)	Number of ASMs (%)	Major exclusion criteria
Adewuya & Ola, 2005 [49]; Adewuya & Oseni, 2005[a] [55]	102	14.46 (1.98) [12–18]	Yoruba ethnic group: 96[b]	36	8.9 (3.55)	7.5 (3.03)	Complex partial: 45 Generalized: 33 Simple partial: 10 Secondary generalized: 6 Mixed seizures: 6	0 in last month: 55 1–2 in last month: 33 ≥3 in last month: 12	Monotherapy: 64 Polytherapy: 36	'Severe & profound' intellectual disability; Nonverbal
Austin et al. 2004[c] [59]; Caplin et al. 2002 [60]; Dunn et al. 2009[d] [61]	175	11.9 (1.8) [9–14]	White: 91 African American/ other: 9	49	6.5 (3.85)	5.2 (3.85)	Generalized tonic-clonic: 22 Complex partial: 38 Partial with secondary generalized: 25 Absence: 19 Elementary partial: 7 AAM: 1 Unknown: 1	NR	≥1 ASMs at study entry: 100	Intellectual disability; Comorbid 'major chronic physical disorder'; Progressive brain disorder; Epilepsy diagnosis < 6 months
Çengel-Kültür et al. 2009 [68]	41	14 (1.6) [NR]	NR	59	6.7 (3.54)	NR	Generalized: 90 Secondary generalized: 7 Partial: 1	< 2 per year: 7 > 1 per month: 32 1–3 per 6 months: 61	Monotherapy: 100	Intellectual disability Comorbid chronic illness; Non-idiopathic epilepsy
Dunn et al. 1999 [50]; Haber et al. 2003[e,f] [51]	115	14.4 (NR) [NR]	White: ~90[g]	48	4.9 (NR)	NR	NR	NR	≥ 1 ASMs at study entry: 100[j]	Intellectual disability Comorbid chronic illness Epilepsy diagnosis < 1 year[f]
Eddy et al. 2010 [56]	50	12.2 (1.4) [10–16]	NR	48	NR	NR	Seizure free: 100	Seizure free: 100	≥ 1 ASMs at study entry: 100	Non-controlled epilepsy
Güven et al. 2015 [48]	166	13.5 (2.57) [9–17]	NR	49	NR	NR	NR	NR	NR	'Mental disabilities'; Comorbid chronic illness; Epilepsy diagnosis < 6 months
Kellerman et al. 2017 [62]	99	14.7 (1.6) [12–17]	White non-Hispanic: 68 White Hispanic: 2 Black /African American: 27 Other: 3	68	8.1 (4.30)	6.6 (1.60)	Generalized convulsive: 32 Partial epilepsy: 41 Unspecified: 16 Generalized nonconvulsive: 11	0 currently: 43.8 ≤ 11 per year: 35.4 1–3 per month: 7.3 1 per week: 4.2 > 1 per week: 3.1 Multiple per day: 6.3	None: 1 Monotherapy: 43 Polytherapy: 56	IQ < 85; Neurodevelopmental disorder; Severe psychiatric disorder
Kwong et al. 2016 [19], 2016 [63]	140	14.5 (2.9) [10–18]	NR	49	M: 8.3 (4.90)[h] F: 8.8 (3.80)[h]	5.6 (3.90)	Focal: 66 Generalized: 34 Undefined: 1	0 for > 12 months: 66 ≥ 1 during last year but < 2 per month: 19 ≥ 1 per month: 10 > 1 per week: 4	None: 25 Monotherapy: 59 Polytherapy: 16	Seizure within last 24 h; Attended special needs school; Neurodegenerative disorder; Surgery ≤ 4 weeks prior; Pseudo-seizures
Lai et al. 2015 [64]	61	13.4 (2.6) [10–18]	White: 76 Non-Hispanic: 79	38	NR	5 (4.10)	Primary generalized: 50 Frontal: 28 Temporal: 16 Occipital: 4 Parietal: 2	0 in last 3 months: 64 1–3 in last 3 months: 16 3 + in last 3 months: 24 Daily: 18 Weekly: 13 Monthly: 36 Yearly: 33	Monotherapy: 70 Polytherapy: 30	NR

(*continued on next page*)

Table 3 (*continued*)

Author	N	Mean age (years) (SD) [range]	Ethnicity or race (%)	Female (%)	Mean age at seizure onset (years) (SD)	Mean epilepsy duration (years) (SD)	Seizure type(s) (%)	Seizure frequency (%)	Number of ASMs (%)	Major exclusion criteria
Miniksar et al. 2022 [65]	56	14 (NR) [11–16]	NR	59	NR	1 year: 14 > 2 years: 21 < 5 years: 21[i]	Focal: 45 Generalized: 31 Focal + generalized: 14	Daily: 9 1 per month: 25 1 per 6 months: 2 1 per year: 16 > 2 years without seizure: 29	Monotherapy: 73 Polytherapy: 27	'Moderate or severe' intellectual disability'; ASD
Puka et al. 2017[j] [38]	65	15.6 (1.9) [12–18]	NR	43	7.7 (4.39)	6.9 (4.40)	Medical refractory localization-related: 100	Daily or weekly: 51 Monthly or yearly: 49	0–1 ASMs: 26 2 ASMs: 52 ≥ 3 ASMs: 22	Prior epilepsy surgery; Planned non-resective epilepsy surgery; Neurodegenerative disorder; Genetic epilepsy syndromes; Primary generalized epilepsy; Epileptic encephalopathies
Rizou et al. 2015 [52]	100	13.9 (2.21) [NR]	NR	41	NR	NR	NR	NR	NR	Non–'normal' IQ; Seizure free ≥ 1 years; Comorbid chronic illness; 'Mental disorder'; Surgery ≤ 1 year; Medication change ≤ 6 months prior
Shatla et al. 2011 [69]	23	11.8 (NR) [NR]	NR	35	NR	NR	Generalized tonic-clonic: 65 Focal: 35	NR	Polytherapy: 100	Comorbid medical condition (requiring daily medication); Intellectual disability; ASD
Wagner et al. 2009 [54], 2012 [70], 2012[k] [53]	77	14.4 (2.21) [9–17]	White: 69Non-white: 31	55	NR	6.8 (4.44)	Partial: 74 Generalized: 26	< 12 in last year: 58 ≥ 12 in last year: 22 Unknown: 19	Monotherapy: 75 Polytherapy: 25	IQ ≤ 85; Epilepsy; diagnosis < 1 year; Severe mental health diagnosis; Intellectual disability; ASD
Wagner et al. 2013 [66]	93	14 (2.0) [10–17]	Black: 30 White: 67Other: 3	53	8 (5)	NR	General nonconvulsive: 22 General convulsive: 15 Partial: 59 Unspecified: 8	0 in last year: 20 1–3 in last year: 28 4–11 in last year: 23 ≥ 1 per month in last year: 12 ≥ 1 per week in last year: 10 ≥ 1 per day in last year: 8	None: 2 Monotherapy: 65 Polytherapy: 35	IQ < 85; 'Severe mental illness'; Epilepsy diagnosis < 6 months
Young et al. 2023 [67]	289	15.4 (1.9) [11–18]	NR	38	9.9 (3.90)	5.5 (3.60)	Generalized tonic-clonic or focal to bilateral tonic-clonic seizures during past year: 33	0 in last year: 46 ≥ 1 per month in last year: 16 1–11 per year: 38	None: 5 Monotherapy: 62 Polytherapy: 33	Intellectual disability; Seizure within prior 48 h; Neurological deficit; Taking medication for comorbid chronic medical or psychiatric illness; Epilepsy diagnosis < 1 year

Note. NR = Not Reported; ASMs = Antiseizure medications; AAM = Atonic, Akinetic Motor; ASD = Autism Spectrum Disorder; IQ = Intelligence Quotient; M = Male, F = Female.

[a]12 fewer participants were included in Adewuya & Oseni (2005) [55], leading to slightly different participant characteristics; [b]this information was extracted from Adewuya & Oseni (2005) (n = 90) [55]; [c]only the 'chronic' epilepsy sample was included as the 'new onset' sample did not meet eligibility criteria; [d]two fewer participants were included in Austin et al. (2004) [59] & Dunn et al. (2009) [61], leading to slightly different participant characteristics; [e]46 fewer participants were included in Haber et al. (2003) [51], leading to slightly different participant characteristics; [f]study entry was four years prior; [g]authors report that approximately 90 %

of the sample where White; [h]mean age at onset for those scoring above HADS-A cut-off; [i]Miniksar et al. (2023) [65] did not report the mean epilepsy duration of their sample but they did report the frequency of participants whose epilepsy duration was 1 year, < 2 years, < 5 years. Therefore, this information was included in the table; [j]only the 'adolescent' sample (aged 12–18) were included as the 'children' sample (aged 6–11) did not meet eligibility criteria; [k]13 fewer participants were included in Wagner et al. (2012) [70], 2012 [53]), leading to slightly different participant characteristics.

Table 4
Assessment of risk of bias of included studies.

Author	Unbiased selection of cohort	Sample size calculation	Adequate description of cohort	Validated measure of anxiety and/or depression	Validated measure(s) of psychosocial variables	Control of confounders	Analysis appropriate
Adewuya & Ola, 2005 [49]; Adewuya & Oseni, 2005 [55]	Yes	N/S	Yes	Yes	Yes	Partial[a]	Partial[b]
Austin et al. 2004 [59]; Caplin et al. 2002 [60]; Dunn et al. 2009 [61]	Partial	N/S	Partial	Yes	Partial[c]	No	Yes
Çengel-Kültür et al. 2009 [68]	Partial	N/S	Yes	Yes	Yes	No	Partial
Dunn et al. 1999 [50]; Haber et al. 2003 [51]	Yes	N/S	Partial	Yes	Partial	Partial	Partial[d]
Eddy et al. 2010 [56]	Yes	N/S	Partial	Yes	Yes	No	Yes
Güven et al. 2015 [48]	Partial	Partial	Partial	Yes	Yes	No	Yes
Kellerman et al. 2017 [62]	Partial	N/S	Yes	Yes	Yes	No	Yes
Kwong et al. 2016 [19], 2016 [63]	Partial	N/S	Yes	Yes	Yes	Partial[e]	Yes
Lai et al. 2015 [64]	Partial	N/S	Yes	Yes	Partial	No	Yes
Miniksar et al. 2022 [65]	Partial	N/S	Yes	Yes	Yes	No	Yes
Puka et al. 2017 [38]	Partial	N/S	Yes	Yes	Yes	Yes	Partial
Rizou et al. 2015 [52]	Yes	N/S	Partial	Yes	Partial	Partial	Partial
Shatla et al. 2011 [69]	Partial	N/S	Partial	Yes	Yes	No	Partial
Wagner et al. 2009 [54], 2012 [70], 2012 [53]	Partial	N/S	Yes	Yes	Yes	Partial[f]	Partial[g]
Wagner et al. 2013 [66]	Partial	N/S	Yes	Yes	Yes	No	Yes
Young et al. 2023 [67]	Partial	N/S	Yes	Yes	Partial	No	Yes

Note. N/S = Not specified; [a]while Adewuya & Ola (2005) [49] controlled for all important confounders, Adewuya & Oseni (2005) [55] did not (as only the correlation analysis was extracted for this review, we only assessed the risk of bias for this analysis); [b]while Adewuya & Oseni (2005) [55] had an appropriate sample size to conduct correlation analysis, Adeuwya & Ola (2005) [49] did not have an appropriate sample size to conduct multiple regression; [c]while Austin et al. (2004) [59] & Caplin et al. (2002) [60] used validated measures to assess psychosocial variables, Dunn et al. (2009) [61] included single item subscales to assess certain psychosocial variables; [d]while Dunn et al. (1999) [50] had an appropriate sample size to conduct multiple regression, Haber et al. (2003) [51] did not; [e]while Kwong et al. (2016) [19] controlled for all important confounders, Kwong et al. (2016) [63] did not (as only the correlation analysis was extracted for this review, we only assessed the risk of bias for this analysis); [f]Wagner et al. (2012) [70] controlled for all important confounders (only simple linear regression was conducted as no important confounders were significantly associated with the outcome variable). However, Wagner et al. (2012) [53] and Wagner et al. (2009) [54] did not; [g]while Wagner et al. (2012) [70] had an appropriate sample size to conduct simple regression, Wagner et al. (2012) [53] and Wagner et al. (2009) [54] did not have an appropriate sample size to conduct multiple regression.

3.2.3.3. Other parent-specific factors. Anxiety was significantly associated with the general impact of epilepsy on parents (*t*-test only) [55].

3.3. Psychosocial factors associated with depression

3.3.1. Intrapersonal factors

3.3.1.1. Coping responses. Two studies (three articles) [50,51,53] assessed epilepsy-specific coping responses (one study [two articles] from a parental perspective and one study from an adolescent and parental perspective). When assessed from a parental perspective, findings were mixed. One study [53] found that depression was significantly associated with 'developing competence and optimism' (ρ = -0.27); while the other study [50] found that after accounting for clinical, demographic, and other psychosocial variables, depression was not significantly associated with either 'positive coping' (i.e., developing competence & optimism, complying with treatment, seeking support) or 'negative coping' (i.e., being irritable and withdrawing). The same study (reported in a different article) [51] assessed the impact of the difference between mother's and father's perceptions of their child's 'negative coping'. When entered in a multiple regression model with clinical, demographic, and other psychosocial variables, the absolute difference between parent's perception of their child's 'negative coping' was significantly associated with depression (β not reported).

When assessed from an adolescent perspective, 'positive coping' (i.e., problem solving, cognitive restructuring, social support) was not significantly associated with depression but 'negative coping' (i.e., withdrawing, being self-critical, emotional dysregulation, blaming others, defeatist attitude) was, even after controlling for sex, number of ASMs, and seizure severity (β not reported) [53].

3.3.1.2. Epilepsy-specific beliefs and attitudes. Three studies (four articles) [49–51,54] assessed attitude towards having epilepsy. Findings were mixed. Two studies (three articles) [50,51,54] found that attitude towards having epilepsy was significantly associated with depression after accounting for clinical, demographic, and/or other psychosocial variables (β not reported); while one study [49] found no significant association. All three studies assessing seizure self-efficacy found that it was significantly associated with depression (r = -0.32 to -0.58) [48,60], even after controlling for other psychosocial variables (β not reported) [54]. Both studies assessing perceived epilepsy-related stigma found that it was significantly associated with depression (r = 0.48; OR = 4.35) [49,59], even after seizure frequency, number of ASMs, and other psychosocial variables were controlled (β not reported) [49]. One study [55] assessed the impact of epilepsy on adjustment and development and found that it was significantly associated with depression (*t*-test only).

Table 5
Summary of significant findings from included articles grouped by outcome.

Author	Dependent variable	Analysis	Independent variables (psychosocial)	Independent variables entered into multivariate analysis[a]	Significant findings
			Anxiety		
Adewuya & Ola, 2005 [49] (article 1)[b]	DISC-IV (caseness)	*t*-test; multiple regression (forward selection)	**Intrapersonal** Attitude towards epilepsy (CATIS); perceived stigma (3-item measure[c]) **Interpersonal** Family resources (FIRM); family stressors (FILE-FS) **Parent-specific** Parental perceived stigma (5-item measure[d]); parental psychopathology (GHQ)	Seizure frequency, number of ASMs, perceived stigma, parental perceived stigma, parental psychopathology, family stressors	**Univariate** *Intrapersonal:* Perceived stigma (t = NR**; OR = 2.73 [1.00–7.44]) *Interpersonal:* Family stressors (t = NR**; OR = 4.56 [1.87–11.12]) *Parent-specific:* Parental perceived stigma (t = NR*; OR = 3.57 [1.37–9.33]); parental psychopathology (t = NR*; OR = 5.27 [1.86–14.17]) **Multivariate** None
Adewuya & Oseni, 2005 [55] (article 2)[b]	DISC-IV (caseness)	*t*-test	**Intrapersonal** Impact of epilepsy on adjustment and development (ICIS-C) **Interpersonal** Family functioning (ICIS-F)[g] **Parent-specific** Impact of epilepsy on parents(ICIS-P)	N/A	**Univariate***Intrapersonal:* None *Interpersonal:* Family functioning(t = NR**) *Parent-specific:* Impact of epilepsy on parents (t = NR**)
Dunn et al. 2009 [61]	CSI/ASI generalized anxiety subscale (continuous & caseness)	Spearman correlation	**Intrapersonal** Mixed anxiety & depression (CBCL-A/D)	N/A	**Univariate** *Intrapersonal:* Mixed anxiety & depression (ρ = 0.48* for-9-12Y/O; ρ = 0.62* for 13–14 Y/O)
Eddy et al. 2010 [56]	MASC	Spearman correlation	**Intrapersonal** QoL (YQOL-R); sense of self (YQOL–R-S); general life satisfaction (YQOL–R-G) **Interpersonal** Quality of family & peer relationships (YQOL–R-R); satisfaction with broader social and cultural environment (YQOL-R-E)	N/A	**Univariate** *Intrapersonal:* QoL (ρ = -0.29*)[e] *Interpersonal:* Quality of family & peer relationships (ρ = -0. 29*)[e]
Kwong et al. 2016 [19] (article 1)[f]	HADS-A (caseness)	Univariate odds ratio; multiple regression (forward selection)	**Intrapersonal** Depression (HADS-D)	Sex, age, medical comorbidities, tenure of accommodation, Comprehensive Social Security Scheme, age at seizure onset, duration of epilepsy, seizure type, seizure frequency at onset, not on ASMs, epilepsy aetiology, seizure free for ≥ 12 months, depression	**Univariate** *Intrapersonal:* Depression (OR = 1.21***) **Multivariate** *Intrapersonal:* Depression (OR = 1.22**)
Kwong et al. 2016 [63] (article 2)[f]	HADS-A	Spearman correlation; univariate odds ratio	**Intrapersonal** Self-esteem (overall, 'general', 'academic', 'social', & 'parent-related' subscales; CFSEI-2)	N/A	**Univariate***Intrapersonal:* Global self-esteem (ρ = -0.41***; OR = 1.19**); general self-esteem (ρ = -0.48***; OR = 1.29***); academic self-esteem (ρ = -0.26**; OR = 1.13*); social self-esteem (ρ = -0.22*); parent-related self-esteem (OR = 1.15*)
Lai et al. 2013 [64]	NeuroQOL anxiety subscale	*t*-test; ANOVA; spearman correlation	**Intrapersonal** Emotional functioning (PEDS-QL-	N/A	**Univariate** *Intrapersonal:*

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Table 5 (*continued*)

Author	Dependent variable	Analysis	Independent variables (psychosocial)	Independent variables entered into multivariate analysis[a]	Significant findings
			EF); global mental health (PROMIS-M); QoL (single-item measure[g h]); emotional well-being (single-item measure[h])		Emotional functioning (ρ = -0.51**); global mental health (ρ = -0.60***); QoL (ρ = -0.40**)
			Interpersonal Social functioning (PEDS-QL-S)		*Interpersonal:* Social functioning (ρ = -0.37**)
Puka et al. 2017 [38]	GAD-7	Pearson correlation; simple regression; multiple regression (backwards elimination)	**Intrapersonal** Depression (QIDS-SR16)	Sex, parental depression, parental anxiety, family resources	**Univariate** *Intrapersonal:* Depression (r = 0.66***)
			Interpersonal Family functioning (F-APGAR)[i]; family resources (FIRM-MHSS); family stressors (FILE)		*Interpersonal:* Family resources (β = -0.25*)
			Parent-specific Parental depression (QIDS-SR16); parental anxiety (GAD-7)		*Parent-specific:* Parental depression (β = 0.25*); parental anxiety (β = 0.39**) **Multivariate** *Parent-specific:* Parental anxiety (β = 0.35**)
			Depression		
Adewuya & Ola, 2005 [49] (article 1)[b]	DISC-IV (caseness)	*t*-test; multiple regression (forward selection) *t*-test	**Intrapersonal** Attitude towards epilepsy (CATIS); perceived stigma (3-item measure[c])	Perceived stigma, seizure frequency, number of ASMs, family stressors, parental psychopathology	**Univariate** *Intrapersonal*: Perceived stigma (t = NR***; OR = 4.35 [1.56–12.11]) *Interpersonal:* Family stressors (t = NR*; OR = 3.26 [1.33–7.98])
			Interpersonal Family resources (FIRM); family stressors (FILE-FS)		*Parent-specific:* Parental psychopathology (t = NR**) **Multivariate** *Intrapersonal:* Perceived stigma (β = NR, adjusted R^2 = 0.04***)
			Parent-specific Parental perceived stigma (5-item measure[d]); parental psychopathology (GHQ)		
Adewuya & Oseni, 2005 [55] (article 2)[b]	DISC-IV (caseness)	*t*-test	**Intrapersonal** Impact of epilepsy on adjustment and development (ICIS-C)	N/A	**Univariate** *Intrapersonal:* Impact of epilepsy on adjustment and development (t = NR*)
			Interpersonal Family functioning (ICIS-F)[i]		*Interpersonal:* Family functioning (t = NR**)
			Parent-specific Impact of epilepsy on parents (ICIS-P)		*Parent-specific* None
Austin et al. 2004 [59] (article 1)[j]	CDI	Pearson correlation Spearman correlation	**Intrapersonal** Perceived stigma (8-item measure[k])	N/A	**Univariate** *Intrapersonal:* Perceived stigma (r = 0.48***)
Caplin et al. 2002 [60] (article 2)[j]	CDI	Pearson correlation	**Intrapersonal** Seizure self-efficacy(SSES-C)	N/A	**Univariate***Intrapersonal:* Seizure self-efficacy (r = -0.32***)
Dunn et al. 2009 [61] (article 3)[j]	CSI-4/ASI-4 major depression subscale	Spearman correlation	**Intrapersonal** Withdrawal (CBCL-D/W)	N/A	**Univariate** *Intrapersonal:*

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Table 5 (*continued*)

Author	Dependent variable	Analysis	Independent variables (psychosocial)	Independent variables entered into multivariate analysis[a]	Significant findings
	(continuous & caseness)				Withdrawal(ρ = 0.36* for 9–12 Y/O; ρ = 0.27* for 13–14 Y/O)
Dunn et al. 1999 [50] (article 1)[k]	CDI	Pearson correlation; multiple regression (stepwise)	**Intrapersonal** Attitude towards epilepsy (CATIS); coping resources (CHIC)[i]; locus of control (48-item measure[l]) **Interpersonal** Family resources (FIRM); family functioning (F-APGAR)[m]; family stressors (FILE-SF) **Parent-specific** Parental perceived stigma (5-item scale[d]); parental depression (CES-D)	Age, gender, age of seizure onset, seizure severity, attitude towards epilepsy, family functioning[m], negative coping, LoC-general unknown, LoC-social powerful other, parental perceived stigma	**Univariate** *Intrapersonal:* Attitude towards epilepsy (r = -0.55***; r = NR*); positive coping (r = -0.19*); negative coping (r = 0.30**); LoC-social powerful other (r = 0.42***); LoC-general unknown (r = 0.41***) *Interpersonal:* Family functioning (r = -0.49***)[l] *Parent-specific:* Parental perceived stigma (r = 0.28**) **Multivariate** *Intrapersonal:* Attitude towards epilepsy (β = NR; cumulative R^2 = 0.31***); LoC-social powerful other (β = NR; cumulative R^2 = 0.50**); LoC-general unknown (β = NR; cumulative R^2 = 0.53***) *Interpersonal:* Family functioning (β = NR; cumulative R^2 = 0.45***)[l]
Haber et al. 2003 [51] (article 2)$_k$	CDI	Pearson correlation; multiple regression (stepwise)	**Intrapersonal** Attitude towards epilepsy (CATIS); coping resources (CHIC)[i,n] **Interpersonal** Family resources (FIRM-MH)[n]; family functioning (F-APGAR)[m,n] **Parent-specific** Parental attitude towards epilepsy (6-item scale[o])[n]; parental perceived stigma (5-item scale[d])[n]	Age, gender, family SES, epilepsy severity, attitude towards epilepsy, family functioning[p], asolute difference between mother's and father's scores (for child negative coping, family resources, family functioning, attitude towards epilepsy, and perceived stigma)	**Univariate** *Intrapersonal:* Attitude towards epilepsy (r = NR*); absolute difference between mothers' and fathers' perceptions of negative coping (r = NR*) *Interpersonal:* Family functioning (r = NR*)[p] *Parent-specific:* None **Multivariate** *Intrapersonal:* Attitude towards epilepsy (β = NR**); absolute difference between mothers and father's perception of negative coping (β = NR**; *adj* R^2 = 0.09) *Interpersonal:* Family-functioning (β = NR***)[p]
Eddy et al. 2010 [56]	CDI	Spearman correlation	**Intrapersonal** QoL (YQOL-R); sense of self (YQOL–R-S); general life satisfaction (YQOL–R-G) **Interpersonal** Quality of family & peer relationships (YQOL–R-R); satisfaction with broader social and cultural environment (YQOL-R-E)	N/A	**Univariate** *Intrapersonal:* Sense of self (ρ = -0.34*)[e] *Interpersonal:* Quality of family & peer relationships (ρ = -0.32*)[e]
Güven et al. 2015 [48]	CDI	Pearson correlation	**Intrapersonal** Seizure self-efficacy (overall, 'self-management' & 'environmental influences' subscales; SSES-C)	N/A	**Univariate** *Intrapersonal:* Seizure self-efficacy (overall: r = -0.58**; self-management subscale: r = -0.56**; environmental influences subscale: r = -0.46**)
Kellerman et al. 2017 [62]	NDDI-E-Y[q] (continuous & caseness)	Odds ratios; simple regression	**Intrapersonal** Ineffectiveness (CDEI-2-I); self-esteem (CDI-2-S); negative mood (CDI-2-N)	N/A	**Univariate** *Intrapersonal:* Ineffectiveness (β = 0.66***; adj R^2 = 0.43; *OR* = 1.33***); negative mood (β = 0.54*** adj R^2 = 0.29; *OR* = 1.19***); negative

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Author	Dependent variable	Analysis	Independent variables (psychosocial)	Independent variables entered into multivariate analysis[a]	Significant findings
			Interpersonal Interpersonal problems (CDI-2-IP)		self-esteem ($\beta = 0.62$***; adj $R^2 = 0.38$; $OR = 1.32$***) *Interpersonal:* Interpersonal problems ($\beta = 0.61$ ***; adj $R^2 = 0.36$; $OR = 1.30$***)
Kwong et al. 2016 [19] (article 1)[f]	HADS-D (caseness)	Univariate odds ratio; multiple regression (forward selection)	**Intrapersonal** Anxiety (HADS-A)	Sex, age, medical comorbidities, tenure of accommodation, Comprehensive Social Security Scheme, age at seizure onset, duration of epilepsy, seizure type, seizure frequency at onset, not on ASMs, epilepsy aetiology, seizure free for ≥ 12 months, anxiety	**Univariate** *Intrapersonal:* Anxiety ($OR = 1.17$**) **Multivariate** *Intrapersonal:* Anxiety ($OR = 1.62$**)
Kwong et al. 2016 [63] (article 2)[f]	HADS-D	Spearman correlation; univariate odds ratio	**Intrapersonal** Self-esteem (overall, 'general', 'academic', 'social', & 'parent-related' subscales; CFSEI-2)	N/A	**Univariate** *Intrapersonal:* Overall self-esteem ($\rho = -0.51$***; $OR = 1.34$***); general self-esteem ($\rho = -0.49$***; $OR = 1.37$***); academic self-esteem ($\rho = -0.40$***; $OR = 1.22$**); social self-esteem ($\rho = -0.28$**); parent-related self-esteem ($\rho = -0.37$***; $OR = 1.3$***)
Lai et al. 2013 [64]	NeuroQOL depression subscale	*t*-test; ANOVA; spearman correlation	**Intrapersonal** Emotional functioning (PEDS-QL-EF); global mental health (PROMIS-M); QoL (single-item measure[g,h]); emotional well-being (single-item measureh) **Interpersonal** Social functioning (PEDS-QL-S)	N/A	**Univariate** *Intrapersonal:* Emotional functioning ($\rho = -0.66$***); global mental health ($\rho = -0.71$***); QoL ($\rho = -0.43$***) *Interpersonal:* Social functioning ($\rho = -0.49$***)
Miniksar et al. 2022 [65]	CDI	Pearson correlation	**Intrapersonal** Suicidal probability (SPS-T); hopelessness (SPS-H); suicidal ideation (SPS-SI); negative self-evaluation (SPS-N); hostility (SPS-HO); dysfunctional personality (PID-5-BF-T); negative affectivity (PID-5-BF-NA); detachment (PID-5-BF-D); antagonism (PID-5-BF-A); disinhibition (PID-5-BF-DI); psychoticism (PID-5-BF-P)	N/A	**Univariate** *Intrapersonal:* Suicidal probability ($r = 0.83$**); hopelessness ($r = 0.69$**); suicidal ideation ($r = 0.65$**); negative self-evaluation ($r = 0.62$**); hostility ($r = 0.65$**); dysfunctional personality ($r = 0.69$**); negative affectivity ($r = 0.57$**); detachment ($r = 0.51$**); antagonism ($r = 0.37$**); disinhibition ($r = 0.40$**); psychoticism ($r = 0.53$**)
Puka et al. 2017 [38]	QIDS-SR16	Pearson correlation; simple regression; multiple regression (backwards elimination)	**Intrapersonal**Anxiety (GAD-7) **Interpersonal** Family functioning (F-APGAR)[i]; family resources (FIRM-MHSS); family stressors (FILE) **Parent-specific** Parental depression (QIDS-SR16); parental anxiety (GAD-7)	Parental employment status, household income, family resources, family stressors, parental anxiety	**Univariate** *Intrapersonal:* Anxiety ($r = 0.66$***) *Interpersonal:* Family resources ($\beta = -0.33$**); family stressors ($\beta = 0.33$**) *Parent-specific:* Parental anxiety ($\beta = 0.36$**) **Multivariate** *Parent-specific:* Parental anxiety ($\beta = 0.30$*)
Shatla et al. 2011 [69]	CDI	Pearson correlation	**Parent-specific** Global parental stress (PSI)	N/A	**Univariate** *Parent-specific:* Global parental stress (r = NR*)
Wagner et al. 2009 [54] (article 1)[r]	CDI	Multiple regression (standard); moderator analysis (interaction-term); mediation analysis (Sobel test statistic)	**Intrapersonal** Hopelessness (HSC); seizure self-efficacy (SSES-C); attitude towards epilepsy (CATIS)	Hopelessness, seizure self-efficacy, attitude towards epilepsy	**Multivariate** *Intrapersonal:* Hopelessness (β = NR*); seizure self-efficacy (β = NR*); attitude towards epilepsy (β = NR*) Hopelessness + seizure self-efficacy + attitude towards epilepsy: adj $R^2 = 0.53$ Hopelessness mediated the effect of attitude toward illness ondepression after adjusting for self-efficacy (Sobel test statistic = NR*)

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Table 5 (*continued*)

Author	Dependent variable	Analysis	Independent variables (psychosocial)	Independent variables entered into multivariate analysis[a]	Significant findings
Wagner et al. 2012 [70] (article 2)[r]	BASC-II	Simple linear regression	**Parent-specific** Parental seizure self-efficacy (ESES)	N/A	**Univariate** *Parent-specific:* Parental seizure self-efficacy (β = NR; adj R^2 = 0.14**)
Wagner et al. 2012 [53] (article 3)[r]	CDI	Pearson & spearman correlation; *t*-test; Kruskal-Wallis test; multiple regression (stepwise)	**Intrapersonal** Coping responses (CHIC; Kidcope)[m]	Sex, ethnicity, number of ASMs, seizure severity, negative coping[p]	**Univariate** *Intrapersonal:* Coping - develops competence and optimism(ρ = -0.27*)[i]; negative coping (total score ρ = 0.43**, r = -0.54**; frequency score ρ = 0.58***, t or H^s = NR*; efficacy score ρ = 0.46***, t or H^s = NR*)[l] **Multivariate** *Intrapersonal:* Negative coping (total score β = NR***)[p]
Wagner et al. 2013 [66]	NDDI-E-Y	Spearman correlation; x^2 test	**Intrapersonal** Internalizing symptoms (PSC-I); externalizing problems (PSC-E)	N/A	**Univariate** *Intrapersonal:* Internalizing symptoms (ρ = 0.47***; x^2 = NR***); externalizing problems (ρ = 0.28**)
			Mixed anxiety & depression		
Çengel-Kültür et al. 2009 [68]	CBCL anxiety/ depression subscale	Pearson correlation	**Parent-specific** Parental psychopathology (SCL-R-90)	N/A	**Univariate** *Parent-specific:* Parental psychopathology (r = 0.32*)
Dunn et al. 1999 [50]	CBCL-YSR anxiety/ depression subscale	Pearson correlation; multiple regression (stepwise)	**Intrapersonal** Attitude towards epilepsy (CATIS); coping resources (CHIC)[i]; locus of control (48-item measure[l]) **Interpersonal** Family resources (FIRM); family functioning (F-APGAR)[m]; family stressors (FILE-SF) **Parent-specific** Parental perceived stigma (5-item scale[d]); parental depression (CES-D)	Age, gender, age of seizure onset, seizure severity, attitude towards epilepsy, family functioning[p], negative coping, LoC-general unknown, LoC-social powerful other, parental perceived stigma	**Univariate** *Intrapersonal:* Attitude towards epilepsy (r = -0.50***); negative coping (r = 0.30**); LoC-social powerful other (r = 0.42***); LoC-general unknown (r = 0.39***) *Interpersonal:* Family functioning (r = -0.38***)[p] *Parent-specific:* Parental perceived stigma (r = 0.26*) **Multivariate** *Intrapersonal:* Attitude towards epilepsy (β = NR; cumulative R^2 = 0.31***); LoC-social powerful other (β = NR; cumulative R^2 = 0.44**) *Interpersonal:* Family functioning (β = NR cumulative R^2 = 0.38*)[p]
Dunn et al. 2009 [61]	CBCL anxiety/ depression subscale (continuous & caseness)	Spearman & point biserial rank correlation	**Intrapersonal** Generalized anxiety (CSI/ASI); PTSD (CSI/ASI); panic attacks (CSI/ASI)	N/A	**Univariate** *Intrapersonal:* Generalized anxiety (ρ = 0.48* for 9–12 Y/O; ρ = 0.62* for 13–14 Y/O); PTSD (r_{pb} = 0.46* for 9–12 Y/O; ρ = 0.43* for 13–14 Y/O); panic attacks (r_{pb} = 0.53* for 13–14 Y/O)
Rizou et al. 2015 [52]	RCADS	Pearson correlation; multiple regression (hierarchical)	**Intrapersonal** Illness perceptions (BIPQ); autonomous motivation for treatment adherence (TSRQ) **Interpersonal** Autonomous parental support & involvement (POPS)	*Block 1:* Gender *Block 2:* Seizure severity *Block 3:* IP-consequences, IP-timeline, IP-personal control, IP-treatment control, IP-identity, IP-concern, IP-emotional representation	**Univariate** *Intrapersonal:* Illness perceptions (IP)–timeline (r = 0.53***); IP–personal control (r = 0.21*); IP-treatment control (r = 0.23*); IP-emotional representations (r = 0.45***); IP-identity (r = 0.41***); IP-concern (r = 0.55***); IP-consequences (r = 0.41***) *Interpersonal* None **Multivariate** *Intrapersonal:*

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Table 5 (*continued*)

Author	Dependent variable	Analysis	Independent variables (psychosocial)	Independent variables entered into multivariate analysis[a]	Significant findings
					IP-timeline (β = 0.38**); IP-personal control (β = -0.42*); IP–treatment control (β = 0.36*); IP-emotional representations (β = 0.33*)
Young et al. 2023 [67]	CBCL- YSR anxiety/ depression subscale	*t*-test	**Parent-specific** Parental perceived stigma (3-item scale[t])	N/A	**Univariate** *Parent-specific:* Parental perceived stigma (t = NR*)

Note. Adj = adjusted; ASMs = Antiseizure medications; BASC-II = Behavior Assessment System for Children 2nd edition; BIPQ = Brief Illness Perceptions Questionnaire; CATIS = Child Attitude Towards Illness Scale; CBCL = Child Behaviour Checklist; CBCL-YSR = Child Behavior Checklist Youth Self-report; CBCL-A/D = Child Behavior Checklist–Anxiety/Depression subscale; CBCL-W/D = Child Behavior Checklist-Withdrawn/Depressed subscale; CDI = Children's Depression Inventory; CDI-2-I = Children's Depression Inventory-2–Ineffectiveness subscale; CDI-2-S = Children's Depression Inventory-2–Negative Self-esteem subscale; CDI-2-N = Children's Depression Inventory-2–Negative Mood subscale; CDI-2-IP = Children's Depression Inventory-2–Interpersonal Problems subscale; CFSEI-2 = Culture-Free Self-Esteem Inventory for Children; CHIC = Coping Health Inventory for Children; CSI/ASI = Child Symptom Inventory/Adolescent Symptom Inventory; ESES = Epilepsy Self-Efficacy Scale; F-APGAR = Family Adaptability, Partnership, Growth, Affective, and Resolve scale; FIRM = Family Inventory of Resources Management; FIRM-MH = Family Inventory of Resources Management-Family Mastery and Health subscale; FIRM-MHSS = Family Inventory of Resources Management-Family Mastery and Health and Extended Family Social Support subscales combined; FILE = Family Inventory of Life Events and Changes; FILE-FS = Family Inventory of Life Events and Changes–Family Stressors subscale; GAD-7 = Generalized Anxiety Disorder assessment scale (7-item version); GHQ = Global Health Questionnaire; HADS = Hospital Anxiety & Depression Scale; HSC = Hopelessness Scale for Children; ICIS-C = Impact of Childhood Illness Scale–Child subscale; ICIS-P = Impact of Childhood Illness Scale–Parent subscale; ICIS-F = Impact of Childhood Illness Scale–Family subscale; IP = Illness Perceptions; LoC = Locus of Control; MASC = Multidimensional Anxiety Scale for Children; NDDI-E-Y = Neurological Disorders Depression Inventory for Epilepsy–Youth; Neuro-QoL = The Neurology Quality of Life Measurement System Patient Health Questionnaire; PTSD = Post-Traumatic Stress Disorder; PEDS-QL-EF = Paediatric Quality of Life Inventory–Emotional Functioning subscale; PEDS-QL-S = Paediatric Quality of Life Inventory–Social Functioning subscale; PID-5-BF-T = Personality Inventory for DSM-5-Brief Form-Children–Total; PID-5-BF-NA = Personality Inventory for DSM-5-Brief Form-Children–Negative Affectivity subscale; PID-5-BF-D = Personality Inventory for DSM-5-Brief Form-Children–Detachment subscale; PID-5-BF-A = Personality Inventory for DSM-5-Brief Form-Children–Antagonism subscale; PID-5-BF-DI = Personality Inventory for DSM-5-Brief Form-Children–Disinhibition subscale; PID-5-BF-P = Personality Inventory for DSM-5-Brief Form-Children–Psychoticism subscale; PROMIS-M = Patient Reported Outcomes Measurement and Information System–Global Mental Health subscale; PSI = Parenting Stress Index; QIDS-SR16 = Quick Inventory of Depressive Symptomatology (16-item version); QoL = Quality of Life; RCADS = Revised Children's Anxiety & Depression Scale; SPS-T = Suicide Probability Scale-Total; SPS-H = Suicide Probability Scale–Hopelessness subscale; SPS-SI = Suicide Probability Scale–Suicidal Ideation subscale; SPS-HO = Suicide Probability Scale–Hostility subscale; SSES-C = Seizure Self-Efficacy Scale for Children; SCAS = Spence Children's Anxiety Scale; SCL-R-90 = Symptom Checklist-90-Revised; Y/O = Years Old; YQOL-R = Youth Quality of Life Instrument-Research; YQOL-R-E = Youth Quality of Life Instrument-Research–Environmental domain; YQOL-R-S = Youth Quality of Life Instrument-Research–Self domain; YQOL-R-G = Youth Quality of Life Instrument-Research–General domain; YQOL-R-R = Youth Quality of Life Instrument-Research–Relationship domain; *OR* = Odds Ratio; β = Standardized Beta coefficient; r = Pearson correlation coefficient; r^{pb} = Point biserial rank correlation coefficient; ρ = Spearman's Rho correlation coefficient; x^2 = chi-squared; ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

[a]Variables underlined were included in the final model; [b]Adewuya & Ola, 2005 [49] and Adewuya & Oseni, 2005 [55] are the same study; [c]3-item stigma scale developed by Jacoby et al., (1994) [71]; [d]5-item stigma scale adapted from an adult stigma scale developed by Ryan et al. (1980) [72]; [e]after adjusting for multiple comparisons, findings were no longer significant; [f]Kwong et al. 2016 [19] and Kwong et al. 2016 [63] are the same study; [g]single-item scale asking participants to rate how much they agree with the following statement: '*I am content with the quality of my life right now*'; [h]single-item scale asking participants how much they had changed on a specific domain over the past 6 months; [i]measured from a parental perspective; [j]Austin et al. 2004 [59], Caplin et al. 2002 [60] and Dunn et al. 2009 [61] are the same study; [k]Dunn et al. (1999) [50] and Haber et al. 2003 [51] are the same study; [l]48-item perception of control scale developed by Connell (1985) [73]; [m]measured from an adolescent and parental perspective; [n]absolute difference between parental scores calculated and used in analysis; [o]6-item parental attitude scale developed by Haber et al. (2003) [51]; [p]measured from an adolescent perspective; [q]Two depression outcome measures (NDDI-E-Y & Neuro-QOL SF) were used in Kellerman et al. (2017) [62]. Findings from the NDDI-E-Y were chosen as this scale has been more widely used in the literature; [r] Wagner et al. 2009 [54], Wagner et al. 2012 [70] and Wagner et al. 2012 [53] are the same study; [s]it was unclear if analysis conducted was *t*-test or Kruskal-Wallis; [t]3-item stigma scale adapted from a stigma scale developed by Jacoby et al. (1994) [71].

3.3.1.3. General beliefs and attitudes. Perceived locus of control was assessed in one study [50]. After controlling for clinical, demographic, and other psychosocial variables, an external locus of control regarding social interactions and a general unknown locus of control were significantly associated with depression (β not reported). Self-esteem was assessed in two studies [62,63]. Depression was significantly associated with both global (ρ = -0.51; β = 0.62; *OR* = 1.32 to 1.34) [62,63] and specific aspects of self-esteem (ρ = -0.28 to 49; *OR* = 1.22 to 1.37) [63]. Sense of self was assessed in one study [56] and was significantly associated with depression (ρ = -0.34). Negative self-evaluation was assessed in one study [65] and was significantly associated with depression (r = 0.62) but after correcting for multiple comparisons, this association was no longer significant.

3.3.1.4. Alternative mental health difficulties. Two studies [19,38] examined the association between depression and anxiety. Depression was significantly associated with anxiety (r = 0.66; *OR* = 1.17) [19,38], even after controlling for gender (*OR* = 1.62) [19].

Other mental health difficulties were assessed in single studies. When assessed cross-sectionally, depression was significantly associated with mental wellbeing (ρ = -0.66 to -0.71) [64]. However, when assessed prospectively, mean change in depression from baseline to 6-month follow-up was not significantly associated with mean change in mental wellbeing [64]. Depression was also significantly associated with being 'withdrawn/depressed' (r = 0.36 in those aged 9–12; r = 0.27 in those aged 13–14) [61], internalizing symptoms (ρ = 0.47) [66], and negative mood (β = 0.54; *OR* = 1.19) [62].

3.3.1.5. Other intrapersonal factors. Two studies [56,64] assessed QoL cross-sectionally and one [61] assessed QoL prospectively. When assessed cross sectionally, Lai et al. (2015) found that QoL was significantly associated with depression (ρ = -0.43) [64]; whereas Eddy et al. (2010) found no significant association [56]. When assessed prospectively, Lai et al. (2015) found no significant association between mean change in QoL from baseline to 6-month follow-up and mean change in depression [64]. Two studies [54,65] assessed hopelessness and found that it was significantly associated with depression (r = 0.69) [65], even after controlling for other psychosocial variables (β not reported) [54].

Hopelessness also partially mediated the relationship between depression and attitude towards having epilepsy [54].

Single studies examined other intrapersonal factors. Depression was significantly associated with suicidal probability (r = 0.83) [65], suicidal ideation (r = 0.65) [65], hostility (r = 0.65) [65], negative externalizing problems (ρ = 0.28) [66], and negative evaluation of one's abilities and academic performance, defined as 'ineffectiveness' (β = 0.66; OR = 1.33) [62]. Depression was not significantly associated with general life satisfaction [56].

One study [65] assessed maladaptive personality traits. Depression was significantly associated with overall dysfunctional personality (r = 0.69) and the personality trait-domains of 'negative affectivity' (r = 0.57), 'psychoticism' (r = 0.53), 'detachment' (r = 0.51), 'disinhibition' (r = 0.4), and 'antagonism' (r = 0.37).

3.3.2. Interpersonal factors

3.3.2.1. Family factors. Three studies (four articles) [38,50,51,55] assessed family functioning (two studies from a parental perspective and one study [two articles] from an adolescent and parental perspective). When assessed from a parental perspective, findings were mixed. Adewuya & Oseni, (2005) found that family functioning was significantly associated with depression (*t*-test only) [55]; while Puka et al. (2017) and Dunn et al. (1999) found no significant association [38,50]. Haber et al. (2003) assessed the impact of the absolute difference between mother's and father's perception of family functioning on depression and found no significant association [51]. When assessed from an adolescent perspective, family functioning was significantly associated with depression even after accounting for clinical, demographic, and/or other psychosocial variables (β not reported) [50,51].

Three studies (four articles) [38,49–51] assessed family adaptive resources. When entered in a multiple regression model with clinical, demographic, and/or other psychosocial variables, none of the studies found a significant association with depression.

3.3.2.2. Other interpersonal factors. Single studies assessed other interpersonal factors. Depression was significantly associated with social functioning (ρ = -0.49) [64] and interpersonal problems (β = 0.61; OR = 1.30) [62]. Depression was also significantly associated with quality of family and peer relationships (ρ = -0.32) but after correcting for multiple comparisons, this association was no longer significant [56]. Depression was not significantly associated with one's broader social and cultural environment [56].

3.3.3. Parent-specific factors

3.3.3.1. Parental epilepsy specific beliefs and attitudes. Two studies [49,50] measured parental perceived stigma towards epilepsy. After accounting for clinical, demographic, and/or other psychosocial variables, neither study found a significant association with depression. One of these studies (reported in a different article) [51] also assessed the impact of the difference between mother's and father's perceived stigma towards epilepsy and the impact of the difference between mother's and father's attitude towards epilepsy on depression. When entered in a multiple regression model with clinical, demographic, and other psychosocial variables, neither the absolute difference between parent's perceived stigma nor the absolute difference between parent's attitude towards epilepsy was significantly associated with depression. The one study [70] assessing parental seizure self-efficacy found it was significantly associated with depression (β not reported).

3.3.3.2. Parental mental health difficulties. Three studies [38,49,50] assessed parental mental health difficulties. Findings were mixed. When entered in a multiple regression model with clinical, demographic, and/or other psychosocial variables, depression was significantly associated with parental anxiety (β = 0.35) [38] but was not significantly associated with parental psychopathology [49] or parental depression [38,50].

3.3.3.3. Other parent-specific risk factors. Single studies assessed other parent-specific factors. Depression was significantly associated with parental stress (strength of the association not reported) [69]. Depression was not significantly associated with the general impact of epilepsy on parents [55].

3.4. Psychosocial factors associated with mixed anxiety & depression

3.4.1. Intrapersonal factors

Intrapersonal factors were only assessed in single studies. After controlling for clinical, demographic, and other psychosocial variables, mixed anxiety & depression was significantly associated with having a positive attitude towards epilepsy (β not reported) [50], an external locus of control regarding social interactions (β not reported) [50], and four illness perception domains: expecting epilepsy to last a long time (β = 0.38), perceiving oneself to have less personal control over epilepsy (β = 0.42), believing treatment can help (β = -0.36), and expecting epilepsy to have a high emotional impact (β = 0.33) [52]. Mixed anxiety & depression was not significantly associated with the following illness perception domains: perceived consequences of having epilepsy, perceived understanding of epilepsy, and perception of identity due to having epilepsy (i.e., the name or label given to having epilepsy) [52]. After controlling for clinical, demographic, and other psychosocial variables, mixed anxiety & depression was not significantly associated with a general external locus of control [50].

Mixed anxiety & depression was also significantly associated with 'negative coping' (r = 0.30) [50], generalized anxiety (r = 0.48 for those aged 9–12; r = 0.62 for those aged 13–14) [61], symptoms of post-traumatic stress disorder (r_{pb} = 0.46 for those aged 9–12, r = 0.43 for those aged 13–14) [61], and panic attacks (r_{pb} = 0.53 for those aged 9–12) [61]. Mixed anxiety & depression was not significantly associated with autonomous motivation for treatment adherence [52].

3.4.2. Interpersonal factors

Interpersonal factors were only assessed in single studies. After controlling for clinical, demographic, and other psychosocial variables, mixed anxiety & depression was significantly associated with family functioning when assessed from an adolescent perspective (β not reported) but not when assessed from a parental perspective [50]. Mixed anxiety & depression was not significantly associated with family resources [50] or autonomous parental support and involvement [52].

3.4.3. Parent-specific factors

Parental perceived stigma towards epilepsy was assessed in two studies [50,67] and was significantly associated with mixed anxiety & depression (r = 0.26 [50], *t*-test only [67]). Mixed anxiety & depression was also significantly associated with parental psychopathology (r = 0.32) [68] but was not significantly associated with parental depression [50].

4. Discussion

This review critically appraised and synthesised the findings of studies examining the relationship between psychosocial variables and anxiety and/or depression in adolescents aged 9–18 years with epilepsy. Sixteen studies, reported across 23 articles, were included. A wide range of psychosocial variables were tested (37 for depression, 20 for anxiety, 14 for mixed anxiety & depression). At least one psychosocial variable was associated with anxiety and/or depression in each study, highlighting that psychosocial variables are consistently associated with anxiety and depression in adolescents with epilepsy. Intrapersonal

factors were more consistently associated with anxiety and depression than interpersonal or parent-specific factors. Alternative mental health difficulties were the most frequently assessed variable and were consistently associated with anxiety and depression (e.g., anxiety was consistently positively associated with depression and mental well-being). This is in line with findings from a systematic review of adults with epilepsy [12] and with findings in other adolescent physical health populations [74–77]. Attitude towards having epilepsy (significant in two of three studies [three of four articles]), seizure self-efficacy (significant in all three studies), and self-esteem (significant in two of two studies) were consistently associated with depression. Attitude towards having epilepsy and self-esteem were also respectively associated with anxiety and mixed anxiety & depression (both significant in one of one studies). This is in line with findings from a systematic review of adults with epilepsy, in which seizure self-efficacy was associated with depression; and self-esteem was associated with both anxiety and depression [12]. Attitude towards illness, disease management self-efficacy (a similar construct to seizure self-efficacy), and self-esteem are also associated with anxiety and depression in adolescents with other physical health conditions [78–80]. As negative attitude towards illness, low disease management self-efficacy, and low self-esteem negatively impact adherence to medical treatment in epilepsy and other physical health populations [81–83], the association between these variables and anxiety and/or depression may be underpinned by a shared pathway mediated by adherence to medical treatment. However, more robust research is needed to better understand the mechanisms underlying this relationship. Nevertheless, attitude towards having epilepsy and self-esteem may be important intervention targets for anxiety and depression in adolescents with epilepsy whereas seizure self-efficacy may be an important intervention target for depression.

Perceived stigma was associated with depression (significant in two of two studies) but not with anxiety (not significant in one of one studies). Several reviews suggest perceived stigma is likely an important risk factor for anxiety and/or depression in epilepsy [14,84–86]. However, in their systematic review of adults with epilepsy, Gandy et al. (2012) found that perceived stigma was only associated with depression in one of three studies [12]; and that perceived stigma only accounted for 0.26 % of the variance in anxiety. Thus, Gandy et al. (2012) concluded that the role of perceived stigma in the development of anxiety and depression in epilepsy may be overestimated [12]. Our findings partly support this conclusion and suggest that the role of perceived stigma as a risk factor for anxiety in epilepsy may be overestimated. However, perceived stigma may still be an important risk factor for depression.

Findings from this review suggest certain interpersonal and parent-specific factors may also be important risk factors for anxiety and/or depression in adolescents with epilepsy, although confidence in such findings is limited. Regarding interpersonal factors, single studies found that when assessed from an adolescent perspective, perceived family functioning was associated with depression and mixed anxiety & depression. However, when assessed from a parental perspective, perceived family functioning was not associated with mixed anxiety & depression and was only associated with depression in one of three studies. The difference in perceived family functioning dependant on the informant (i.e., parent *vs.* adolescent) highlights the importance of assessing psychosocial variables and symptoms of anxiety and/or depression in adolescents with epilepsy from multiple perspectives [87,88].

Regarding parent-specific factors, parental perception of their child being stigmatised due to having epilepsy was associated with mixed anxiety & depression (significant in two of two studies); though this association was weak. Single studies also found that parental stress and parental anxiety were associated with anxiety and depression; and parental psychopathology was associated with mixed anxiety & depression. Support for the role of these variables as important risk factors for anxiety and depression are strengthened by similar findings in other youth physical health populations in which the interpersonal and parent-specific factors outlined above are associated with several mental health outcomes [89–94]. Potential reasons for the associations outlined above are provided.

Parental anxiety about epilepsy is associated with 'overprotective' behaviours in parents of youth with epilepsy [95]. Parental overprotective behaviour is a predictor for anxiety and depression in the general youth population [96–98]. For those with epilepsy, adolescence usually involves the transition of responsibility of epilepsy management from parent to adolescent. This can lead to discrepancies between parent and adolescent about the adolescent's perceived level of autonomy [99]. It may be that the associations between the parent-specific factors (i.e., parental mental health difficulties and parental perceived stigma) and anxiety and/or depression found in this study are mediated or moderated by a discrepancy in perceived level of autonomy between the parent and adolescent. Such a discrepancy may partly explain why the impact of perceived family functioning differed between parent and adolescent.

The association between parental mental health difficulties and anxiety and/or depression in adolescents with epilepsy may also be influenced by adolescents adopting beliefs similar to their parents. Adolescents with physical health conditions tend to seek information relating to their condition from those whom they have a close and long-standing relationship with [100]. Thus, if parents are highly anxious and worrying about their child's epilepsy, then adolescents with epilepsy may adopt similar worrisome beliefs, potentially leading to increased levels of anxiety.

This synthesis provides a valuable insight into a broad range of psychosocial risk factors associated with anxiety and depression in adolescents with epilepsy and in turn suggests many potential interventions. Several limitations of the available studies preclude strong recommendations. First, as all but one study was cross-sectional, causation cannot be inferred. Identified risk factors may not lead to the development of anxiety and/or depression in adolescents with epilepsy but instead may be a consequence of anxiety and/or depression. Second, over half of the studies ($n = 10$) failed to control for clinical, demographic, or other psychosocial variables in their analyses. Without accounting for such variables, it is unclear whether identified risk factors are a consequence of other uncontrolled factors. It is also unclear how such variables may interact with each other. Third, only two studies measured adolescent anxiety and/or depression from multiple perspectives (i.e., parent and adolescent), whereas four relied solely on parent-proxy report. While assessing anxiety and/or depression from an adolescent perspective is priority [101,102], using a multi-informant perspective may provide more detailed insight into adolescent's experience of anxiety and/or depression [87,88,101]. Fourth, although a range of psychosocial variables were tested, many were tested in few studies. This makes it difficult to conclude whether the lack of association between such variables and anxiety and/or depression is due to such variables not being important risk factors or due to there being insufficient research investigating the role of such variables. Finally, the included studies used heterogenous outcome measures and data analysis procedures, limiting confidence in conclusions drawn. Despite these limitations, the findings have important clinical implications.

4.1. Clinical implications

Anxiety and depression were consistently positively associated with each other as well as alternative mental health difficulties. This is unsurprising given that the co-occurrence of anxiety and depression in epilepsy is common [103,104]. People presenting with anxiety and depression often experience more difficulties and respond less well to psychological and pharmacological intervention than those presenting with only anxiety or depression [105–107]. This highlights the clinical importance of screening adolescents with epilepsy for multiple types of mental health difficulties and supports current clinical guidance which recommends screening for symptoms of both anxiety and depression in

adolescents with epilepsy as part of regular review [108].

However, findings from this study indicate that clinicians need to go beyond screening for anxiety and depression and screen for a range of psychosocial factors also. This could help identify psychosocial risk factors which make adolescents with epilepsy susceptible to anxiety and depression and/or areas which could be a target of psychological intervention. Supporting this approach, Kazak et al. (2011) demonstrated that, compared to those receiving routine assessment only, screening for a range of psychosocial risk factors amongst newly diagnosed paediatric cancer patients led to patients and families receiving a wider range of psychosocial care corresponding to their identified needs [109]. It has been recommended that at each epilepsy clinic visit, clinicians should, at minimum, enquire about changes to patient's mental health; while a more detailed assessment should be conducted for all new patients and at routine time intervals such as annually or following any recent changes to ASM protocols [21,110]. During this more detailed assessment, it may be beneficial to screen for potential psychosocial risk factors identified in this review such as attitude towards having epilepsy, seizure self-efficacy, self-esteem, perceived stigma, family functioning and parental mental health difficulties.

A common approach in epilepsy clinics is to monitor those who do not meet clinical levels of anxiety and/or depression and refer them to specialist psychologist services for intervention once they do meet criteria [111]. However, as most studies in this review assessed anxiety and/or depression on a continuum, the psychosocial variables associated with anxiety and/or depression in this review are not restricted to clinical levels of anxiety and/or depression (i.e., anxiety and/or depressive disorders). Thus, screening and identifying potential psychosocial risk factors associated with anxiety and/or depression amongst adolescents with epilepsy who do not meet diagnostic criteria for anxiety and/or depressive disorders could lead to such individuals receiving lower-intensity interventions targeting identified risk factors to reduce their likelihood of developing clinical levels of anxiety and/or depression. For instance, educating adolescents with epilepsy on seizure management, improving family dynamics, providing support to parents to reduce their mental health difficulties, and providing adolescents with epilepsy and their families with psycho-educational material related to epilepsy could increase seizure self-efficacy, reduce parental mental health difficulties, and improve family functioning [112–115].

When considering clinical implications for those who require specialist psychological intervention (i.e., for those who do not respond well to lower level interventions or those presenting with anxiety and/or depressive disorders), traditional cognitive behavioural therapies which target unrealistic appraisals of events, including how one appraises their illness may be beneficial given attitude towards having epilepsy (which included items about illness appraisals), perceived stigma, seizure self-efficacy, and four illness perception domains (expecting epilepsy to last a long time, perceiving oneself to have less personal control over epilepsy, believing treatment can help, and expecting epilepsy to have a high emotional impact) were all associated with anxiety and/or depression. However, as it is unclear from the studies included whether the appraisals of adolescents with epilepsy were unrealistic, and as studies only assessed associations, it is too early to conclude this. As appraisals made by adolescents with epilepsy may be realistic (e.g., "I am treated differently than my peers due to having epilepsy", "having epilepsy could prevent me from being able to drive"), challenging such appraisals might be of limited efficacy in people with physical health conditions such as epilepsy [116–119].

4.2. Future research implications

While the findings of this review highlight psychosocial factors consistently associated with anxiety and/or depression, the evidence-base is limited by the lack of prospective studies, which precludes identifying cause and effect relationships. To better understand which psychosocial factors lead to the development and maintenance of anxiety and depression, future studies need to look beyond associations and employ more sophisticated statistical modelling techniques such as path analysis and structural equation modelling. This would enable the causal role of psychosocial factors and the interplay between biological/biomedical and psychosocial factors to be investigated within a well-defined theoretical framework. Given that adolescents with epilepsy often present with both anxiety and depressive symptoms, future research would also benefit from focusing on identifying psychological risk factors which cause and maintain both anxiety and depression. Exploring psychological factors which have been shown to predict both anxiety and depression in other physical health populations, such as worry and rumination, seems most appropriate [120–122]. Moreover, most studies included adolescents across different phases of the adolescent trajectory. The adolescent trajectory involves several important developmental milestones such as identity development, transition from dependence on caregiver to becoming an independent adult, and seeking acceptance from peer groups [123–125]. Adolescents with epilepsy contend with additional challenges such as transition of responsibility of epilepsy management from parent to child, increased fear of seizures in social situations, and increased recognition and realisation of restrictions accompanying an epilepsy diagnosis [14,126]. Thus, the psychosocial risk factors associated with anxiety and/or depression in adolescents with epilepsy may differ depending on their developmental phase. Future research would benefit from focusing on adolescents at specific developmental phases across the adolescent trajectory. Finally, due to the unpredictability of many aspects of epilepsy such as seizures [127,128] and given that anxiety and depression can highly fluctuate over short intervals [129], future research should employ methodologies such as experience sampling methodology which accounts for this unpredictability and variability.

4.3. Limitations of the review

As this systematic review was restricted to published studies written in English, it is possible that relevant grey-literature studies and studies published in other languages may have been excluded introducing potential language and cultural bias. Moreover, all studies recruited participants through clinics or epilepsy centres. As youth with well-controlled epilepsy and those from minority groups are less likely to present in clinics and epilepsy centres [87,130,131], the generalizability of findings to the wider adolescent epilepsy population is unclear. Finally, included studies were restricted to those that reported findings specifically for adolescents with epilepsy aged 9–18. This decision was made pragmatically i.e., in the UK, adolescents generally transition to adult epilepsy services by 18 years of age [132]. However, some definitions of adolescence extend to 24 years of age [133]. Therefore, using a more liberal definition of adolescence may have resulted in the identification of additional relevant studies.

4.4. Conclusion

This review suggests that several psychosocial variables may be important risk factors for anxiety and/or depression in adolescents with epilepsy. This highlights that the management of epilepsy in adolescents needs to go beyond the assessment of biological and biomedical factors (e.g., age, comorbid somatic conditions, seizure frequency and severity) and incorporate assessment of psychosocial factors. To advance understanding of the psychological mechanisms underpinning and maintaining anxiety and/or depression in adolescents with epilepsy, more prospective research which explicitly tests the role of psychological mechanisms accounted for within theoretical models of anxiety and/or depression is needed. This would help guide the development of more efficacious psychological interventions for adolescents with epilepsy.

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Data access statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2023.109522.

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