Emotional Distress in Young People with Epilepsy

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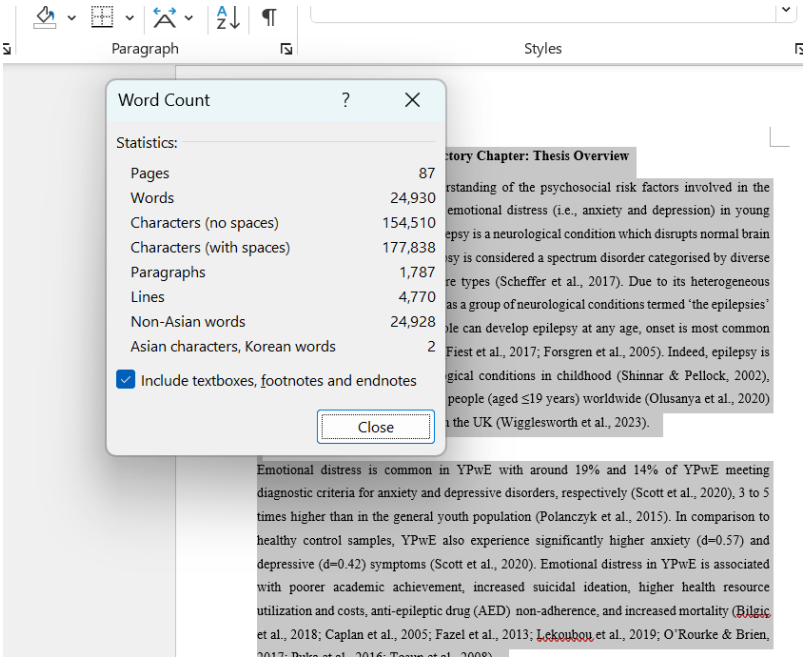

Introductory Chapter: Thesis Overview

This thesis aims to advance understanding of the psychosocial risk factors involved in the development and maintenance of emotional distress (i.e., anxiety and depression) in young people with epilepsy (YPwE). Epilepsy is a neurological condition which disrupts normal brain activity, leading to seizures. Epilepsy is considered a spectrum disorder categorised by diverse aetiologies, syndromes, and seizure types (Scheffer et al., 2017). Due to its heterogeneous nature, epilepsy is often referred to as a group of neurological conditions termed 'the epilepsies' (Scheffer et al., 2017). While people can develop epilepsy at any age, onset is most common in childhood and older adulthood (Fiest et al., 2017; Forsgren et al., 2005). Indeed, epilepsy is one of the most common neurological conditions in childhood (Shinnar & Pellock, 2002), affecting around 22 million young people (aged ≤19 years) worldwide (Olusanya et al., 2020) and around 60,000 young people in the UK (Wigglesworth et al., 2023).

Emotional distress is common in YPwE with around 19% and 14% of YPwE meeting diagnostic criteria for anxiety and depressive disorders, respectively (Scott et al., 2020), 3 to 5 times higher than in the general youth population (Polanczyk et al., 2015). In comparison to healthy control samples, YPwE also experience significantly higher anxiety (d = 0.57) and depressive (d = 0.42) symptoms (Scott et al., 2020). Emotional distress in YPwE is associated with poorer academic achievement, increased suicidal ideation, higher health resource utilization and costs, anti-epileptic drug (AED) non-adherence, and increased mortality (Bilgiç et al., 2018; Caplan et al., 2005; Fazel et al., 2013; Lekoubou et al., 2019; O'Rourke & Brien, 2017; Puka et al., 2016; Tosun et al., 2008).

YPwE are also at increased risk of experiencing neurological, physical, cognitive, and social difficulties (Aguiar et al., 2007; Beghi et al., 2002; Ettinger, 2006; McCagh et al., 2009; Menlove & Reilly, 2015; Reilly et al., 2014; Scott et al., 2020; Sherman et al., 2007), all of which are associated with poorer quality of life (QoL; Cengiz et al., 2019; Curt LaFrance et al., 2011; Giovagnoli et al., 2014; Johnson et al., 2004; Reilly et al., 2015; Vickrey et al., 2000; Zhong et al., 2022). Epilepsy management has traditionally focused on enhancing QoL by managing the medical aspects of epilepsy (i.e., reduction of seizure frequency and intensity, reduction of AED side-effects; Bishop et al., 2002; Blumer et al., 2004; Elliott & Richardson, 2014; Michaelis et al., 2020). Over the last 30 years, the medical management of epilepsy has progressed greatly and around 70% of YPwE could be seizure free with appropriate surgery or

AEDs (Englot et al., 2013; World Health Organization, 2019). However, there is growing evidence that psychosocial risk factors, particularly emotional distress, account for a larger amount of variance in QoL than seizure frequency or severity and AED side-effects (Baca et al., 2011; Reilly et al., 2015; Sano et al., 2014; Stevanovic et al., 2011). Ensuring YPwE receive appropriate support to reduce emotional distress is therefore essential.

Despite increased awareness of the prevalence and consequences of emotional distress in YPwE, the identification and management of emotional distress in YPwE continues to be an area of considerable unmet need (Gandy, 2023). A recent survery of 433 epilepsy specialisits working across 67 countries, 167 of whom worked primarily with YPwE, found approximately 60% do not routinely screen patients with epilepsy for emotional distress, and approximately 25% rely on 'watchful waiting' for those identified as experiencing emotional distress (Gandy et al., 2021). Moreover, only 13% of paediatric epilepsy clinics in England and Wales offer mental health services (Royal College of Paediatrics and Child Health, 2018). This has led to several campaigns, international consensus statements, national initiatives on epilepsy, and clinical practice guidelines recommending increased recognition and support for YPwE experiencing emotional distress (Barry, 2003; Barry et al., 2008; Centers for Disease Control and Prevention, 2003; Dunn et al., 2016; Epilepsy Scotland, 2020; Institute of Medicine, 2012; Kerr et al., 2011; Mula et al., 2022; National Institute for Health and Care Excellence, 2022; Villanueva et al., 2023; Young Epilepsy, 2022). As such, the World Health Organization (2022) has identified addressing the mental health needs of YPwE as a key target for improvement.

In response to the aforementioned recommendations, a proliferation of research has investigated potential risk factors for emotional distress in YPwE. Exploration of risk factors associated with emotional distress in epilepsy can be broadly categorised into four main areas: sociodemographic (e.g., age, gender), AEDs (e.g., AED type, mono- *vs.* poly-therapy), epilepsy-specific characteristics (e.g., seizure type and frequency, age of epilepsy onset), and psychosocial risk factors (e.g., perceived stigma, attitude towards epilepsy; Hermann et al., 2000). Research has primarily focused on identifying sociodemographic, AED and epilepsy-specific risk factors (Gandy et al., 2012; Hermann et al., 2000) but has thus far produced mixed findings (Dunn et al., 2016; Ekinci et al., 2009; Seyfhashemi & Bahadoran, 2013). While identification of psychosocial risk factors has received less attention than the other three areas (Gandy et al., 2012), psychosocial risk factors appear to influence the severity of emotional

distress in people with epilepsy to a greater degree than risk factors across the other three areas (Baker et al., 2019; Fisher & Noble, 2017; Fisher et al., 2018; Kwong et al., 2016; Lu & Elliott, 2012).

While emotional distress is common in YPwE, it is more prevalent in adolescents with epilepsy (AwE) than in younger children (LaGrant et al., 2020; Oguz et al., 2002; Thome-Souza et al., 2004; Wagner et al., 2015)[1]. For instance, in a sample of 6,730 YPwE living in North America, 9.3% and 7.6% of YPwE aged 6-12 were diagnosed with an anxiety or depressive disorder, respectively, according to ICD-9 criteria, compared with 18.9% and 20.6% of YPwE aged 13-18, respectively (Wagner et al., 2015). In the general population, emotional distress is also more common in adolescents than in younger children (Costello et al., 2011). It is postulated that this is due to the physical, social, and psychological changes that occur during adolescence (Andrews et al., 2021; Angold & Worthman, 1993; Paus et al., 2008). During adolescence, children experience profound changes to their physical appearance, develop their own identity, transition from dependence on caregiver to becoming an independent adult, and seek acceptance from peer groups (Best & Ban, 2021; Casey et al., 2010; Pfeifer & Berkman, 2019). Epilepsy may pose additional challenges for adolescents 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 (Ekinci 2009; Coppola et al., 2019). The psychosocial risk factors associated with emotional distress in YpWE can also differ between adolescents and younger children (Puka et al., 2017).

Developing an understanding of the psychosocial risk factors associated with emotional distress in AwE is necessary to inform development and implementation of age-appropriate psychological interventions to reduce emotional distress in this group. While several studies have examined whether psychosocial factors are associated with emotional distress in AwE, no systematic review has been conducted. Systematically appraising and synthesising the evidence-base will inform clinicians and researchers about which psychosocial factors could be a target for intervention and about further research needed to advance understanding of the psychosocial risk factors involved in the development and maintenance of emotional distress in AwE.

[1] The age range used to define AwE differ across cited studies. Age ranges included 12-17, 12-18, and 13-18 years of age.

Chapter 1 therefore presents a systematic review of 16 studies examining the relationship between psychosocial factors and emotional distress in AwE, all but one of which were cross-sectional. Twenty-seven psychosocial factors were significantly associated with emotional distress in AwE. Intrapersonal factors were more consistently associated with emotional distress than interpersonal or parent-specific factors. Intrapersonal factors consistently positively associated with emotional distress were alternative types of emotional distress (e.g., anxiety was positively associated with depression), having a negative attitude towards having epilepsy, lower seizure self-efficacy, lower self-esteem, and perceived stigma. 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 also positively associated with emotional distress but there was less evidence supporting such associations. The review provides a discussion of the clinical implications of these findings and recommendations for future research. One future research recommendation was to explicitly test the role of potential psychological mechanisms underpinning emotional distress in AwE accounted for within theoretical models of emotional distress. This would help guide the development of more efficacious psychological interventions for AwE.

Building on the findings outlined in Chapter 1, Chapter 2 presents the findings of an empirical study exploring the utility of a theoretical model of emotional distress which accounts for the potential psychological mechanisms that underpin emotional distress in AwE; the Self-Regulatory Executive Function (S-REF) model (Wells & Matthews, 1994, 1996). Due to the unpredictability of many aspects of epilepsy such as seizures (Lacey et al., 2015; Mensah et al., 2007); and given that emotional distress can highly fluctuate over short intervals (Moberly & Watkins, 2008), a method which accounts for this unpredictability and variability - experience sampling methodology (ESM) - was used. ESM requires participants to complete a short assessment about their 'momentary' experiences in their everyday settings several times daily (Shiffman et al., 2008). This reduces recall biases, enables the assessment of variability in experiences over time, and more accurately captures cause and effect relationships (Fahrenberg et al., 2007). According to the S-REF model, maladaptive metacognitive beliefs and processes are essential to the development and continuation of emotional distress. The S-REF model posits that maladaptive metacognitive beliefs, particularly positive and negative metacognitive beliefs about worry and rumination lead to anxiety and depression by steering individuals to engage in worry and rumination. Therefore, the aim of this study was to examine the role of

momentary positive and negative metacognitive beliefs in predicting momentary worry and rumination, and momentary anxiety and depression in AwE.

The ESM study involved participants completing a set of baseline questionnaires followed by a 10-day ESM assessment period. ESM assessments were completed on an app downloaded onto participants' smartphones. Participants were prompted to complete the ESM assessment five times daily. Eighteen participants completed the baseline questionnaires and ESM assessment period. Findings supported the utility of the S-REF model in AwE by showing momentary metacognitive beliefs were associated with momentary worry and rumination, and momentary anxiety and depression. After acknowledging study limitations, the chapter concludes with a discussion of the implications of the findings and recommendations for future research.

Journal Submission

The systematic review (Chapter 1) has been submitted to Health Psychology Review and is currently under review (see Appendix A for author guidelines). The empirical ESM paper (Chapter 2) will be submitted to Epilepsy & Behaviour (see Appendix B for author guidelines).

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Chapter 1. Psychosocial Factors Associated with Emotional Distress in Adolescents with Epilepsy: A Systematic Review

Abstract

Emotional distress is common in adolescents with epilepsy (AwE). Identifying psychosocial risk factors for emotional distress is essential for AwE to receive appropriate support. This systematic review synthesised findings of studies examining the relationship between psychosocial factors and emotional distress in AwE. Outcomes were anxiety, depression, and general distress. Six electronic databases were searched for studies which: used cross-sectional or prospective designs; quantitatively evaluated the relationship between psychosocial factors and emotional distress; presented results for AwE aged 9-18 years; and used validated measures of emotional distress. Psychosocial factors were categorised as intrapersonal, interpersonal, or parent-specific factors. Sixteen studies (23 papers) were included. All but one were cross-sectional. Regarding intrapersonal factors, alternative types of emotional distress 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 distress 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 emotional distress in AwE are needed.

Keywords: Psychosocial, Risk Factors, Epilepsy, Adolescents, Emotional Distress, Young People

1 Introduction

Epilepsy is one of the most common neurological conditions in childhood (Shinnar & Pellock, 2002), affecting around 22 million young people (aged ≤ 19[2]) worldwide (Olusanya et al., 2020). Epilepsy accounts for approximately 13 million disability adjusted life years each year (Singh & Sander, 2020) and is responsible for approximately 0.5% of the global burden of disease (World Health Organization, 2019). Around 19% and 14% of young people (aged ≤ 18[2]) with epilepsy (YPwE) meet diagnostic criteria for anxiety and depressive disorders, respectively (Scott et al., 2020), 3 to 5 times higher than in the general youth population (Polanczyk et al., 2015). In comparison to healthy control samples, YPwE also experience significantly higher anxiety (d = 0.57) and depressive (d = 0.42) symptoms (Scott et al., 2020). Anxiety and/or depression (i.e., emotional distress) in YPwE is associated with poorer academic achievement, increased suicidal ideation, reduced quality of life (QoL), and higher health resource utilization (Bilgiç et al., 2018; Caplan et al., 2005; Puka et al., 2016; Tosun et al., 2008). It is therefore imperative that YPwE have access to appropriate interventions to reduce emotional distress. To inform the development and implementation of appropriate interventions, identifying risk factors associated with emotional distress in YPwE is essential.

Potential risk factors associated with emotional distress in epilepsy have been categorised into four main areas: sociodemographic (e.g., age, gender), antiepileptic drugs (AEDs; e.g., AED type, mono- *vs.* poly-therapy), epilepsy-specific characteristics (e.g., seizure type and frequency, age of epilepsy onset), and psychosocial risk factors (Hermann et al., 2000). Research has primarily focused on identifying sociodemographic, AED and epilepsy-specific risk factors (Gandy et al., 2012; Hermann et al., 2000) and has thus far produced mixed findings (Dunn et al., 2016; Ekinci et al., 2009; Seyfhashemi & Bahadoran, 2013). While efforts to identify psychosocial risk factors has received less attention than the other three areas (Gandy et al., 2012), there is growing evidence that psychosocial risk factors (i.e., subjective psychological and/or social variables) have a greater impact on emotional distress in people with epilepsy than risk factors across the other three areas (Baker et al., 2019; Fisher & Noble, 2017; Fisher et al., 2018; Kwong et al., 2016a; Lu & Elliott, 2012). Moreover, as many sociodemographic, epilepsy-specific, and medication factors are either not readily modifiable (e.g., age, seizure type) or are effective in alleviating the neurological effects of epilepsy (e.g., AEDs may reduce seizure frequency and severity), the clinical utility of identifying risk factors

[2] Cited epilepsy diagnosis prevalence rates included young people aged 1-19, whereas cited prevalence rates of anxiety and depression in YpWE included young people aged 5-18.

across these areas is questionable. For instance, if a specific AED is identified as a risk factor for emotional distress but effectively alleviates the neurological effects of epilepsy, switching to a different AED to reduce emotional distress may negatively impact seizure frequency and severity. Therefore, identifying psychosocial risk factors associated with emotional distress in YPwE that could be ameliorated through psychological intervention appears a more clinically useful path (Gandy et al., 2012; Shallcross et al., 2015).

Despite limited understanding of the psychosocial risk factors associated with emotional distress in YPwE, 10 trials have evaluated the efficacy of psychological interventions for emotional distress in YPwE (Bennett, Au, et al., 2021; Blocher et al., 2013; Dorris et al., 2017; Li et al., 2016; Martinović et al., 2006; Rizou et al., 2017; Shore et al., 2008; Snead et al., 2004; Tajrishi et al., 2015; Wagner et al., 2010). 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; Bennett, Au, et al., 2021; Blocher et al., 2013; Dorris et al., 2017; Rizou et al., 2017; Shore et al., 2008; Snead et al., 2004; Tajrishi et al., 2015; Wagner et al., 2010); while only two were full-scale trials primarily designed to test intervention efficacy (i.e., phase II trials; Li et al., 2016; Martinović et al., 2006). Findings are mixed; seven trials reported a significant reduction in emotional distress from pre- to post-intervention (Bennett, Au, et al., 2021; Blocher et al., 2013; Li et al., 2016; Martinović et al., 2006; Rizou et al., 2017; Shore et al., 2008; Tajrishi et al., 2015) and three reported a significant reduction from pre-intervention to 3- or 6-month follow-up (Blocher et al., 2013; Martinović et al., 2006; Shore et al., 2008). Alternatively, three reported no significant reduction in emotional distress from pre- to post-intervention (Dorris et al., 2017; Snead et al., 2004; Wagner et al., 2010) and one reported no significant reduction from pre-intervention to 3-month follow-up (Dorris et al., 2017). These findings indicate that psychological interventions may reduce emotional distress in YPwE. 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 factors mediated treatment effects, it is unclear which psychosocial factors targeted for modification in these interventions were influential (or not) in the reduction of emotional distress.

Prior to conducting large-scale high-quality psychological intervention trials for emotional distress in YPwE, it is important to develop a better understanding of the psychosocial factors associated with emotional distress in YPwE. This could help inform the development of

theoretically-driven psychological interventions, considered best practice in intervention development (Craig et al., 2008; O'Cathain et al., 2019). The psychosocial risk factors associated with emotional distress in YPwE can differ depending on the life stage of a young person (e.g., young childhood *vs.* adolescence; Puka et al., 2017). As adolescence is a time of physical, social, and psychological change, developing an understanding of the psychosocial risk factors associated with emotional distress in YPwE during adolescence is a prerequisite to developing effective and age-appropriate psychological interventions for this group. While several studies have examined whether psychosocial factors are associated with emotional distress in adolescents with epilepsy (AwE), 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 factors and emotional distress in AwE.

2 **Method**

This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021). 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 emotional distress and a psychosocial variable (multivariate analyses were included if emotional distress was the outcome variable); 3) reported findings specifically for AwE aged 9-18; 4) assessed emotional distress 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 on baseline data or if emotional distress was measured at follow-up. Intervention studies were included if relevant analyses were conducted on pre-intervention data (post-intervention data were 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.

Emotional distress was defined as anxiety, depression, or general distress (i.e., a combination of anxiety and depression). Psychosocial variables were defined as subjective psychological and/or social characteristics located directly within the AwE (i.e., intrapersonal); involving the relationship between the AwE and another (i.e., interpersonal); or located directly within the parent of the AwE (i.e., parental-specific).

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 young people (see Figure 1 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 (e.g., Ekinci et al., 2009; Gökçen & Turgut, 2021; Reilly et al., 2011) were hand-searched to ensure relevant articles were not missed. Searches were updated in March 2023 to identify additional relevant studies.

	Search strategy (Medline, Web of Science, PsycINFO, CINAHL, psycARTICLE, AMED)
1	epilep*[tiab]
2	anxiet*[tiab] OR anxious*[tiab] OR depress*[tiab] OR "affective disorder*"[tiab] OR mood[tiab] OR psych*[tiab] OR emotional*[tiab] OR distress*[tiab]
3	child*[tiab] OR p?ediatric[tiab] OR adolescen*[tiab] OR teenage*[tiab] OR youth[tiab] OR young[tiab]
4	Rat[tiab] OR genet*[tiab] OR genes[tiab] OR psychogenic[tiab]
5	1 AND 2 AND 3 NOT 4
Filters: English Language only; journals only **Abbreviations: tiab = title or abstract only**	

Figure 1. Search Strategy for Electronic databases

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 and CM) each independently assessed approximately half of all titles and abstracts. At this stage, agreement between JT and the other reviewers (CH & 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 (CM & CD) each independently assessed a random 10% of full-text articles. At both stages, discrepancies were resolved

through discussion between two reviewers (i.e., JT & CH; 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 C), 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., AwE 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, standardised beta coefficients or odds ratios [*ORs*], and percentage of individual variance explained; R^2 values for overall models and unstandardised beta coefficients were not extracted). There was considerable variability in the statistics reported for multivariate analysis. While only standardised beta coefficients are included in the narrative write-up, additional statistics (e.g., R^2 values) are included where possible in Table 5. Articles that reported data from the same study were interpreted and referred to as a single study with all relevant papers listed. Each outcome variable (anxiety, depression, and general distress) was examined separately.

Psychosocial variables were grouped into three categories: intrapersonal (i.e., coping responses, epilepsy-specific beliefs and attitudes, general beliefs and attitudes, emotional distress, and 'other' intrapersonal factors); interpersonal (i.e., family variables and 'other' interpersonal factors); and parent-specific factors (i.e., parental epilepsy-specific beliefs and attitudes and 'other' parent-specific factors). Due to heterogeneity across studies, meta-analysis was considered inappropriate. Therefore, data were synthesised narratively. Correlation coefficient values of ≤.30, .40 to .60, and ≥.70, and *OR* values of ≤1.68, 1.69 to 3.47, and ≥6.70 were interpreted as weak, moderate, and strong, respectively (Chen et al., 2010; Dancey & Reidy, 2007).

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 Agency for Healthcare Research and Quality (Williams et al., 2010; see Appendix D). One reviewer (JT) independently assessed the quality of all included studies, while two reviewers (CM & CD) each independently assessed

approximately half of included studies. Discrepancies were resolved through discussion between reviewers (i.e., JT & CM; JT & CD). 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 emotional distress).

3 **Results**

The electronic database search retrieved 8,716 papers. 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 papers were assessed for eligibility. Overall, 23 papers corresponding to 16 studies were eligible and included (Figure 2).

Study characteristics are displayed in Table 1. Seven studies (12 papers) were conducted in North America and all but one study were cross-sectional. Nine studies (14 papers) measured one emotional distress outcome (e.g., anxiety, depression, or general distress), six studies (eight papers) measured two emotional distress outcomes, and one study (one paper) measured all three emotional distress outcomes. Depression was the most frequently assessed outcome (13 studies, 20 papers), followed by anxiety (six studies, eight papers), and general distress (five studies, five papers). 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 general distress, three used self-report measures and two used parent-proxy measures. The most used depression outcome measure was the Children's Depression Index (CDI; Kovacs, 1992) used in seven studies (10 papers); and the most used general distress outcome measure was the anxiety/depression subscale of the Child Behavior Checklist (CBCL; Achenbach, 1991; Achenbach & Leslie, 2001) used in four studies (four papers). No anxiety outcome measure was used in more than one study. A glossary of the outcome measures used are shown in Table 2.

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 AEDs was reported in 14 studies and ranged from 75% to 100%.

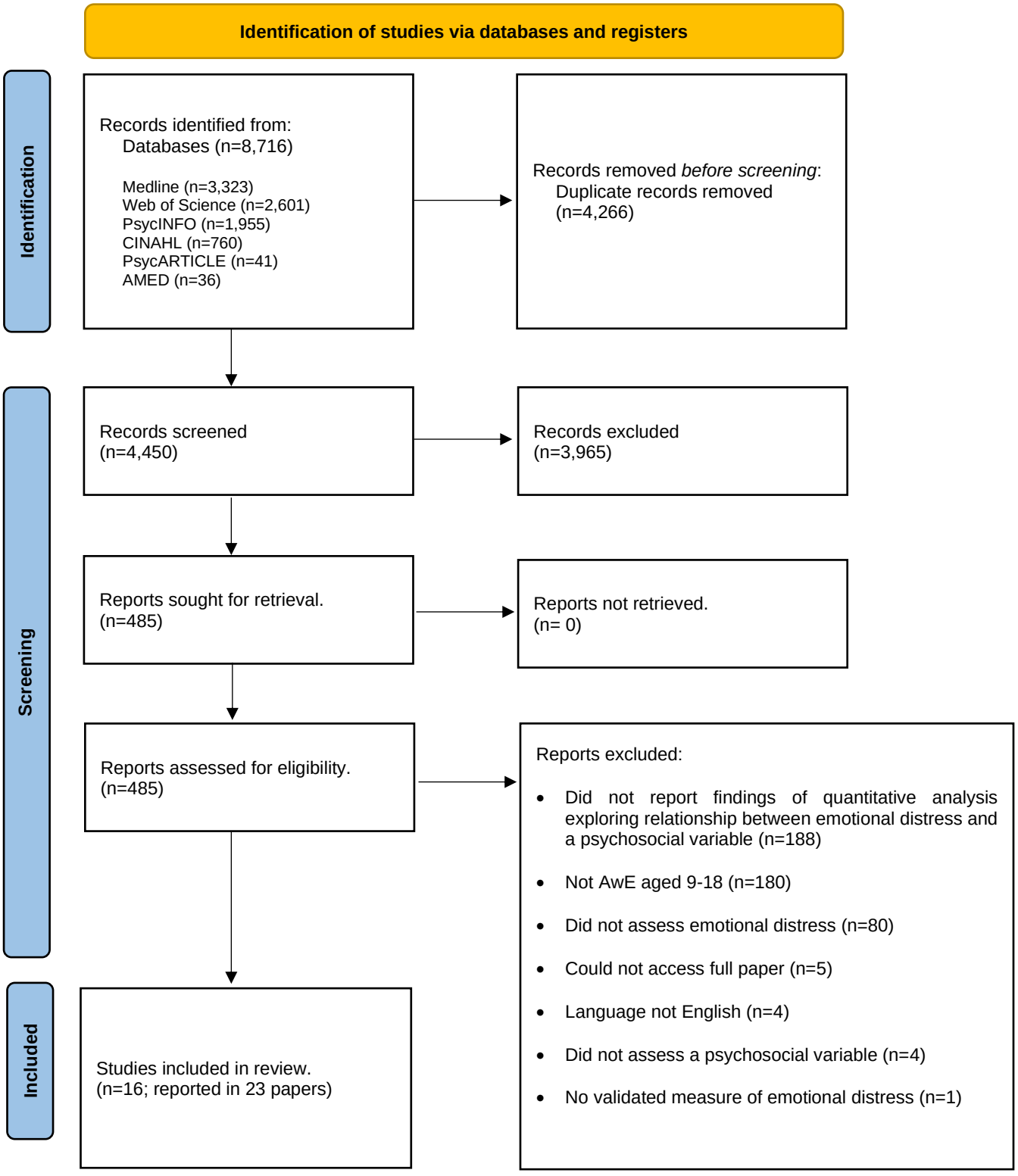

Figure 2. PRISMA diagram summarising the screening process for included studies.

Only six studies (eight papers) included multivariate analysis investigating whether psychosocial variables are associated with emotional distress (in which emotional distress 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.

3.1 Risk of bias

Assessment of 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 (Güven & İşler, 2015) 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 papers) conducting multivariate analyses, only three studies (three papers; Adewuya & Ola, 2005; Kwong et al., 2016a; Puka et al, 2017) controlled for all relevant confounders (i.e., variables significantly associated with emotional distress from univariate analysis and clinical/sociodemographic variables associated with emotional distress in YPwE in prior reviews, i.e., age, gender, seizure frequency, number of AEDs, duration of epilepsy; Ekinci et al., 2009; Reilly et al., 2011). The other three studies (five papers; Dunn et al, 1999; Haber et al., 2003; Rizou et al., 2015; Wagner et al., 2009, 2012b) 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 papers; Adewuya & Ola, 2005; Adewuya & Oseni, 2005; Eddy et al., 2010; Rizou et al., 2015) 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 IV's entered in the model for multivariate analysis; Green, 1991; VanVoorhis & Morgan, 2007). Nine studies (12 papers; Austin et al., 2004; Caplin et al., 2002; Dunn et al., 2009; Eddy et al., 2010; Güven et al., 2015; Kellerman et al., 2017; Kwong et al., 2016a, 2016b; Lai et al., 2015; Miniksar et al., 2022; Wagner et al., 2013; Young et al., 2023) had an adequately powered sample to conduct their analyses; while seven studies (11 papers; Adewuya & Ola, 2005; Adewuya & Oseni, 2005; Çengel-Kültür et al., 2009; Dunn et al., 1999; Haber et al., 2003; Puka et al., 2017; Rizou et al., 2015; Shatla et al., 2011; Wagner et al., 2009, 2012a, 2012b) 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 **Adewuya & Oseni, 2005**	Consecutive	Neuropsychiatric outpatient clinics	Cross-sectional	Nigeria
Austin et al., 2004 **Caplin et al., 2002** **Dunn et al., 2009**	Purposive	Paediatric neurology outpatient clinics, schools (via school nurses), paediatric neurologist private practices	Cross-sectional	USA
Çengel-Kültür et al., 2009	Purposive	Paediatric clinic	Cross-sectional	Turkey
Dunn et al., 1999 **Haber et al., 2003**	Purposive	Paediatric neurology outpatient clinics, neurologist private practices	Cross-sectional	USA
Eddy et al., 2010	Consecutive	Paediatric neuropsychiatry clinic	Cross-sectional	UK
Güven et al., 2015	Purposive	Paediatric neurology clinics	Cross-sectional	Turkey
Kellerman et al., 2017	Purposive	Epilepsy clinic	Cross-sectional	USA
Kwong et al., 2016a, 2016b	Purposive	Neurology outpatient clinics	Cross-sectional	Hong Kong
Lai et al., 2015	Purposive	Paediatric hospital, hospitals, medical centre	Prospective (6-month follow-up)	USA
Miniksar et al., 2022	Purposive	Paediatric neurology outpatient clinics	Cross-sectional	Turkey
Puka et al., 2017	Purposive	Epilepsy centres	Cross-sectional	Canada
Rizou et al., 2015	Consecutive	Paediatric epilepsy clinic	Cross-sectional	Greece
Shatla et al., 2011	Prospective	Paediatric epilepsy clinic	Cross-sectional	Egypt
Wagner et al., 2009, 2012a, 2012b	Purposive	Paediatric epilepsy clinic	Cross-sectional	USA
Wagner et al., 2013	Purposive	Epilepsy centre	Cross-sectional	USA
Young et al., 2023	Purposive	Paediatric outpatient clinics	Cross-sectional	South Korea

Table 2. Glossary of emotional distress measures used in included studies.

Validated outcome measure/ clinical interview	Abbreviation	Assessment method	Outcome	Studies used (n)	Papers 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	General distress (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	General distress (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) and Adewuya & Oseni, (2005) 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 last 12 months, the authors concluded the relevant psychiatric diagnosis was currently present.

Table 3. Participant characteristics from included studies.

Author	N	Age (years) Mean (SD) [range]	Ethnicity or race (%)	Gender (%)	Mean age at seizure onset (years)	Mean epilepsy duration Years (SD)	Seizure type(s) (%)	Seizure frequency (%)	Number of AEDs (%)
Adewuya & Ola, 2005; Adewuya & Oseni, 2005[a]	102	14.46 (1.98) [12-18]	Yoruba ethnic group: 96[b]	M: 64 F: 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
Austin et al., 2004[c]; Caplin et al., 2002; Dunn et al., 2009[d]	175	11.9 (1.8) [9-14]	White: 91 African American/ other: 9	M: 51 F: 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 AEDs at study entry: 100
Çengel-Kültür et al., 2009	41	14 (1.6) [NR]	NR	M: 41 F: 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
Dunn et al., 1999; Haber et al., 2003[e,f]	115	14.4 (NR) [NR]	White: ~90[g]	M: 62 F: 48	4.9 (NR)	NR	NR	NR	≥ 1 AEDs at study entry: 100[j]
Eddy et al., 2010	50	12.2 (1.4) [10-16]	NR	M: 52 F: 48	NR	NR	Seizure free: 100	Seizure free: 100	≥ 1 AEDs at study entry: 100
Güven et al, 2015	166	13.5 (2.57) [9-17]	NR	M: 51 F: 49	NR	NR	NR	NR	NR
Kellerman et al., 2017	99	14.7 (1.6) [12-17]	White non-Hispanic: 68 White Hispanic: 2 Black/African American: 27	M: 32 F: 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	None: 1 Monotherapy: 43 Polytherapy: 56

			Other: 3					Multiple per day: 6.3	
Kwong et al., 2016a, 2016b	140	14.5 (2.9) [10-18]	NR	M: 51 F: 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
Lai et al., 2015	61	13.4 (2.6) [10-18]	White: 76 Non-Hispanic: 79	M: 62 F: 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
Miniksar et al., 2022	56	14 (NR) [11-16]	NR	M:41 F: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
Puka et al., 2017[j]	65	15.6 (1.9) [12-18]	NR	M: 57 F: 43	7.7 (4.39)	6.9 (4.40)	Medical refractory localization-related: 100	Daily or weekly: 51 Monthly or yearly: 49	0-1 AEDs: 26 2 AEDs: 52 ≥ 3 AEDs: 22
Rizou et al., 2015	100	13.9 (2.21) [NR]	NR	M: 59 F: 41	NR	NR	NR	NR	NR
Shatla et al., 2011	23	11.8 (NR) [NR]	NR	M: 65 F: 35	NR	NR	Generalized tonic-clonic: 65 Focal: 35	NR	Polytherapy: 100
Wagner et al., 2009, 2012a, 2012b[k]	77	14.4 (2.21) [9-17]	White: 69 Non-white: 31	M: 45 F: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

Wagner et al., 2013	93	14 (2.0) [10-17]	Black: 30 White: 67 Other: 3	M: 47 F: 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
Young et al., 2023	289	15.4 (1.9) [11-18]	NR	M: 62 F: 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

Note. NR = Not Reported; AEDs = Anti-epileptic drugs; AAM = Atonic, Akinetic Motor; M = Male, F = Female.
[a]12 fewer participants were included in Adewuya & Oseni (2005), leading to slightly different participant characteristics; [b]This information was extracted from Adewuya & Oseni (2005; *n* = 90); [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) & Dunn et al.,(2009), leading to slightly different participant characteristics; [e]46 fewer participants were included in Haber et al., (2003), 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) 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., (2012a, 2012b), 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 emotional distress	Validated measure(s) of psychosocial variables	Control of confounders	Analysis appropriate
Adewuya & Ola, 2005; Adewuya & Oseni, 2005	Yes	N/S	Yes	Yes	Yes	Partial[a]	Partial[b]
Austin et al., 2004; Caplin et al., 2002; Dunn et al., 2009	Partial	N/S	Partial	Yes	Partial[c]	No	Yes
Çengel-Kültür et al., 2009	Partial	N/S	Yes	Yes	Yes	No	Partial
Dunn et al., 1999; Haber et al., 2003	Yes	N/S	Partial	Yes	Partial	Partial	Partial[d]
Eddy et al., 2010	Yes	N/S	Partial	Yes	Yes	No	Yes
Güven et al., 2015	Partial	Partial	Partial	Yes	Yes	No	Yes
Kellerman et al., 2017	Partial	N/S	Yes	Yes	Yes	No	Yes
Kwong et al., 2016a, 2016b	Partial	N/S	Yes	Yes	Yes	Partial[e]	Yes
Lai et al., 2015	Partial	N/S	Yes	Yes	Partial	No	Yes
Miniksar et al., 2022	Partial	N/S	Yes	Yes	Yes	No	Yes
Puka et al., 2017	Partial	N/S	Yes	Yes	Yes	Yes	Partial
Rizou et al., 2015	Yes	N/S	Partial	Yes	Partial	Partial	Partial
Shatla et al., 2011	Partial	N/S	Partial	Yes	Yes	No	Partial
Wagner et al., 2009, 2012a, 2012b	Partial	N/S	Yes	Yes	Yes	Partial[f]	Partial[g]
Wagner et al., 2013	Partial	N/S	Yes	Yes	Yes	No	Yes
Young et al., 2023	Partial	N/S	Yes	Yes	Partial	No	Yes

Note. N/S = Not specified; [a]While Adewuya & Ola (2005) controlled for all important confounders, Adewuya & Oseni (2005) 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) had an appropriate sample size to conduct correlation analysis, Adeuwya & Ola (2005) did not have an appropriate sample size to conduct multiple regression; [c]While Austin et al., (2004) & Caplin et al., (2002) used validated measures to assess psychosocial variables, Dunn et al (2009) included single item subscales to assess certain psychosocial variables; [d]While Dunn et al., (1999) had an appropriate sample size to conduct multiple regression, Haber et al., (2003) did not; [e]While Kwong et al. (2016a) controlled for all important confounders, Kwong et al. (2016b) 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., (2012a) 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., (2012b) and Wagner et al., (2009) did not; [g]While Wagner et al., (2012a) had an appropriate sample size to conduct simple regression, Wagner et al., (2012b) and Wagner et al., (2009) did not have an appropriate sample size to conduct multiple regression.

3.2 Psychosocial factors associated with anxiety

There was limited evidence that any of the psychosocial variables assessed in the included studies were consistently significantly associated with anxiety (see Table 5).

3.2.1 Intrapersonal factors

3.2.1.1 Epilepsy-specific beliefs and attitudes. One study (two papers; Adewuya & Ola, 2005; Adewuya & Oseni, 2005) 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 (Kwong et al., 2016b) measured self-esteem and one (Eddy et al., 2010) measured sense of self (a similar construct to self-esteem). Anxiety was significantly associated with both global and specific aspects of self-esteem (ρ = -.22 to -.48; *OR* = 1.13 to 1.29) but was not significantly associated with sense of self.

3.2.1.3 Emotional distress. Four studies (Dunn et al., 2009; Kwong et al., 2016a; Lai et al., 2015; Puka et al., 2017) assessed the relationship between anxiety and alternative types of emotional distress. Anxiety was significantly associated with depression (r = .66; *OR* = 1.21; Kwong et al., 2016a; Puka et al., 2017), even after controlling for clinical and demographic variables (*OR* = 1.22; Kwong et al., 2016a). Anxiety was also significantly associated with general distress (r = .48 for those aged 9-12; r = .62 for those aged 13-14; Dunn et al., 2009). When assessed cross-sectionally, anxiety was significantly associated with emotional well-being (defined as 'emotional functioning' and 'general mental health'; ρ = -.51 to -.60; Lai et al., 2015). However, when assessed prospectively, mean change in anxiety from baseline to 6-month follow-up was not significantly associated with mean change in emotional well-being (Lai et al., 2015).

3.2.1.4 Other intrapersonal factors. Two studies (Eddy et al., 2010; Lai et al., 2015) assessed quality of life (QoL). Eddy et al. (2010) found that QoL was significantly associated with anxiety (ρ = -.40). 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 = -.29). 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. General life satisfaction was assessed in one study (Eddy et al., 2010) and was not significantly associated with anxiety.

3.2.2. Interpersonal factors

3.2.2.1 Family factors. Two studies (Adewuya & Ola, 2005; Puka et al., 2017) assessed adaptive family resources (i.e., family mastery, family esteem & communication, family social support, financial well-being). After accounting for gender, number of AEDs and/or parental anxiety, adaptive family resources were not significantly associated with anxiety. Two studies (Adewuya & Oseni, 2005; Puka et al., 2007) assessed family functioning (both from a parental perspective). Findings were mixed. Adewuya & Oseni (2005) found a significant association with anxiety (*t*-test only); while Puka et al. (2007) found no significant association.

3.*2.2.2 Other interpersonal factors*. Single studies assessed other interpersonal factors. Anxiety was significantly associated with social functioning (ρ = -.37; Lai et al., 2015). Anxiety was also significantly associated with quality of family and peer relationships (ρ = -.29) but after correcting for multiple comparisons, this association was no longer significant (Eddy et al., 2010). Anxiety was not significantly associated with satisfaction with one's broader social and cultural environment (Eddy et al., 2010).

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 (Adewuya & Ola, 2005). 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 emotional distress. Two studies (Adewuya & Ola et al., 2005; Puka et al., 2017) assessed parental emotional distress 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 = .35; Puka et al., 2017) but was not significantly associated with parental psychopathology (Adewuya & Ola, 2005) or parental depression (Puka et al., 2017).

3.2.3.3 Other parent-specific factors. Anxiety was significantly associated with the general impact of epilepsy on parents (*t*-test only; Adewuya & Oseni, 2005).

3.3 Psychosocial factors associated with depression

3.3.1 Intrapersonal factors

3.3.1.1 Coping responses. Two studies (three papers; Dunn et al., 1999; Haber et al., 2003; Wagner et al., 2012b) assessed epilepsy-specific coping responses (two studies from a parental perspective and one from a child perspective). When assessed from a parental perspective, findings were mixed. One study (Wagner et al., 2012b) found that depression was significantly associated with 'developing competence and optimism' (ρ = -.27); while the other study (Dunn et al., 1999) 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 paper; Haber et al., 2003) 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 a child 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 gender, number of AEDs, and seizure severity (β not reported; Wagner et al., 2012b).

3.3.1.2 Epilepsy-specific beliefs and attitudes. Three studies (four papers; Adewuya & Ola, 2005; Dunn et al., 1999; Haber et al., 2003; Wagner et al., 2009) assessed attitude towards having epilepsy. Findings were mixed. Two studies (three papers; Dunn et al., 1999; Haber et al., 2003; Wagner et al., 2009) 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 (Adewuya & Ola, 2005) found no significant association. All three studies assessing seizure self-efficacy found that it was significantly associated with depression (r = -.32 to -.58; Caplin et al., 2002; Güven & İşler, 2015), even after controlling for other psychosocial variables (β not reported; Wagner et al., 2009). Both studies assessing perceived epilepsy-related stigma found that it was significantly associated with depression (r = .48; OR = 4.35; Adewuya & Ola, 2005; Austin et al., 2004), even after seizure frequency, number of AEDs, and other psychosocial variables were

controlled (β not reported; Adewuya & Ola, 2005). One study (Adewuya & Oseni, 2005) assessed the impact of epilepsy on adjustment and development and found that it was significantly associated with depression (*t*-test only).

3.3.1.3 General beliefs and attitudes. Perceived locus of control was assessed in one study (Dunn et al., 1999). 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 (Kellerman et al., 2017; Kwong et al., 2016b). Depression was significantly associated with both global (ρ = -.51; β = .62; *OR* = 1.32 to 1.34; Kellerman et al., 2017; Kwong et al., 2016b) and specific aspects of self-esteem (ρ = -.28 to 49; *OR* = 1.22 to 1.37; Kwong et al., 2016b). Sense of self was assessed in one study (Eddy et al., 2010) and was significantly associated with depression (ρ = -.34) Negative self-evaluation was assessed in one study (Miniksar et al., 2022) and was significantly associated with depression (*r* = .62) but after correcting for multiple comparisons, this association was no longer significant.

3.3.1.4 Emotional distress. Two studies (Kwong et al., 2016a; Puka et al., 2017) examined the association between depression and anxiety. Depression was significantly associated with anxiety (*r* = .66; *OR* = 1.17; Kwong et al., 2016a; Puka et al., 2017), even after controlling for gender (*OR* = 1.62; Kwong et al., 2016a).

Other forms of emotional distress were assessed in single studies. When assessed cross-sectionally, depression was significantly associated with emotional well-being (ρ = -.66 to -.71; Lai et al., 2015). However, when assessed prospectively, mean change in depression from baseline to 6-month follow-up was not significantly associated with mean change in emotional well-being (Lai et al., 2015). Depression was also significantly associated with being 'withdrawn/depressed' (*r* = .36 in those aged 9-12; *r* = .27 in those aged 13-14; Dunn et al., 2009), internalizing symptoms (ρ = .47; Wagner et al., 2013), and negative mood (β = .54; *OR* = 1.19; Kellermann et al., 2017).

3.3.1.5 Other intrapersonal factors. Two studies (Lai et al., 2015; Eddy et al., 2010) assessed QoL cross-sectionally and one (Lai et al., 2015) assessed QoL prospectively. When assessed cross sectionally, Lai et al. (2015) found that QoL was significantly associated with depression (ρ = -.43); whereas Eddy et al., (2010) found no significant association. 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. Two studies (Miniksar et

al., 2022; Wagner et al., 2009) assessed hopelessness and found that it was significantly associated with depression (r = .69; Miniksar et al., 2022), even after controlling for other psychosocial variables (β not reported; Wagner et al., 2009). Hopelessness also partially mediated the relationship between depression and attitude towards having epilepsy (Wagner et al., 2009).

Single studies examined other intrapersonal factors. Depression was significantly associated with suicidal probability (r = .83; Miniksar et el., 2022), suicidal ideation (r = .65; Miniksar et el., 2022); hostility (r = .65; Miniksar et al., 2022), negative externalizing problems (ρ = .28; Wagner et al., 2013), and negative evaluation of one's abilities and academic performance, defined as 'ineffectiveness' (β = .66; *OR* = 1.33; Kellermann et al., 2017). Depression was not significantly associated with general life satisfaction (Eddy et al., 2010).

One study (Miniksar et al., 2022) assessed maladaptive personality traits. Depression was significantly associated with overall dysfunctional personality (r = .69) and the personality trait-domains of 'negative affectivity' (r = .57), 'psychoticism' (r = .53), 'detachment' (r = .51), 'disinhibition' (r = .4), and 'antagonism' (r = .37).

3.3.2 Interpersonal factors

3.3.2.1 Family factors. Three studies (four papers; Adewuya & Oseni, 2005; Dunn et al., 1999; Haber et al; Puka et al., 2017) assessed family functioning (two studies from a parental perspective and one from a child 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); while Puka et al., (2017) and Dunn et al., (1999) found no significant association. 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. When assessed from a child perspective, family functioning was significantly associated with depression even after accounting for clinical, demographic, and/or other psychosocial variables (β not reported; Dunn et al., 1999; Haber et al., 2003).

Three studies (four papers; Adewuya & Ola, 2005; Dunn et al., 1999; Haber et al., 2003; Puka et al., 2017) 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 = -.49; Lai et al., 2015) and

interpersonal problems (β = .61; *OR* = 1.30; Kellermann et al., 2017). Depression was also significantly associated with quality of family and peer relationships (ρ = -.32) but after correcting for multiple comparisons, this association was no longer significant (Eddy et al., 2010). Depression was not significantly associated with one's broader social and cultural environment (Eddy et al., 2010).

3.3.3. Parent-specific factors

3.3.3.1 Parental epilepsy specific beliefs and attitudes. Two studies (Adewuya & Ola, 2005; Dunn et al., 1999) 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 paper; Haber et al., 2003) 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 parents perceived stigma nor the absolute difference between parent's attitude towards epilepsy was significantly associated with depression. The one study (Wagner 2012a) assessing parental seizure self-efficacy found it was significantly associated with depression (β not reported).

3.3.3.2 Parental emotional distress. Three studies (Adewuya & Ola, 2005; Dunn et al., 1999; Puka et al., 2017) assessed parental emotional distress. 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 = .35; Puka et al., 2017) but was not significantly associated with parental psychopathology (Adewuya & Ola, 2005) or parental depression (Dunn et al., 1999; Puka et al., 2017).

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; Shatla et al., 2011). Depression was not significantly associated with the general impact of epilepsy on parents (Adewuya & Oseni, 2005).

3.4 Psychosocial factors associated with general distress

3.4.1 Intrapersonal factors

Intrapersonal factors were only assessed in single studies. After controlling for clinical, demographic, and other psychosocial variables, general distress was significantly associated

with having a positive attitude towards epilepsy (β not reported; Dunn et al., 1999), an external locus of control regarding social interactions (β not reported; Dunn et al., 1999), and four illness perception domains: expecting epilepsy to last a long time (β = .38), perceiving oneself to have less personal control over epilepsy (β = .42), believing treatment can help (β = -.36), and expecting epilepsy to have a high emotional impact (β = .33; Rizou et al., 2015). General distress 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; Rizou et al., 2015). After controlling for clinical, demographic, and other psychosocial variables, general distress was not significantly associated with a general external locus of control (Dunn et al., 1999).

General distress was also significantly associated with 'negative coping' (r = .30; Dunn et al., 1999), generalized anxiety (r = .48 for those aged 9-12; r = .62 for those aged 13-14; Dunn et al., 2009), symptoms of post-traumatic stress disorder (r_{pb} = .46 for those aged 9-12, r = .43 for those aged 13-14; Dunn et al., 2009), and panic attacks (r_{pb} =.53 for those aged 9-12; Dunn et al., 2009). General distress was not significantly associated with autonomous motivation for treatment adherence (Rizou et al., 2015).

3.4.2 Interpersonal factors

Interpersonal factors were only assessed in single studies. After controlling for clinical, demographic, and other psychosocial variables, general distress was significantly associated with family functioning when assessed from a child perspective (β not reported) but not when assessed from a parental perspective (Dunn et al., 1999). General distress was not significantly associated with family resources (Dunn et al., 1999) or autonomous parental support and involvement (Rizou et al., 2015).

3.4.3 Parent-specific factors

Parental perceived stigma towards epilepsy was assessed in two studies (Dunn et al., 1999; Young et al., 2023) and was significantly associated with general distress (r = .26, t-test only). General distress was also significantly associated with parental psychopathology (r = .32; Çengel-Kültür et al., 2009) but was not significantly associated with parental depression (Dunn et al., 1999).

Table 5. Summary of significant findings from included studies grouped by emotional distress outcome.

Author (year)	Dependent variable	Analysis	Independent variables (psychosocial)	Independent variables entered into multivariate analysis[a]	Significant findings
			Anxiety		
Adewuya & Ola, 2005	DISC-IV (caseness)	*t*-test; multiple regression (forward selection)	**Intrapersonal** Attitude towards epilepsy (CATIS); perceived stigma (3-item measure[b]) **Interpersonal** Family resources (FIRM**)**; family stressors (FILE-FS) **Parent-specific** Parental perceived stigma (5-item measure[c]); parental psychopathology (GHQ)	Seizure frequency, number of AEDs, 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	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	CSI/ASI generalized anxiety subscale	Spearman correlation	**Intrapersonal** General distress (CBCL-A/D)	N/A	**Univariate** *Intrapersonal* General distress (ρ = 0.48* for-9-12Y/O; ρ = 0.62* for 13-14 Y/O)

	(continuous & caseness)				
Eddy et al., 2010	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** *Interpersonal* QoL (ρ = -0.29*)[d] **Interpersonal** Quality of family & peer relationships (ρ = -0. 29*)[d]
Kwong et al., 2016a;	HADS-A (caseness)	Univariate odds ratio; multiple regression (forward selection)	**Intrapersonal** Depression (HADS-D)	Gender, 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 AEDs, epilepsy aetiology, seizure free for ≥12 months, depression	**Univariate** *Intrapersonal:* Depression (*OR* = 1.21***) **Multivariate** *Intrapersonal* Depression (*OR* = 1.22**)
Kwong et al., 2016b	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	NeuroQOL anxiety subscale	*t*-test; ANOVA; spearman correlation	**Intrapersonal** Emotional functioning (PEDS-QL-EF); global mental health (PROMIS-M); QoL (single-item measure[e,f]); emotional well-being (single-item measure[f])	N/A	**Univariate** *Intrapersonal* 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	GAD-7	Pearson correlation; simple regression; multiple regression (backwards elimination)	**Intrapersonal** Depression (QIDS-SR16) **Interpersonal** Family functioning (F-APGAR)[g]; family resources (FIRM-MHSS); family stressors (FILE) **Parent-specific** Parental depression (QIDS-SR16); parental anxiety (GAD-7)	Gender, parental depression, parental anxiety, family resources	**Univariate** *Intrapersonal* Depression (r = 0.66***) *Interpersonal* Family resources (β = -0.25*) *Parent-specific* Parental depression (β = 0.25*); parental anxiety (β = 0.39**) **Multivariate** *Parent-specific* Parental anxiety (β = 0.35**)
			Depression		
Adewuya & Ola, 2005	DISC-IV (caseness)	*t*-test; multiple regression (forward selection)	**Intrapersonal** Attitude towards epilepsy (CATIS); perceived stigma (3-item measure[b]) **Interpersonal** Family resources (FIRM**)**; family stressors (FILE-FS) **Parent-specific** Parental perceived stigma (5-item measure[c]); parental psychopathology (GHQ)	Perceived stigma, seizure frequency, number of AEDs, 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]) *Parent-specific* Parental psychopathology (t = NR**) **Multivariate** *Intrapersonal:* Perceived sigma (β = NR, adjusted R^2 = 0.04***)

Adewuya & Oseni, 2005	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 Impact of epilepsy on adjustment and development (*t* = NR*) *Interpersonal* Family functioning (*t* = NR**) *Parent-specific* None
Austin et al., 2004	CDI	Pearson correlation	**Intrapersonal** Perceived stigma (8-item measure[i])	N/A	**Univariate** *Intrapersonal* Perceived stigma (*r* = 0.48***)
Caplin et al., 2002	CDI	Pearson correlation	**Intrapersonal** Seizure self-efficacy (SSES-C)	N/A	**Univariate** *Intrapersonal* Seizure self-efficacy (*r* = -0.32***)
Dunn et al., 2009	CSI-4/ASI-4 major depression subscale (continuous & caseness)	Spearman correlation	**Intrapersonal** Withdrawal (CBCL-D/W)	N/A	**Univariate** *Intrapersonal* Withdrawal (ρ = 0.36* for 9-12 Y/O; ρ = 0.27* for 13-14 Y/O)
Dunn et al., 1999	CDI	Pearson correlation; Multiple regression (stepwise)	**Intrapersonal** Attitude towards epilepsy (CATIS); coping resources (CHIC)[g]; locus of control (48-item measure[j]) **Interpersonal** Family resources (FIRM); Family functioning (F-APGAR)[k]; family stressors (FILE-SF) **Parent-specific** Parental perceived stigma (5-item scale[c]); parental depression (CES-D)	**Dunn et al., 1999** Age, gender, age of seizure onset, seizure severity, attitude towards epilepsy, family functioning[i], 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] *Parent-specific* None
Haber et al., 2003	CDI	Pearson correlation; multiple regression (stepwise)	**Intrapersonal** Attitude towards epilepsy (CATIS); coping resources (CHIC)[g,m] **Interpersonal** Family resources (FIRM-MH)[m]; Family functioning (F-APGAR)[k,m] **Parent-specific** Parental attitude towards epilepsy (6-item scale[n])[m]; parental perceived stigma (5-item scale[c])[m]	**Haber et al., 2003** Age, gender, family SES, epilepsy severity, attitude towards epilepsy, family functioning[l] Absolute 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*)[l] *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***)[l] *Parent-specific* None

Eddy et al., 2010	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*)[d] *Interpersonal* Quality of family & peer relationships (ρ = -0.32*)[d]
Güven et al, 2015	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	NDDI-E-Y[n] (continuous & caseness)	Odds ratios; simple regression	**Intrapersonal** Ineffectiveness (CDEI-2-I), self-esteem (CDI-2-S), negative mood (CDI-2-N) **Interpersonal** Interpersonal problems (CDI-2-IP)	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 self-esteem (β = 0.62***; adj R^2 = 0.38; *OR* = 1.32***) *Interpersonal* Interpersonal problems (β = 0.61 ***; adj R^2 = 0.36; *OR* = 1.30***)
Kwong et al., 2016a	HADS-D (caseness)	Univariate odds ratio; multiple regression (forward selection)	**Intrapersonal** Anxiety (HADS-A)	**Kwong et al., 2016a** Gender, 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 AEDs, epilepsy aetiology, seizure free for ≥12 months, anxiety	**Univariate** *Intrapersonal* Anxiety (*OR* = 1.17**) **Multivariate** *Intrapersonal* Anxiety (*OR* = 1.62**)
Kwong et al., 2016b	HADS-D	Spearman correlation;	**Intrapersonal** Self-esteem (overall, 'general', 'academic', 'social', & 'parent-related' subscales; CFSEI-2)	**Kwong et al., 2016b** N/A	**Univariate** *Intrapersonal*

		univariate odds ratio			Overall self-esteem (ρ = -0.51***; *OR* = 1.34***); general self-esteem (ρ = -0.49***; *OR* = 1.37***), academic self-esteem (ρ = -0.40***; *OR* = 1.22**); social self-esteem (ρ = -0.28**); parent-related self-esteem (ρ = -0.37***; *OR* = 1.3***)
Lai et al., 2013	NeuroQOL depression subscale	*t*-test; ANOVA; spearman correlation	**Intrapersonal** Emotional functioning (PEDS-QL-EF); global mental health (PROMIS-M); QoL (single-item measure[e,f]); emotional well-being (single-item measure[f]) **Interpersonal** Social functioning (PEDS-QL-S)	N/A	**Univariate** *Intrapersonal* Emotional functioning (ρ = -0.66***); global mental health (ρ = -0.71***); QoL (ρ = -0.43***) *Interpersonal* Social functioning (ρ = -0.49***)
Miniksar et al., 2022	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	QIDS-SR16	Pearson correlation; simple regression; multiple regression (backwards elimination)	**Intrapersonal** Anxiety (GAD-7) **Interpersonal** Family functioning (F-APGAR)[g]; 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 (β = -0.33**); family stressors (β = 0.33**) *Parent-specific* Parental anxiety (β = 0.36**) **Multivariate** *Parent-specific* Parental anxiety (β = 0.30*)
Shatla et al., 2011	CDI	Pearson correlation	**Parent-specific** Global parental stress (PSI)	N/A	**Univariate** *Parent-specific*

					Global parental stress (r = NR*)
Wagner et al., 2009	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)	**Wagner et al., 2009** 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 on depression after adjusting for self-efficacy (Sobel test statistic = NR*)
Wagner et al., 2012b	CDI	Pearson & spearman correlation; *t*-test; Kruskal-Wallis test; multiple regression (stepwise)	**Intrapersonal** Attitude towards epilepsy (CATIS), coping responses (CHIC; Kidcope)[k]	**Wagner et al., 2012b** Gender, ethnicity, number of AEDs, seizure severity; negative coping[l]	**Univariate** *Intrapersonal* Coping - develops competence and optimism (ρ = -0.27*)[g]; negative coping (total score ρ = 0.43**, r = -0.54**; frequency score ρ = 0.58***, t or H^o = NR*; efficacy score ρ = 0.46***, t or H^o = NR*)[l] **Multivariate** *Intrapersonal* Negative coping (total score β = NR***)[l]
Wagner et al., 2012a	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., 2013	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**)
			General distress		

Çengel-Kültür et al., 2009	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	CBCL-YSR anxiety/ depression subscale	Pearson correlation; multiple regression (stepwise)	**Intrapersonal** Attitude towards epilepsy (CATIS); coping resources (CHIC)[g]; Locus of control (48-item measure[j]) **Interpersonal** Family resources (FIRM); family functioning (F-APGAR)[k]; family stressors (FILE-SF) **Parent-specific** Parental perceived stigma (5-item scale[c]); parental depression (CES-D)	Age, gender, age of seizure onset, seizure severity, attitude towards epilepsy, family functioning[i], 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***)[l] *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*)[l]
Dunn et al., 2009	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	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* IP-timeline (β = 0.38**); IP-personal control (β = -0.42*); IP–treatment control (β = 0.36*); IP-emotional representations (β = 0.33*) *Interpersonal* None
Young et al., 2023	CBCL- YSR anxiety/ depression subscale	*t*-test	**Parent-specific** Parental perceived stigma (3-item scale[p])	N/A	**Univariate** *Parent-specific* Parental perceived stigma (t = NR*)

Note. Adj = adjusted; 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; IP = Illness Perceptions; ICIS-P = Impact of Childhood Illness Scale–Parent subscale; ICIS-F = Impact of Childhood Illness Scale–Family subscale; 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 = Standardised 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]3-item stigma scale developed by Jacoby et al., (1994); [c]5-item stigma scale adapted from an adult stigma scale developed by Ryan et al., (1980); [d]after adjusting for multiple comparisons, findings were no longer significant; [e]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'*; [f]single-item scale asking participants how much they had changed on a specific domain over the past 6 months; [g]measured from a parental perspective; [h]p=0.05 but authors reported as significant; [i]8-item stigma scale developed by Austin et al., (2004); [j]48-item perception of control scale developed by Connell (1985); [k]measured from a child and parental perspective; [l]measured from a child perspective; [m]absolute difference between parental scores calculated and used in analysis; [m]6-item parental attitude scale developed by Haber et al., (2003); [n]Two depression outcome measures (NDDI-E-Y & Neuro-QOL SF) were used in Kellerman et al., (2017). Findings from the NDDI-E-Y were chosen as this scale has been more widely used in the literature; [o]it was unclear if analysis conducted was *t*-test or Kruskal-Wallis; [p]3-item stigma scale adapted from a stigma scale developed by Jacoby et al., (1994).

4 Discussion

This review critically appraised and synthesised the findings of studies examining the relationship between psychosocial variables and emotional distress in adolescents aged 9-18 years with epilepsy. Sixteen studies, reported across 23 papers, were included. A wide range of psychosocial variables were tested (37 for depression, 20 for anxiety, 14 for general distress). At least one psychosocial variable was associated with emotional distress in each study, highlighting that psychosocial variables are consistently associated with emotional distress in AwE. Intrapersonal factors were more consistently associated with emotional distress than interpersonal or parent-specific factors. Alternative types of emotional distress were the most frequently assessed variables and were consistently associated with emotional distress (e.g., anxiety was consistently positively associated with depression). This is in line with findings from a systematic review of adults with epilepsy (Gandy et al., 2012) and with findings in paediatric physical health populations (Buchberger et al., 2016; Eccleston et al., 2004; Hjemdal et al., 2007; Modi et al., 2011).

Attitude towards having epilepsy (significant in three of four papers), seizure self-efficacy (significant in all three papers), and self-esteem (significant in two of two papers) were consistently associated with depression. Attitude towards having epilepsy and self-esteem were also respectively associated with general distress and anxiety (both significant in one of one papers). 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 (Gandy et al., 2012). Attitude towards illness, disease management self-efficacy (a similar construct to seizure self-efficacy), and self-esteem are also associated with emotional distress in young people with other physical health conditions (Armstrong et al., 2011; Ferro & Boyle, 2015; Herts et al., 2017; Ramsey et al., 2016). 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 (Kennard et al., 2004; Kyngäs, 2007; Xie et al., 2020), the association between these variables and emotional distress 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, seizure self-efficacy, and self-esteem may be important intervention targets for emotional distress in AwE.

Perceived stigma was associated with depression (significant in two of two papers) but not with anxiety (not significant in one of one papers). Several reviews suggest perceived stigma is

likely an important risk factor for emotional distress in epilepsy (Beyenburg et al., 2005; Ekinci et al., 2009; Hesdorffer & Lee, 2009; Mula & Kaufman, 2020). 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; 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 emotional distress in epilepsy may be overestimated. 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 emotional distress in AwE, although confidence in such findings is limited. Regarding interpersonal factors, single studies found that when assessed from a child perspective, perceived family functioning was associated with general distress and depression. However, when assessed from a parental perspective, perceived family functioning was not associated with general distress and was only associated with depression in one of three studies. Regarding parent-specific factors, parental perception of their child being stigmatised due being epileptic was associated with general distress (significant in two of two studies); though this association was weak. Single studies also found that parental stress and anxiety were associated with anxiety and depression; and parental psychopathology was associated with general distress. Support for the role of these variables as important risk factors for emotional distress are strengthened by similar findings in other paediatric physical health populations in which the interpersonal and parent-specific factors outlined above are associated with several mental health outcomes (Bakula et al., 2019; Bassi et al., 2021; Hickling et al., 2021; Leeman et al., 2016; Masnari et al., 2019; Trojanowski et al., 2021). Potential reasons for the associations outlined above are provided.

Parental anxiety about epilepsy is associated with ‘overprotective’ behaviours in parents of YPwE (Chapieski et al., 2005), a predictor for emotional distress in children and adolescents (Oldehinkel et al., 2006; Van Oort et al., 2011; Young et al., 2013). For YPwE, adolescence usually involves the transition of responsibility of epilepsy management from parent to child. This can lead to discrepancies between parent and adolescent about the adolescent’s perceived level of autonomy (Chew et al., 2019). Such discrepancies may moderate or mediate the association between the parent-specific factors (i.e., parental distress and parental perceived

stigma) and emotional distress in AwE found in this study and could explain why the impact of perceived family functioning differed depending on the informant.

The association between parental distress and emotional distress in AwE may also be influenced by AwE adopting beliefs similar to their parents. Young people with physical health conditions tend to seek information relating to their condition from those whom they have a close and long-standing relationship with (Young et al., 2003). Thus, if parents are highly anxious and worrying about their child's epilepsy, then AwE 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 emotional distress 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 emotional distress in AwE but instead may be a consequence of emotional distress. Likewise, 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. 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

Emotional distress was consistently associated with alternative types of emotional distress (e.g., anxiety was consistently positively associated with depression). This is unsurprising given that the co-occurrence of anxiety and depression in epilepsy is common (Jones et al., 2003; Kanner et al., 2004). 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 (Howland et al., 2008; Kerr et al., 2011; Nilsen et al., 2013). This highlights the clinical importance of screening AwE for multiple types of emotional distress and supports current clinical guidance which recommends screening for symptoms of both anxiety and depression in AwE as part of regular review (National Institute for Health and Care Excellence [NICE], 2022).

However, findings from this study indicate that clinicians need to go beyond screening for emotional distress and screen for a range of psychosocial factors also. This could help identify

psychosocial risk factors which make AwE susceptible to emotional distress 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 cancer patients led to patients and families receiving a wider range of psychosocial care corresponding to their identified needs. 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 AED protocols (Barry et al., 2008; Michaelis et al., 2018). 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 distress.

A common approach in epilepsy clinics is to monitor those who do not meet clinical levels of anxiety and depression and refer them to specialist psychologist services for intervention once they do meet criteria (Gandy et al., 2021). However, as most studies in this review assessed emotional distress on a continuum, the psychosocial variables associated with emotional distress in this review are not restricted to clinical levels of emotional distress (i.e., anxiety and/or depressive disorders). Thus, screening and identifying potential psychosocial risk factors associated with emotional distress amongst AwE who do not meet diagnostic criteria for anxiety and depressive disorders could lead to such individuals receiving lower-intensity interventions targeting identified risk factors to reduce their likelihood of developing clinical levels of emotional distress. For instance, educating AwE on seizure management, improving family dynamics, providing support to parents to reduce their distress, and providing AwE and their families with psycho-educational material related to epilepsy could increase seizure self-efficacy, reduce parental distress, and improve family functioning (Austin et al., 2002; Fong et al., 2019; Frizzell et al., 2011; Pfäfflin et al., 2012).

One major difficulty with providing AwE with low-intensity psychological interventions is that there is often a lack of clarity among epilepsy health care professionals (HCPs) about their role in managing mental health difficulties. Many epilepsy HCPs report feeling undertrained and under-skilled to manage the mental health difficulties of AwE (Gandy et al., 2021) and identify screening and management of mental health difficulties as the most critical area for their clinical development (Mula et al., 2017). One way to overcome this barrier is to integrate mental health specialists into epilepsy care settings (Gandy, 2023; Gandy et al., 2021). This is

not currently common practice in neurological settings (Mula et al., 2017), with only 13% of paediatric epilepsy clinics in in England and Wales offering mental health services (Royal College of Paediatrics and Child Health, 2018). Clinical practice guidelines highlight the key role of epilepsy specialist nurses in providing timely education and support to AwE and their families (NICE, 2022). Embedding an integrated care model within epilepsy services would enable mental health specialists (e.g., psychiatrists or clinical psychologists) to be part of multi-disciplinary team meetings and provide training and consultation to other professionals (e.g., epilepsy specialist nurses). Such integrated care models have been implemented in paediatric hospital settings and have demonstrated increased identification and reduction of several physical and mental health outcomes amongst both patients and family members (Bennett, Kerry, et al., 2021; Caccavale et al., 2020; Catanzano et al., 2021; Guilfoyle et al., 2015).

Preliminary evidence also indicates that HCPs embedded in epilepsy clinics can successfully deliver higher intensity psychological interventions. Bennett, Au, et al. (2021) conducted a study to determine the feasibility of a CBT-based telephone-delivered psychological intervention for YPwE. The intervention was delivered by epilepsy HCPs with limited experience delivering psychological interventions. All HCPs were trained by mental health professionals and received weekly supervision from a clinical psychologist. After receiving formal training, all HCPs were competent in delivering the intervention and YPwE who received the intervention demonstrated significant reductions in emotional distress pre- to post-intervention.

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 emotional distress. However, as it is unclear from the studies included whether the appraisals of AwE were unrealistic, and as studies only assessed associations, it is too early to conclude this. As appraisals made by AwE may be realistic (e.g., “I am treated differently than my peers due to having epilepsy”, “having epilepsy prevents me from being able to drive”), challenging such appraisals might be of limited efficacy in people with physical

health conditions such as epilepsy (Dodd et al., 2021; McPhillips et al., 2019; Noble et al., 2018; Temple et al., 2020).

4.2 Future research implications

While the findings of this review highlight psychosocial factors consistently associated with emotional distress, 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 emotional distress, 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 AwE 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 (Brown et al., 2020; Cherry et al., 2023; Trick et al., 2016). Finally, due to the unpredictability of many aspects of epilepsy such as seizures (Lacey et al., 2015; Mensah et al., 2007) and given that emotional distress can highly fluctuate over short intervals (Moberly & Watkins, 2008), 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. Finally, included studies were restricted to those that reported findings specifically for AwE aged 9-18. This decision was made pragmatically i.e., in the UK, AwE generally transition to adult epilepsy services by 18 years of age (Epilepsy Action, 2020). However, some definitions of adolescence extend to 24 years of age (Sawyer et al., 2018). 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 emotional distress in AwE. 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 emotional distress in AwE, more prospective research which explicitly tests the role of psychological mechanisms accounted for within theoretical models of emotional distress is needed. This would help guide the development of more efficacious psychological interventions for AwE.

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Chapter 2. Experience Sampling Methodology Study of Anxiety and Depression in Adolescents with Epilepsy: The Role of Metacognitive Beliefs and Perseverative Thinking

Abstract

The existing evidence-base for the efficacy of psychological interventions for emotional distress in young people with epilepsy (YPwE) is limited. To inform the development of psychological interventions for YPwE, understanding the psychological mechanisms underpinning and maintaining emotional distress, grounded within a well-defined theoretical model, is considered best practice. The Self-Regulatory Executive Function (S-REF) model specifies that maladaptive metacognitive beliefs are fundamental in the development and maintenance of perseverative thinking and emotional distress. Perseverative thinking and emotional distress can highly fluctuate over short intervals in YPwE. It is therefore important to account for this variability when testing the utility of psychological models. Experience sampling methodology (ESM) was therefore used to explore the momentary relationship between metacognitive beliefs, perseverative thinking, and emotional distress in YPwE. Eighteen participants diagnosed with epilepsy (aged 12-17 years) completed the 10-day ESM period. Participants were prompted to complete the ESM assessment five times daily. The ESM assessment assessed participant's momentary levels of metacognitive beliefs, perseverative thinking (i.e., worry and rumination), and emotional distress (i.e., anxiety and depression). A series of multilevel regression analyses indicated that momentary metacognitive beliefs were significantly positively associated with momentary worry and rumination, and momentary anxiety and depression. After controlling for momentary worry and rumination, respectively, momentary metacognitive beliefs did not account for additional variance in momentary anxiety or depression. Findings provide support for the utility of the S-REF model for emotional distress in YPwE. Metacognitive therapy (MCT), which is underpinned by the S-REF model, may be an appropriate intervention for emotional distress in YPwE. Implications of utilising ESM in clinical practice and future research are discussed.

Keywords: Experience Sampling, Metacognitive Beliefs, Worry, Rumination, Anxiety, Depression

1. Introduction

Epilepsy is one of the most common neurological conditions in the world [1], affecting around 60,000 young people (aged ≤19 years) in the UK [2] and around 760,000 young people in North America [3]. Around 19% and 14% of YPwE (aged ≤18 years) meet diagnostic criteria for anxiety and depressive disorders, respectively [4], which is 3-5 times higher than that reported in the general youth population [5]. Anxiety and depression in YPwE are associated with adverse antiepileptic drug (AED) effects [6] and have a larger negative impact on quality of life (QoL) than seizure frequency or duration [7]. Anxiety and depression also increase the risk of suicide [8,9], the incidence being 2.3 times higher in YPwE than in the general youth population [10]. Providing effective psychological interventions for YPwE is therefore essential [4,11]. However, the existing evidence-base for the efficacy of psychological interventions for anxiety and depression in YPwE is limited [12,13]. As such, when deciding which psychological interventions should be used for YPwE, National Institute for Health and Care Excellence (NICE) guidelines for YPwE (2022) recommend following recommendations from alternative NICE guidelines not grounded in data based on YPwE [14-16].

The alternative NICE guidelines cited above advocate a stepped-care approach to treating mental health difficulties, in which clinical decision-making about appropriate psychological interventions are based, in-part, on the severity of patients' symptoms. These alternative guidelines recommend interventions based on CBT principles as first-line treatment for those with mild anxiety or depression as well as group interpersonal psychotherapy (IPT) or group non-directive supportive therapy (NDST) for those with mild depression. Whereas CBT is recommended as first-line treatment for those with moderate-to-severe anxiety or depression [14-16]. No trials have evaluated the efficacy of group IPT or NDST for depression in YPwE, while seven trials have evaluated the efficacy of CBT-based interventions for emotional distress (i.e., anxiety and/or depression) in YPwE [17-23]. Only one of these trials was a full-scale trial primarily designed to test intervention efficacy (i.e., phase II trial) [20]; while six were primarily designed to evaluate the feasibility and acceptability of the interventions (i.e., phase I trials) [17-19, 21-23]. Findings are mixed; four trials reported a statistically significant reduction in emotional distress from pre- to post-intervention [17,18,20,21] and two reported a significant reduction from pre-intervention to 3-month follow-up [18,20]. Conversely, three reported no significant reduction in emotional distress from pre- to post-intervention [19,22,23]; and one reported no significant reduction from pre-intervention to 3-month follow-up [19].

Considering the conflicting findings regarding the efficacy of CBT for emotional distress in YPwE and given most trials are phase I intervention trials with underpowered samples, data regarding the efficacy of CBT for emotional distress in YPwE remains inconclusive. However, current evidence suggests that CBT achieves only modest treatment effects for young people and adults with physical health conditions [24,25], including adults with epilepsy [26]. Reasons for these modest treatment effects are not entirely clear. However, it has been suggested 'reality-testing' negative automatic thoughts (NATs), a defining feature of CBT, may be of limited benefit in a physical health context given that people's NATs are often realistic (e.g., 'I am unable to control my seizures') [25-28]. Moreover, a recent systematic review of psychosocial variables associated with emotional distress in YPwE found conflicting evidence regarding the association between emotional distress and illness appraisals [29], the modification of which is a central premise of CBT [30]. Thus, psychological interventions that focus on how and why people respond negatively to NATs (as opposed to focusing on the content of NATs) may be more useful for alleviating anxiety and depression in YPwE. One such intervention is Metacognitive Therapy (MCT) [31].

Preliminary evidence indicates that MCT may be an effective intervention for anxiety and depression in adults with physical health conditions [32-37], adolescents and young adults with cancer [38], and adolescents with common mental health disorders [39-43]. Prior to evaluating the efficacy of MCT in YPwE, the clinical utility of the psychological model underpinning MCT, the Self-Regulatory Executive Functioning (S-REF) model [44,45], needs to be established [46,47].

According to the S-REF model, anxiety and depression are maintained and intensified by a negative and continued response style called the cognitive attentional syndrome (CAS). The CAS includes perseverative thinking (i.e., worry and rumination), attentional focus on threat, and unhelpful coping behaviours (e.g., thought suppression, substance misuse, avoidance). The model postulates that the CAS is activated by stored metacognitive beliefs (i.e., beliefs about thinking, emotions, and conceptual processing strategies). While several metacognitive belief domains are highlighted in the S-REF model, they are often clustered into two general types: *positive metacognitive beliefs* and *negative metacognitive beliefs*. Positive metacognitive beliefs refer to beliefs about the benefits of, or need to, engage in perseverative thinking (e.g., "I must ruminate in order to find answers to my sadness", "worrying helps me cope"); whereas negative metacognitive beliefs refer to beliefs about the uncontrollability and danger of

perseverative thinking (e.g., “my ruminating is uncontrollable”, “worrying will make me go crazy”).

Preliminary evidence supports the utility of the S-REF model for anxiety and depression in adults with epilepsy; positive and negative metacognitive beliefs were associated with anxiety and depression in adults with epilepsy; these relationships were partially mediated by perseverative thinking in the form of worry [45,48]. However, the relationship between metacognitive beliefs, perseverative thinking (i.e., worry and rumination), and anxiety and depression in YPwE has not been explored. Moreover, the two studies investigating the utility of the S-REF model in epilepsy have several methodological shortcomings. First, both studies relied solely on retrospective self-report measures, which are often affected by recall biases [49]. As people with epilepsy often experience memory problems [50], recall biases may be more likely to occur in this population. Second, data were only collected at a single time-point. Emotional distress and engagement in perseverative thinking can highly fluctuate over short intervals [51]. Thus, collecting data at a single time-point increases risk of inaccuracy. Due to the unpredictability of seizures, the occurrence of which are associated with increased distress [52,53], perseverative thinking and emotional distress may be more likely to fluctuate in people with epilepsy than the general population. Moreover, there is evidence that retrospective and daily measures of psychological variables measure different constructs. For instance, one study found that retrospective measures of worry only accounted for a small amount of variance in daily worry [54]. Another study demonstrated that daily rumination predicted higher cortisol level whereas retrospective measures of rumination did not [55]. Finally, as both studies are cross-sectional, it is impossible to establish temporal precedence. Thus, an alternative methodology that overcomes the limitations of traditional retrospective self-report methods and accounts for the daily variability in perseverative thinking and emotional distress in YPwE is needed.

One such method is experience sampling methodology (ESM). ESM involves asking participants to complete a short assessment about their current ‘momentary’ experiences several times daily in everyday settings [56]. This minimises recall bias, enables the assessment of variability in experiences over time, and more accurately captures cause and effect relationships [49]. It also enables the assessment of emotional distress and related factors as they occur in their natural environment alongside daily tasks, increasing external validity [57].

ESM has been used to assess the relationship between metacognitive beliefs and perseverative thinking (i.e., worry and rumination) in adult populations [58-62]. However, to our knowledge, ESM has never been used to assess the relationship between metacognitive beliefs and perseverative thinking in YPwE. Therefore, the aims of this study were to assess the influence of metacognitive beliefs on perseverative thinking (i.e., worry and rumination) and emotional distress (i.e., anxiety and depression) in YPwE using ESM. More specifically, using ESM we explored whether momentary metacognitive beliefs were associated with momentary worry and rumination (aim 1), and momentary anxiety and depression (aim 2). Whether momentary worry and rumination were respectively associated with momentary anxiety and depression (aim 3); and whether momentary metacognitive beliefs explained additional variance in momentary anxiety and depression after respectively accounting for momentary worry and rumination (aim 4). Given adolescence is often regarded as a particularly challenging time for young people involving numerous physical and psychological changes [63,64], the study will focus specifically on YPwE aged 12-17 years.

2. Method

2.1 Study design

A prospective cohort design including a baseline assessment and an ESM assessment period was used. There is little theoretical guidance on the appropriate frequency and duration of an ESM assessment period. Based on practical considerations (e.g., ensuring sufficient data is collected whilst minimizing participant demand) and conclusions from a recent ESM study exploring optimal assessment frequency and duration [65], we chose for ESM assessments to occur five times daily for ten consecutive days.

2.2. Participants

Participants were recruited through a National Health Service (NHS) children's hospital in North-West England and through advertisements on social media. To be eligible, participants needed to have a diagnosis of epilepsy (of any type), be aged 12-17 years old, and have access to a smartphone with an android or iOS operating system for the 10-day ESM period. Both participant and their parent/caregiver needed to sufficiently understand English and have capacity to provide informed assent and consent, respectively.

Sample size

Considering the nested nature of ESM, small samples produce large datasets. As power calculations for three-level ESM models are in their infancy [66], most studies base their

sample size on practical considerations. ESM studies assessing emotional distress in neurological populations have used sample sizes ranging from 1-34 [67-78]. Based on practical considerations and approximated guidelines [79], we aimed to recruit, at minimum, 30 participants.

2.3. ESM assessment protocol

ESM assessments were delivered by an app downloaded onto participants' smartphones (SEMA3) [80]. Participants were 'prompted' to complete each ESM assessment by a pre-programmed notification within the app. To capture sufficient variability in daily experiences, prompts were delivered in pseudo-randomised blocks with a minimum of 90 minutes between each prompt. If assessments were not completed within 15 minutes of the prompt, they were no longer accessible. The timeframe during which participants were prompted was individualized by programming the app to only prompt participants during their average waking hours.

2.4. Measures

2.4.1. Baseline assessment

Sociodemographic and epilepsy information (age, gender, ethnicity, type of epilepsy, age at diagnosis, epilepsy duration, AED monotherapy or polytherapy, additional medical conditions) were obtained via medical records (for those recruited through an NHS children's hospital) and self-report (for those recruited through social media).

Metacognitive beliefs were assessed using the Metacognitions Questionnaire for Adolescents (MCQ-A) [81], an adapted version of the Metacognitive Questionnaire–30 (MCQ-30) [82]. The MCQ-A is a 30-item self-report questionnaire measuring five metacognitive belief domains. The MCQ-A has been validated for use with adolescents, has acceptable internal consistency (α = .66-.88 for subscales), and replicable factor structure with the MCQ-30 [81,83].

Anxiety and depression were assessed using a short version of the Revised Child Anxiety and Depression Scale (RCADS-25) [84]. The RCADS-25 is a 25-item self-report questionnaire measuring child and adolescent symptoms of anxiety (15-items) and depression (10-items). The anxiety subscale of the RCADS-25 has sufficient internal consistency (α = .82), test-retest reliability (intraclass correlation coefficient [ICC] = .73), and construct and structural validity. The depression subscale has acceptable internal consistency (α = .79-.80), test-retest reliability (ICC = .70), and construct validity [84,85].

Worry and rumination were assessed using 5-item versions of the Penn State Worry Questionnaire (brief-PSWQ) [86] and the Ruminative Response Scale (brief-RRS) [86]. Both scales have been validated in adolescents, correlate highly with their respective full versions (brief-PSWQ: r = .91–.94; brief-RRS: r = .88–.91), and have acceptable to excellent internal consistency (brief-PSWQ: α = .84–.91; brief-RRS: α = .78–.81) [86].

2.4.2. ESM assessment

The number of items per ESM assessment vary greatly across studies, ranging from 2-135 items [87]. On average, ESM assessments contain around 20-30 items [87]. There is conflicting evidence about whether increasing the number of items per assessment decrease compliance rates [87-89]. We took a cautious approach and only included 18 items in the final ESM assessment. As few ESM assessment measures have been validated [90], items are often developed based on global retrospective questionnaires [91]. Where possible, we used valid and reliable ESM assessment measures (momentary anxiety, depression, worry, rumination). Otherwise, we developed our own measures based on valid and reliable retrospective self-report questionnaires (momentary positive and negative metacognitive beliefs about worry and rumination). Item selection was made based on face validity. Split-half reliability coefficients were calculated for all ESM assessment measures. Mean scores for each measure for the first half of the 10-day ESM period were compared with mean scores for the second half. ESM assessment measures assessed momentary levels of anxiety (3 items), depression (3 items), worry (1 item), rumination (1 item), positive metacognitive beliefs about worry and rumination (2 items), and negative metacognitive beliefs about worry and rumination (2 items). To reduce potential reactivity to negatively valanced items, four items assessing positive affect were included. One item measuring threat-focused attention (a component of the CAS) was also included in the ESM assessment. However, the positive affect and threat-focused attention items were not included in the analysis. Based on feedback during the pilot stage (see 'consultation and piloting of ESM protocol' section), all ESM items were rated on a five-point Likert scale ranging from 0 (not at all) to 4 (very much so) and were preceded by the phrase 'Right now' (See appendix E for all included ESM items).

Momentary anxiety and depression were assessed using an adapted version of the anxiety and depression subscales of the 15-item Profile of Mood States (POMS-15) scale [92]. Each subscale consists of 3 items assessing momentary anxiety and depression, respectively. Both subscales have been used in adolescents [93,94]. In the current sample, both subscales demonstrated excellent reliability (ICC = .97 for both subscales).

Momentary worry and rumination were assessed using an adapted version of a 2-item scale developed by Kircanski et al. (2015) [95]. The 2-item scale measures momentary worry (1-item) and rumination (1-item). Both items demonstrate good convergent and discriminant validity with retrospective self-report questionnaires assessing worry and rumination, respectively [95]. In the current sample, both items demonstrated excellent reliability (ICC = .93 for both items).

Momentary positive and negative metacognitive beliefs were assessed by adapting items from the CAS-1 [31] and the Metacognitions about Symptom Control Scale (MaSCS) [96] to represent momentary experiences. Two subscales were developed: positive metacognitive beliefs about worry and rumination; negative metacognitive beliefs about worry and rumination. The CAS-1 has good concurrent and predictive validity, and good internal consistency (α = .78) in an epilepsy population [97,98].The MaSCS has good concurrent validity and internal consistency (α = .88-.89 for subscales) in a physical health population [96]. In the current sample, the positive metacognitive beliefs subscale demonstrated good reliability (ICC = .87) and the negative metacognitive beliefs subscale demonstrated excellent reliability (ICC = .92).

2.4.3. Consultation and piloting of ESM protocol

Members of a young person's advisory group (Generation R) that supports the design and delivery of paediatric health research in the UK were consulted about study materials, ESM assessment measures, and the ESM schedule. The 10-day ESM schedule was also informally piloted on eleven members of the young person's advisory group. Based on their feedback, language in the participant information sheets was amended, the positive affect items were added to the ESM assessment, and language used in the ESM assessment was revised (e.g., wording of questions was changed from second-person to first-person and a uniform five-point Likert scale ranging from 0 [not at all] to 4 [very much so] was implemented for responses across all ESM items).

2.5. Procedure

Ethical approval was obtained from the NHS Wales Research Ethics Committee 4 (reference: 21/WA/0072). The study was completed in two parts. Part 1 involved completing the baseline assessment. Part 2 involved completing the 10-day ESM assessment period. Interested participants could access and complete the baseline assessment online via Qualtrics. Prior to completing the online baseline assessment, interested participants and their parent/caregiver were required to complete an online assent and consent form, respectively. After completing

the online baseline assessment, those interested in completing the 10-day ESM period could enter their contact details. If entered, the researcher (JT) contacted potential participants to arrange a time to meet with them and their parent/caregiver (remotely via video-platform) to facilitate setting up the ESM app on their smartphone. During the meeting, the researcher (JT) explained the study, answered any questions, and obtained informed assent and consent from participant and parent/caregiver respectively for the ESM aspect of the study. After informed assent and consent were obtained, the researcher (JT) helped the participant download the ESM application ('app') onto their smartphone and ensured the participant understood all the items in the ESM assessment. The participant then completed an example ESM assessment on their smartphone to familiarise themselves with the ESM procedure. Next, the app was programmed to begin on an agreed date and to prompt them within an agreed timeframe for ten consecutive days. During the 10-day ESM period, the researcher (JT) contacted participants to ensure that the app was functional and that they still wanted to participate. At the end of the 10-day ESM period, the researcher (JT) contacted participants to thank them for taking part. Participants who completed both parts of the study received a £15 gift voucher.

2.6. Statistical analysis

Preliminary analyses revealed no baseline data were missing and so no data imputation was required. Compliance rates were investigated (i.e., number of ESM assessments completed). In line with previous ESM studies [51,99,100], participants completing less than one third of assessments were excluded from analyses. Pearson correlation, *t*-tests, or ANOVAs were conducted to explore whether compliance rates significantly differed depending on emotional distress (i.e., baseline anxiety or depression scores, clinically vs. non-clinically depressed or anxious individuals), sociodemographic information (i.e., age, gender, ethnicity), or clinical characteristics (i.e., epilepsy type, age of epilepsy diagnosis, epilepsy duration, seizure severity, AED protocol, additional medical conditions). To assess the extent to which measures were associated with related constructs and to assess the extent to which ESM measures were associated with their corresponding baseline measure, correlation analysis using ESM average scores was conducted (clustering was not accounted for in these analyses). Non-parametric analysis (one-tailed Spearman's correlation co-efficient) was used due to the ESM assessment scores being interval data and most measures demonstrating non-normal distributions. Descriptive statistics, correlational analysis, *t*-tests and ANOVAs were conducted using SPSS version 28.0.1.1.

The data obtained via ESM was nested at three levels: assessments (level 1), days (level 2), individuals (level 3). Multilevel modelling is the most suitable method for analysing repeated, nested data as it accounts for both within- and between-cluster variance (e.g., the variability between worry and anxiety scores within- and between-participants). Multilevel modelling is also able to handle large amounts of missing data without excluding participants [101]. Thus, multilevel modelling was used to explore the relationship between momentary metacognitive beliefs, perseverative thinking (i.e., worry and rumination) and emotional distress (i.e., anxiety and depression). As there was informative clustering within days (level 2), which can result in biased results [102], a 2-level structure (assessments > individuals) was deemed most appropriate for our dataset. Level 1 data (assessments) captures within-person variability (i.e., how much a score on a variable for a specific individual varies from their mean score). Level 2 data (individuals) captures between-person variability (i.e., how much an individual's mean score on a variable varies from the overall sample mean). As a uniform 5-point Likert-scale response scale was used for all ESM measures, it was not necessary to group-centre mean the data.

To explore aim 1 (whether momentary metacognitive beliefs are associated with momentary worry or rumination), multilevel regression models were constructed with momentary worry and rumination as respective outcome variables. Initially, separate multilevel simple regression models were constructed to explore associations between each outcome variable (momentary worry and momentary rumination) and each independent variable (momentary positive metacognitive beliefs about worry and rumination, momentary negative metacognitive beliefs about worry and rumination). Next, to assess the relative contribution of each independent variable, multilevel multiple regression models were constructed for each outcome variable (momentary worry and momentary rumination) with the independent variables significantly associated with each outcome variable in multilevel simple regression models entered simultaneously.

To explore aim 2 (whether momentary metacognitive beliefs are associated with momentary anxiety and depression) and aim 3 (whether momentary worry and rumination are associated with momentary anxiety and depression, respectively), multilevel simple regression models were constructed to explore associations between each outcome variable (momentary anxiety and momentary depression) and each independent variable (momentary positive metacognitive beliefs about worry and rumination, momentary negative metacognitive beliefs about worry

and rumination, momentary worry [for the outcome variable 'momentary anxiety'], momentary rumination [for the outcome variable 'momentary depression']).

To explore aim 4, multilevel multiple regression models were constructed for each outcome variable (momentary anxiety and momentary depression) with the independent variables significantly associated with each outcome variable in multilevel simple regression models entered simultaneously.

A random intercept for each individual was used for each model. Unstandardised beta coefficients were calculated for each model. ICCs were also calculated to explain the proportion of variability explained by clustering (i.e., within participants). As recommended [103], marginal and conditional R^2 were calculated for the multilevel multiple regression models to explain how much variance is accounted for by the independent variables without the variance explained by clustering (marginal R^2) and how much variance is explained by the independent variables and variation explained by clustering combined (conditional R^2). Multilevel modelling was conducted in R using the lme4 package.

Sensitivity analyses were conducted in which all multilevel multiple regression models were repeated with the inclusion of the corresponding baseline measure of the outcome variable investigated as an additional independent variable (e.g., for the model in which momentary worry was the outcome variable, baseline worry was included as an additional independent variable).

We had originally planned to test a more complete account of the theoretical predictions of the S-REF model by assessing the mediational relationship between momentary metacognitive beliefs, perseverative thinking (i.e., worry and rumination) and emotional distress (i.e., anxiety and depression) using time-lagged models. However, recruitment difficulties prevented us from reaching an appropriate sample size for such analysis. We therefore include a reflection of learning points related to recruitment difficulties and study design as an appendix (see Appendix F). The original analysis plan for this study was preregistered in the AsPredicted database (https://aspredicted.org/8v7ga.pdf).

3. Results

3.1. Descriptive statistics

Nineteen participants took part in the study. One participant did not complete the cut-off of at least a third of the ESM assessments and was excluded from analyses. No participants dropped

out during the ESM assessment period. Sample characteristics are summarized in Table 6. Participants had a mean age of 14.3 (range 12-17), were predominantly female (65%), and all but one were White British. The most common seizure type was generalised (50%), followed by focal (39%). Most of the sample were on AED monotherapy (61%). The mean age of epilepsy diagnosis was 8.9 years and mean epilepsy duration was 5.4 years. The mean time elapsed between completing the baseline assessment and starting the 10-day ESM period was 13.3 days (median 9 days). Thirty-three percent and 22% of the sample scored above the clinical threshold for anxiety and depression, respectively. Mean and median scores and standard deviations for all baseline and ESM assessment measures are shown in Table 7. Scores were relatively low across most measures.

3.2. Compliance with ESM protocol

Of a possible 900 ESM assessments, participants completed 599 (66%) within the 15-minute timeframe. Participant compliance rates of ESM assessments ranged from 40-88% (mean 67%). Compliance rates were not significantly associated with emotional distress, sociodemographic information, or clinical characteristics (see Appendix G).

3.3. Correlation analysis

Apart from positive metacognitive beliefs about worry (both the baseline assessment version and the ESM assessment version), significant moderate-to-large correlations were found between most ESM measures (e.g., momentary worry was significantly correlated with other momentary measures) and between most baseline measures (e.g., baseline worry was significantly correlated with most baseline measures). As momentary positive metacognitive beliefs about worry did not significantly correlate with most ESM measures, we separated the positive metacognitive beliefs about worry and rumination subscale into two distinct subscales: *positive metacognitive beliefs about worry* and *positive metacognitive beliefs about rumination.*

Regarding correlations between ESM measures and their corresponding baseline measure, a significant moderate correlation was found between baseline negative metacognitive beliefs about worry and momentary negative metacognitive beliefs about worry and rumination ($\rho = .47$, $p < .05$). Non-significant correlations were found between all other corresponding baseline and ESM measures (see Table 8).

Table 6. Sample characteristics (*n* = 18).

Variable	Category	N (% of participants)
Gender	Male	4 (22.2%)
	Female	13 (72.2%)
	Prefer not to say	1 (5.6%)
Age: mean (range; SD)		14.33 (12-17; 1.24)
Ethnicity	White British	17 (94.4%)
	White & Black African	1 (5.6%)
Seizure type	Generalised	9 (50%)
	Focal	7 (38.9%)
	Unknown	2 (11.1%)
AED protocol	Monotherapy	11 (61.1%)
	Polytherapy	7 (38.9%)
Seizure severity	Mild	5 (27.8%)
	Moderate	8 (44.4%)
	Severe	0 (0%)
	Unknown	5 (27.8%)
Age of epilepsy diagnosis (*n* = 16): mean (range; SD)		8.88 (2-16; 4.49)
Epilepsy duration (*n* = 16): mean (range; SD)		5.38 (0-12; 4.36)
Comorbidity		
None		14 (77.8%)
Another medical condition		4 (22.2%)
Days between baseline assessment and starting ESM protocol: mean (range; SD)		13.33 (3-46; 11.54)
RCADS-25 Anxiety clinical threshold[a]		N/A: 1 (5/6%)[b]
		Below threshold: 10 (55.6%)
		Borderline threshold: 1 (5.6%)
		Above threshold: 6 (33.3%)
RCADS-25 Depression clinical threshold[a]		N/A: 1 (5.6%)[b]
		Below threshold: 12 (66.7%)
		Borderline threshold: 1 (5.6%)
		Above threshold: 4 (22.2%)

Note. AED = Anti-epileptic drugs; ESM = Experience sampling method; RCADS = Revised Children's Anxiety & Depression Scale (25-item version); N/A = Not applicable; *SD* = standard deviation; [a]*T*-scores of 65-70 are classed as borderline clinical threshold for anxiety or depression, *T*-scores of > 70 are classed as above clinical threshold for anxiety or depression. See Appendix H for further information on how T-scores were calculated; [b]As identifying as male or female is required to calculate *T*-scores for the RCADS, this could not be calculated for one participant.

Table 7. Descriptive statistics for each study variable**.**

Variable	Mean (median; *SD*)	Score range
Baseline measures		
1) Anxiety (RCADS-25 anxiety subscale)	15.56 (14.5; 7.06)	0-60
2) Depression (RCADS-25 depression subscale)	12.67 (11.5; 6.04)	0-40
3) Worry (brief-PSWQ)	17.56 (18.5; 5.26)	5-25
4) Rumination (brief-RRS)	12.05 (11.5; 3.35)	5-20
5) Positive metacognitive beliefs about worry (MCQ-A-PBW subscale)	11.22 (11; 3.49)	6-24
6) Negative metacognitive beliefs about worry (MCQ-A-NBW subscale)	16.44 (15.5; 4.73)	6-24
ESM assessment measures		
7) Momentary anxiety	.96 (.79; .92)	0-4
8) Momentary depression	.98 (.55; 1.13)	0-4
9) Momentary worry	1.19 (1.25; .98)	0-4
10) Momentary rumination	1.01 (1.03; .97)	0-4
11) Momentary positive beliefs about worry	.73 (.56; .76)	0-4
12) Momentary positive beliefs about rumination	.65 (.36; .67)	0-4
13) Momentary negative beliefs about worry and rumination	3.16 (3.15; 2.28)	0-8

Note. brief-PSWQ = Penn State Worry Questionnaire (5-item version); brief-RRS = Ruminative Response Scale (5-item version); ESM = Experience sampling method; MCQ-A-PBW = Metacognitions Questionnaire for Adolescents–Positive Beliefs about Worry Subscale; MCQ-A NBW = Metacognitions Questionnaire for Adolescents–Negative Beliefs about Danger and Uncontrollability of Worry Subscale; RCADS = Revised Children's Anxiety & Depression Scale (25-item version). *SD* = standard deviation.

Table 8. Spearman's rho correlations between study variables.

	Baseline measures							*ESM assessment measures*					
Variables	**1)**	**2)**	**3)**	**4)**	**5)**	**6)**	**7)**	**8)**	**9)**	**10)**	**11)**	**12)**	**13)**
Baseline measures													
1) Anxiety (RCADS-25 anxiety subscale)	-	.68***	.78***	.81***	.44*	.69***	.35	.09	.14	.14	-.40	-.23	-.03
2) Depression (RCADS-25 depression subscale)		-	.48*	.75***	.31	.54*	.44*	.23	.15	.21	-.11	.08	.07
3) Worry (brief-PSWQ)			-	.78***	.33	.74***	.22	-.07	.86	.01	-.28	-.26	.18
4) Rumination (brief-RRS)				-	.18	.72***	.26	.05	.15	.13	-.12	-.03	.20
5) Positive metacognitive beliefs about worry (MCQ-A-PBW subscale)					-	.25	.67**	.40	.38	.47*	-.08	-.10	-.06
6) Negative metacognitive beliefs about worry (MCQ-A-NBW subscale)						-	.44*	.14	.45*	.30	-.24	-.01	.47*
ESM assessment measures													
7) Momentary anxiety							-	.83***	.85***	.88***	.05	.37	.47*
8) Momentary depression								-	.84***	.86***	.31	.48*	.40*
9) Momentary worry									-	.89***	.19	.41*	.64**
10) Momentary rumination										-	.29	.57**	.57**
11) Momentary positive beliefs about worry											-	.78***	.06
12) Momentary positive beliefs about rumination												-	.31
13) Momentary negative beliefs about worry and rumination													-

Note. ESM = Experience sampling method; RCADS = Revised Children's Anxiety & Depression Scale (25-item version); brief-PSWQ = Penn State Worry Questionnaire (5-item version); brief-RRS = Ruminative Response Scale (5-item version); MCQ-A-PBW = Metacognitions Questionnaire for Adolescents–Positive Beliefs about Worry Subscale; MCQ-A NBW = Metacognitions Questionnaire for Adolescents–Negative Beliefs about Danger and Uncontrollability of Worry Subscale* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ (one-tailed).

3.4. Multilevel modelling

3.4.1. Aim 1

In the multilevel simple regression analyses for momentary worry and rumination, all three momentary metacognitive belief domains were significantly associated with worry (β = .20-.31) and rumination (β = .17-.31; see Table 9). The ICCs for the independent worry and rumination models ranged from .45-.54, indicating that approximately half of the variability in observed relationships between outcome variables and each significant independent variable was due to within-person variation. When entered simultaneously into a multilevel multiple regression analysis, momentary positive metacognitive beliefs about rumination (β = .16 for worry model; β =.17 for rumination model) and momentary negative metacognitive beliefs about worry and rumination (β = .17 for worry model; β = .20 for rumination model) remained significantly independently associated with momentary worry and rumination but momentary positive metacognitive beliefs about worry did not. The ICCs for the multilevel multiple regression models for worry and rumination were .47 and .50, respectively (see Table 10).

Table 9. Multilevel simple regression for the dependent variables (momentary worry, momentary rumination) and each independent variable.

Momentary worry	***β***	**95% CI**	***p***	**ICC**
Momentary positive metacognitive beliefs about worry	.22	.12 - .32	< .001	.54
Momentary positive metacognitive beliefs about rumination	.31	.21 - .42	< .001	.53
Momentary negative metacognitive beliefs about worry and rumination	.20	.16 - .25	< .001	.45
Momentary rumination	***β***	**95% CI**	***p***	**ICC**
Momentary positive metacognitive beliefs about worry	.17	.07 - .27	< .01	.54
Momentary positive metacognitive beliefs about rumination	.31	.20 - .41	< .001	.54
Momentary negative metacognitive beliefs about worry and rumination	.22	.18 - .26	< .001	.49

Note. CI = confidence interval; ICC = intraclass correlation coefficient; β = unstandardised beta coefficient

3.4.2. Aim 2 & 3

The results of the multilevel simple regression analyses for momentary anxiety and depression are shown in Table 11. Momentary worry (β = .46), momentary positive metacognitive beliefs about rumination (β = .19), and momentary negative metacognitive beliefs about worry and rumination (β = .08) were significantly associated with momentary anxiety. Momentary rumination (β = .32), momentary positive metacognitive beliefs about rumination (β = .13), and momentary negative metacognitive beliefs about worry and rumination (β = .07) were significantly associated with depression. Momentary positive metacognitive beliefs about

worry were not significantly associated with either momentary anxiety or momentary depression. ICCs for the independent anxiety and depression models ranged from .44-.72.

Table 10. Multilevel multiple regression for the dependent variables (momentary worry, momentary rumination) with independent variables entered simultaneously.

Momentary worry	***β***	**95% CI**	***p***
Intercept	.50	.08 - .92	< .05
Momentary positive beliefs about worry	.07	-.04 -.18	ns
Momentary positive metacognitive beliefs about rumination	.16	.04 - .28	< .01
Momentary negative metacognitive beliefs about worry and rumination	.17	.12 - .21	< .001
Model summary Assessments: 589 ICC = .47 Marginal R^2 / Conditional R^2 = .17 / .56			
Momentary rumination	***β***	**95% CI**	***p***
Intercept	.28	-.13 -.69	ns
Momentary positive metacognitive beliefs about worry	.01	-.10 - .11	ns
Momentary positive metacognitive beliefs about rumination	.17	.06 - .28	< .01
Momentary negative metacognitive beliefs about worry and rumination	.20	.15 - .24	< .001
Model summary Assessments: 589 ICC = .50 Marginal R^2 / Conditional R^2 = .21 / .60			

Note. CI = confidence interval; ICC = intraclass correlation coefficient; ns = non-significant; β = unstandardised beta coefficient

3.4.3. Aim 4

The results of the multilevel multiple regression analyses for momentary anxiety and depression are shown in Table 12. After respectively controlling for momentary worry and momentary rumination (and other metacognitive beliefs domains respectively significantly associated with momentary anxiety and momentary depression in the multilevel simple regression analyses; see Table 11), none of the momentary metacognitive belief domains were significantly independently associated with momentary anxiety or depression. Momentary worry was significantly independently associated with momentary anxiety (β = .45) and momentary rumination was significantly independently associated with momentary depression (β = .31) The ICCs for the multilevel multiple regression models for anxiety and depression were for .45 and .66, respectively.

3.5. Sensitivity analysis

The inclusion of the corresponding baseline measure of the outcome variable in the multilevel multiple regression models had little impact on the results. None of baseline measure were significantly independently associated with the relevant outcome variables (see Appendix I).

Table 11. Multilevel simple regression for the dependent variables (momentary anxiety, momentary depression) and each independent variable.

Momentary anxiety	***β***	**95% CI**	***p***	**ICC**
Momentary worry	.46	.41 - .51	< .001	.44
Momentary positive metacognitive beliefs about worry	.05	-.04 - .13	ns	-
Momentary positive metacognitive beliefs about rumination	.19	.10 - .28	< .001	.62
Momentary negative metacognitive beliefs about worry and rumination	.08	.05 - .12	< .001	.59
Momentary depression	***β***	**95% CI**	***p***	**ICC**
Momentary rumination	.32	.26 - .38	< .001	.66
Momentary positive metacognitive beliefs about worry	-.01	-.09 - .07	ns	-
Momentary positive metacognitive beliefs about rumination	.13	.05 - .22	< .01	.72
Momentary negative metacognitive beliefs about worry and rumination	.07	.03 - .10	< .001	.71

Note. CI = confidence interval; ICC = intraclass correlation coefficient; ns = non-significant; *β* = unstandardised beta coefficient

Table 12. Multilevel multiple regression for the dependent variables (momentary anxiety, momentary depression) with independent variables entered simultaneously.

Momentary anxiety	***β***	**95% CI**	***p***
Intercept	.42	.14 - .69	< .01
Momentary worry	.45	.40 - .51	< .001
Momentary positive metacognitive beliefs about rumination	.05	-.02 - .13	ns
Momentary negative metacognitive beliefs about worry and rumination	-.01	-.04 - .02	ns
Model summary Assessments: 589 ICC = .45 Marginal R^2 / Conditional R^2 = .36 / .65			
Momentary depression	***β***	**95% CI**	***p***
Intercept	.65	.22 – 1.08	< .01
Momentary rumination	.31	.25 - .38	< .001
Momentary positive metacognitive beliefs about rumination	.04	-.04 - .12	ns
Momentary negative metacognitive beliefs about worry and rumination	-.00	-.04 - .03	ns
Model summary Assessments: 589 ICC = .66 Marginal R^2 / Conditional R^2 = .13 / .70			

Note. CI = confidence interval; ICC = intraclass correlation coefficient; ns = non-significant; *β* = unstandardised beta coefficient

4. Discussion

This is the first study to explore the potential utility of the S-REF model [104,105] for explaining emotional distress (i.e., anxiety and depression) in YPwE. It is also the first study to explore the fluctuating nature of emotional distress and theoretically related constructs in YPwE by using an innovative methodology, ESM. The study had four aims.

The first aim was to explore whether momentary metacognitive beliefs are associated with momentary worry and momentary rumination. In the multilevel simple regression analyses, all three momentary metacognitive beliefs domains (i.e., positive metacognitive beliefs about worry, positive metacognitive beliefs about rumination, negative metacognitive beliefs about worry and rumination) were significantly positively associated with momentary worry and momentary rumination. These findings are in-line with predictions of the S-REF model and build on previous findings in adults with epilepsy and adults with other physical health populations in which positive and negative metacognitive beliefs about worry were positively associated with worry or rumination [27,44,106,107]. When entered simultaneously into a multilevel multiple regression model for rumination, momentary positive metacognitive beliefs about rumination and momentary negative metacognitive beliefs about worry and rumination were independently positively associated with momentary rumination. These findings, which are in-line with predictions of the S-REF model, are the first to demonstrate that metacognitive beliefs about rumination are associated with rumination in a physical health population. Conversely, when momentary metacognitive beliefs were entered simultaneously into the multilevel multiple regression model for worry, momentary positive metacognitive beliefs about rumination and momentary negative metacognitive beliefs about worry and rumination were independently positively associated with momentary worry but momentary positive metacognitive beliefs about worry were not. This was unexpected. While worry and rumination are both central components of the CAS, positive metacognitive beliefs about worry would primarily be expected to lead to worry whereas positive metacognitive beliefs about rumination would primarily be expected to lead to rumination.

While worry and rumination have traditionally been conceptualised as distinct concepts, worry and rumination correlate highly and share common processes [108-110]. As such, worry and rumination have been conceptualised as part of a wider transdiagnostic construct named ‘repetitive negative thinking’ [111,112]. If worry is part of a wider transdiagnostic construct, positive metacognitive beliefs about rumination would be expected to be associated with worry.

However, this does not explain why momentary positive metacognitive about worry were not independently associated with momentary worry. This finding may be due to positive metacognitive beliefs about worry being involved in the worry process at a different stage. According to the S-REF model, positive metacognitive beliefs about worry are primarily involved in initiating worry as opposed to maintaining it. However, associations between variables in our study were only compared within the same assessment period. The lack of association between worry and positive metacognitive beliefs about worry assessed at the same time-point has been found in other studies [44,61,107]. Our sample size precluded us from investigating this temporal relationship (i.e., whether metacognitive beliefs about worry at assessment 1 predict worry at a later assessment point).

The second and third aims were to explore whether momentary worry and rumination (respectively), and momentary metacognitive beliefs are associated with momentary anxiety and momentary depression. Momentary worry and rumination were significantly positively associated with momentary anxiety and depression, respectively; and momentary positive metacognitive beliefs about rumination and momentary negative metacognitive beliefs about worry and rumination were significantly associated with both momentary anxiety and depression, all of which fit with the S-REF model. The strongest associations were found between momentary worry and anxiety, and momentary rumination and depression (as would also be expected according to the S-REF model). These findings are in-line with the well-established evidence-base demonstrating that perseverative thinking in the form of worry and rumination are prominent in those presenting with anxiety and depression [113-116]. The S-REF model theorises that positive metacognitive beliefs about worry should be significantly associated with anxiety and depression. This was not supported by our data. The same methodological considerations described earlier regarding the time-point in which positive metacognitive beliefs are important may apply.

The final aim was to explore whether momentary metacognitive beliefs explain additional variance in momentary anxiety and depression after respectively accounting for momentary worry and rumination. None of the metacognitive belief domains entered into the multilevel multiple regression models (i.e., positive metacognitive beliefs about rumination and negative metacognitive beliefs about worry and rumination) explained additional variance in anxiety or depression. The S-REF model proposes that positive metacognitive beliefs about worry and rumination indirectly lead to anxiety and depression via worry and rumination (i.e. the relationship between positive metacognitive beliefs and anxiety and depression should be fully

mediated by worry and rumination). Therefore, it is unsurprising that positive metacognitive beliefs about rumination did not account for additional variance after controlling for worry and rumination. Alternatively, the S-REF model proposes that negative metacognitive beliefs about worry and rumination lead to anxiety and depression both indirectly (via worry and rumination) and directly (i.e., the relationship between negative metacognitive beliefs about worry and rumination and anxiety and depression should be partially mediated by worry and rumination). More specifically, the S-REF model postulates that once an individual experiences the negative consequences of worry and rumination (i.e., heightened anxiety and depression), they develop negative metacognitive beliefs about worry and rumination. Such beliefs indirectly exacerbate anxiety and depression by decreasing the likelihood of an individual terminating worry and rumination (due to negative beliefs that such processes are uncontrollable). Thus, the finding that negative metacognitive beliefs about worry and rumination did not account for additional variance after controlling for worry and rumination is surprising.

One reason for this finding could be due to the low levels of anxiety and depression reported by the sample, as this may have resulted in insufficient variance in anxious and depressive symptoms (leading to floor effects). Moreover, the S-REF model was primarily designed to explain emotional distress in clinically distressed samples. While it is not uncommon for individuals who do not meet diagnostic criteria for clinical levels of anxiety and depression to hold positive metacognitive beliefs about worry and rumination [44], according to the S-REF model, it is less common for such individuals to hold negative metacognitive beliefs about worry and rumination. While holding positive metacognitive beliefs would be expected to lead to increased anxiety and depression (indirectly via worry and rumination), individuals are more likely to terminate worry and rumination if they believe such processes are controllable (i.e., if they do not hold negative metacognitive beliefs). Thus, while the S-REF model asserts that negative metacognitive beliefs are of most direct importance in the maintenance and exacerbation of anxiety and depression, negative metacognitive beliefs may typically only arise in individuals who meet diagnostic criteria for anxiety or depression. This notion is supported by the relatively low momentary negative metacognitive beliefs about worry and rumination scores observed in our sample (see Table 7). Lending credence to this explanation, Benedetto et al., (2018) found that amongst adolescents, negative metacognitive beliefs about worry were associated with anxiety in a clinical sample but they were not associated anxiety in a non-clinical sample [117]. Moreover, Papageorgiou & Wells (2003) tested the fit of the S-REF

model in depressed and non-depressed participants. While the S-REF model fitted the data well for the depressed sample, it did not fit well for the non-depressed sample [118].

Another reason for this finding could be due to amalgamating negative metacognitive beliefs about worry and rumination into a unitary scale. According to the S-REF model, negative metacognitive beliefs about worry would be expected be more closely related to anxiety whereas negative metacognitive beliefs about rumination would be expected to be more closely related to depression. If a participant held strong negative metacognitive beliefs about worry but not rumination, this may have been masked. However, due to the wording of items in the ESM assessment, it was not possible to separate out these constructs (i.e., both items assessing negative metacognitive beliefs referred to metacognitive beliefs about both worry and rumination; see Appendix E). To assess the S-REF model more accurately, future studies may benefit from recruiting a sample of YPwE who are clinically anxious or depressed and separating out negative metacognitive beliefs about worry and rumination into two distinct constructs.

4.1. Strengths

The use of ESM enabled the assessment of the relationship between metacognitive beliefs, perseverative thinking (i.e., worry and rumination) and emotional distress (anxiety and depression) in YPwE at a momentary level. This enabled the identification of more complex and dynamic relationships between variables that may be unaccounted for using traditional research designs. The high level of within-person variability for the relationships between metacognitive beliefs, perseverative thinking, and emotional distress demonstrates that such variables appear to fluctuate over short intervals, providing support for the use of more nuanced methodologies which account for this variability, such as ESM. Future research would benefit from combining different assessment methods (i.e., baseline and ESM measures) into multilevel analyses. However, this would require a larger sample size.

A major strength of the study was the use of a smartphone app to administer the ESM assessments. ESM studies have traditionally been administered via ‘paper-pen’ methods were participants carry around a batch of paper-based assessments and are signalled to complete them by a wristwatch ‘beep’. However, ‘paper-pen’ methods cannot ensure participants complete assessments when prompted, potentially leading to forward or backlogging of responses [119]. The smartphone app overcame this issue by accurately ‘timestamping’ when participants competed the assessment and discarding assessments not completed within a

specific timeframe. As participants had to have access to a smartphone to participate, this may have led to a biased sample. While no participants were excluded due to inaccessibility to a smartphone, it is possible that potential participants did not volunteer due to this requirement. Future studies would benefit from providing participants with a smartphone for the duration of the ESM period.

4.2. Limitations

Apart from negative metacognitive beliefs about worry and rumination, the relationship between ESM measures and their corresponding baseline measures were weak and non-significant. This may have been due to type II error. As the correlation analysis was based on average ESM scores, the current sample size (n = 18) was likely underpowered [120]. However, this does not explain the weak correlation coefficients between ESM measures and their corresponding baseline measures. The weak coefficients could suggest that the momentary assessments were not validly assessing what they were intending. Yet, significant moderate-to-large correlations were found between most ESM measures and theoretically related constructs (measured via ESM), demonstrating convergent validity of the ESM measures. Alternatively, it could be that baseline and ESM measures were capturing different aspects of such constructs, which has been demonstrated in prior research (i.e., retrospective measures of worry only account for a small amount of variance in daily worry) [54]. There was also a high level of within-person variability for most variables. Thus, using an average score for ESM measures in the correlation analysis may not be appropriate. Assessment of the reliability and validity of ESM measures is difficult [121-123]. Demonstrating reliability of an assessment measure involves confirmation that it produces consistent scores when repeatedly applied to the same participant. However, this expectation violates the key purpose of ESM, to assess variables which fluctuate over short intervals [88,124]. Demonstrating the validity of an assessment measure involves ensuring it adequately correlates with well-established assessment measures (i.e., retrospective self-report measures) assessing the same construct. However, as ESM measures potentially capture different aspects of constructs measured via retrospective self-report measures, this is of limited value. While the implications of testing the reliability and validity of ESM assessment measures are beginning to receive careful consideration [125], well-established methods for assessing reliability and validity of ESM measures do not currently exist. Until well-established methods are developed, future studies would benefit from asking participants to what extent they think ESM items represents a certain construct [126].

ESM assessment compliance rates were high, suggesting the use of ESM is a feasible approach in YPwE. However, recruitment was difficult. We originally aimed to recruit approximately 30 participants (see Appendix F for reflection of learning points related to recruitment difficulties). This would have enabled us to test a more complete account of the theoretical predictions of the S-REF model by assessing the mediational relationship between momentary metacognitive beliefs, perseverative thinking (i.e., worry and rumination) and emotional distress (i.e., anxiety and depression) using time-lagged models (e.g., whether metacognitive beliefs at assessment 1 predict anxiety at assessment 3, and whether this relationship is mediated by worry at assessment 2). Instead, our analysis was constrained to cross-sectional associations (i.e., whether metacognitive beliefs at assessment 1 are associated with perseverative thinking at assessment 1). Therefore, causality cannot be assumed. The sample size also precluded the inclusion of demographic and clinical characteristics as covariates within the multilevel model analyses. Future studies should explore time-lagged relationships and include demographic and clinical variables in multilevel analyses, with appropriate sample sizes. As we only assessed one aspect of the CAS - perseverative thinking (i.e., worry and rumination) - future studies would also benefit from considering other CAS processes such as attentional focus on threat and unhelpful coping behaviours.

Despite these limitations, our findings provide support for the utility of the S-REF model for emotional distress in YPwE and add to the accumulating evidence base for the utility of the S-REF model for emotional distress in people with physical health conditions [27,106,127,128].

4.3. Clinical implications

Findings of this study provide empirical support for the utility of the S-REF model for emotional distress in YPwE. Thus, MCT [31], which is underpinned by the S-REF model, may be an effective psychological intervention for YPwE experiencing anxiety and depression. It may also be an effective preventative intervention for those at risk of developing anxiety and depression; modifying maladaptive positive metacognitive beliefs may prevent YPwE from developing maladaptive negative metacognitive beliefs and subsequent anxiety or depressive disorders. Preliminary evidence indicates that MCT, which primarily aims to modify maladaptive positive and negative metacognitive beliefs, is an acceptable and effective intervention to reduce anxiety and depression in adults with physical health [32-37], adolescents and young adults with cancer [38], and adolescents with common mental health disorders [39-43]. Prior to examining the effectiveness of MCT for anxiety and depression in YPwE, a better understanding of the temporal and mediational relationships between

momentary metacognitive beliefs, perseverative thinking, and emotional distress in a clinically distressed sample of YPwE is recommended.

The ability of ESM to capture more complex and dynamic relationships between variables in this study also has important clinical implications. Clinicians tend to assess for symptoms of anxiety and depression in YPwE either via general discussion about their mental health (either initiated by the clinician or in response to anxiety and depression symptoms spontaneously reported by YPwE) or via clinician-administered or self-report measures assessing YpWE's level of anxiety and depression over the preceding weeks or months [129]. Clinical decisions around appropriate psychological or pharmacological interventions are then based on these outcomes. However, this study demonstrates that anxiety and depression highly fluctuate across a relatively short timeframe in YPwE. Findings also indicate that momentary experiences of anxiety and depression may conceptually differ from more 'trait-like' experiences of anxiety and depression. Thus, using ESM in YPwE offers a promising and clinically useful alternative or complementary method for the assessment of anxiety and depression in clinical practice. The richer insight provided by ESM could provide a more in-depth understanding of YPwE's mental health needs which could better inform clinical decisions around appropriate psychological or pharmacological interventions. ESM could also be used to better monitor YPwE's psychotherapeutic progress in-between psychological intervention sessions. Observation of patterns between anxious and depressive symptoms and related psychological processes in 'real time' (i.e., via graphs) could enhance patient insight and promote socialisation to specific therapeutic approaches [130]. Monitoring psychological intervention progress via ESM has also been shown to enhance patients' sense of empowerment in decision-making around their care [131]. While patients and clinicians view self-monitoring via ESM as a potentially useful tool to supplement assessment and intervention [132-134], clinicians have raised practical concerns regarding the implementation ESM in clinics (e.g., lacking necessary skills to use ESM technology, lack of best-practice guidelines, how to integrate ESM assessments into electronic health records, time burden) [132,134,135]. Notwithstanding these challenges, the application of ESM in clinical practice offers an innovate approach to assess and monitor YPwE's anxiety and depressive symptoms.

Furthermore, daily self-monitoring of symptoms of anxiety and depression and related psychological processes in YPwE could serve as an intervention on its own. Using ESM as a self-monitoring tool has been shown to improve emotional self-awareness and reduce emotional distress [136-138].

4.4. Conclusion

This study provides promising initial evidence for the utility of the S-REF model to understand emotional distress in YPwE. This suggests that MCT, which is underpinned by the S-REF model, may be an appropriate intervention for anxiety and depression in YPwE. To enable more fine-grained testing of the S-REF model for emotional distress in YPwE, replication of this study with a larger sample is warranted. The use of ESM using a smartphone app appears a promising new direction to assess, monitor and advance understanding of the psychological mechanisms underpinning and maintaining emotional distress in YPwE.

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Appendices

Appendix A. Author Guidelines for Journal of Health Psychology Review.

About the Journal

Health Psychology Review is an international, peer-reviewed journal publishing high-quality, original research. Please see the journal's Aims & Scope for information about its focus and peer-review policy.

Preparing Your Paper

Manuscripts must be written in English. American or British spelling and punctuation are acceptable, provided authors apply the style consistently throughout the manuscript. Manuscripts with incorrect grammar or errors will be returned to authors. Authors are encouraged to proofread their manuscript prior to submission. Authors requiring English language editing services are directed to the Taylor and Francis Author Services website.

Manuscript Length

The editorial team acknowledge that review articles are usually longer than articles reporting findings of primary research. Health psychology review does not impose any length restrictions on submitted articles. However, it is also recognised that articles should be appropriately concise and pithy so that the main focus is not lost and the argument is not encumbered by unnecessary detail. Authors can include supplemental materials such as figures and tables not directly germane to the main argument of the manuscript as online supplemental materials. For meta-analyses and systematic reviews, references for studies included in the review should be only appear in a separate supplemental list that the journal will make available as an online supplement. These materials will not count toward the page length of the manuscript, but will be included as a permanent record of supplemental materials alongside the online version of the manuscript (see later). Manuscripts should be compiled in the following order: title page including acknowledgements and funding details as an author note; abstract; keywords; main text; references; table(s) with caption(s) (on individual pages); figures and figure caption(s).

Structure

Your paper should be compiled in the following order: title page; abstract; keywords; main text introduction, materials and methods, results, discussion; acknowledgments; declaration of interest statement; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figures; figure captions (as a list).

Format-Free Submission

Authors may submit their paper in any scholarly format or layout. Manuscripts may be supplied as single or multiple files. These can be Word, rich text format (rtf), open document format (odt), or PDF files. Figures and tables can be placed within the text or submitted as separate documents. Figures should be of sufficient resolution to enable refereeing.

Appendix B. Author Guidelines for Journal of Epilepsy & Behavior.

Epilepsy & Behavior presents original peer-reviewed articles based on laboratory and clinical research. Topics are drawn from a variety of fields, including clinical neurology, neurosurgery, neuropsychiatry, neuropsychology, neurophysiology, neuropharmacology, and neuroimaging.

Epilepsy & Behavior publishes papers on the study of:

• Localization of ictal and postictal behaviours
• Neuroendocrine aspects of epilepsy
• Psychiatric and psychosocial aspects of epilepsy
• Behavioral aspects of epilepsy surgery
• Cognitive and affective effects of seizure treatment
• Functional imaging
• Animal models

Types of article

Epilepsy & Behavior publishes the following types of articles:

• Original research articles (both clinical and laboratory research)
• Reviews
• Editorials
• Brief communications
• Letters
• Book reviews
• Calendar of events

Article structure

Subdivision - numbered sections

Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Material and methods

Provide sufficient details to allow the work to be reproduced by an independent researcher. Methods that are already published should be summarized, and indicated by a reference. If quoting directly from a previously published method, use quotation marks and also cite the source. Any modifications to existing methods should also be described.

Results

Results should be clear and concise.

Discussion

The Discussion section should explore the significance of the results of the work, not repeat them. Results and Discussion should be separate and may be organized into subheadings. Avoid extensive citations and discussion of published literature.

Conclusions

The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

Keywords

Immediately after the abstract, provide a maximum of 6 keywords, using American spelling and avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Reference style

Text: Indicate references by number(s) in square brackets in line with the text. The actual authors can be referred to, but the reference number(s) must always be given.

List: Number the references (numbers in square brackets) in the list in the order in which they appear in the text.

Appendix C. Data Extraction Sheet Form.

Title of paper:

Name of reviewer completing this form:

Date form completed:

STUDY METHODS

Research question	

POPULATION AND SETTING

Inclusion criteria	
Exclusion criteria	
Method/s of recruitment of participants (How were potential participants approached and invited to participate?)	
Location of study	
Prospective cohort **Cross-sectional Cohort**	
Prospective (follow-up length)	

SAMPLE

	Description as stated in report/paper
Number invited to participate, eligible, excluded, refused	
Sample size taking part (meeting eligibility criteria)	
Sample size at follow-up if prospective	

PARTICIPANTS

	Description as stated in report/paper
Age: range, mean and SD	
Ethnicity and race	
Gender	

CLINICAL CHARACTERISTICS

	Description as stated in report/paper
Type of epilepsy	
Seizure type	
Seizure frequency	
Number of AEDs	
Age of seizure onset or age of epilepsy diagnosis	
Epilepsy duration	

OUTCOME

Psychological outcome **Anxiety (measure)**	**Description as stated in report/paper**
Depression (measure)	
Emotional distress (measure)	
Methods of assessing outcome measures (e.g., self-report, parent proxy, clinical interview	
Is the measure validated?	

Psychosocial variable (repeat for each variable)	Description as stated in report/paper
Variable (measure)	
Methods of assessing outcome measures (e.g., self-report, parent proxy, clinical interview	
Is the measure validated?	

Results	Description as stated in report/paper
Analysis used:	
Statistical findings reported (*list*)	
Statistical information omitted.	

Appendix D. Risk of Bias Form for included studies.

Title of paper

Name of reviewer completing this form:

Date form completed:

Unbiased section of cohort	
Did inclusion/exclusion ensure that the sample they wanted to recruit was recruited	
Participant recruitment	
Was consecutive sample used	
Overall score	

Sample size justified/ power analysis	
Overall score	

Validated measure of distress	
Has the measure been validated? –	
Were single item measures used?	
Overall score	

Validated measure of psychosocial variable	
Have measures been validated? (See attachment for outcomes of interest in each paper)	
Were single item measures used?	
Overall score	

Adequate description of the cohort	
Was demographic information of sample reported? (must include age and gender of sample at minimum)	
Was clinical information of sample reported? (must include whether sample was on AEDs, frequency of seizures, type of seizures, epilepsy duration)	
Overall score	

Analysis controlled for confounding variable	
Was multiple regression conducted?	
For multiple regression, were all sig variables in univariate analysis accounted for?	
Were the following variables included in multiple regression analysis - seizure frequency number of AEDs account, duration of epilepsy, age, gender	
Overall score	

Appropriate analysis	
Was the kind of analysis done appropriate for the kind of outcome data?	
If correlation or simple regression, was sample size 50 or above? If multiple regression, was sample size 104+m (m=however many IVs are included in regression)?	
Overall score	

Appendix E. ESM Assessment Items.

All questions were preceded by the phrase "right now" and rated on a 5-point Likert scale 0 (not at all) – 5 (very much so)

(0) Not at all
(1) A little
(2) Somewhat
(3) A lot
(4) Very much so

ESM items included in study analysis.

Momentary anxiety subscale

1. I feel anxious.
2. I feel uneasy.
3. I feel on edge.

Momentary depression subscale

1. I feel sad.
2. I feel hopeless.
3. I feel discouraged.

Momentary worry subscale

1. I am worrying about things that could happen.

Momentary rumination subscale

1. I am dwelling on my feelings and problems.

Momentary positive metacognitive beliefs about worry subscale

1. I believe that worrying is helpful.

Momentary positive metacognitive beliefs about rumination subscale

1. I believe that ruminating about my problems will help me figure out how to deal with them.

Momentary negative metacognitive beliefs about worry & rumination subscale

1. I believe that worrying or dwelling on thoughts is harmful.
2. I believe that worrying or dwelling is uncontrollable.

Additional ESM items not included in study analysis.

Momentary threat-focused attention

1. My attention is focused on thoughts and feelings I find threatening.

Momentary positive affect subscale

1. I feel *happy.*
2. I feel joyful.
3. I feel energetic.
4. I feel excited.
5. I feel enthusiastic.

Appendix F. Reflection of Learning Points Related to Recruitment Difficulties and Study Design.

Due to recruitment difficulties, iterative changes were made to the recruitment process. We initially recruited participants solely via one NHS children's hospital. Given approximately 200 adolescents were open to the epilepsy service within the NHS children's hospital, we anticipated no difficulties reaching our target sample size. However, recruitment uptake was much lower than anticipated. This led to several extensions to the study recruitment period and expanding our recruitment method to advertisement on social media (a limitation of this is that epilepsy diagnosis and other clinical characteristics were based on self-report). Several epilepsy charities and advocates were contacted to ask if they would promote the study via their social media platforms. One of the largest epilepsy charities in the UK regularly advertised our study on their social media platform. While this increased study recruitment, uptake remained slow. Recruitment difficulties for ESM studies are not uncommon (Christensen et al., 2003; Chen et al., 2016; Palmier-Claus et al., 2010). Recruitment difficulties are also common in clinical trials involving adolescent populations (Kilicel et al., 2023). An important learning point from this study is to be cautious regarding recruitment rates, particularly when using such an innovative methodology.

Recruitment difficulties may also have been due to the recruitment procedure. Initially, parents/caregivers of all YPwE open to the epilepsy services at the NHS children's hospital were sent a letter asking them to share the accompanied invitation letter and information sheet with their child. A disadvantage of this approach is that it is impersonal and, as such, can lead to low participation rates (Aitken et al., 2009). Recruitment rates into clinical studies tend to be higher when potential participants are approached by healthcare professionals (HCPs) during routine appointments (Aitken et al., 2009; Peindl & Wisner, 2003) and those interested in participating are then offered the opportunity to meet with the researcher in clinic. In response to low uptake, this approach was adopted. However, due to time constraints on the researcher, being present in clinics could only happen sporadically. Developing collaborative relationships with HCPs, ensuring they have a good understanding of the study, and reducing the workload required for HCPs to introduce the study are crucial to increase recruitment (Fenlon et al., 2013; Gee et al., Kling et al., 2021; Lamb et al., 2001). While attempts were made to achieve this (e.g., attending multidisciplinary meetings, providing HCPs with information sheets to offer to potential participants, sending regular email reminders, and

ensuring their support was recognised and appreciated), this was somewhat limited and rushed due to this approach being implemented late in the recruitment phase. Thus, to achieve an appropriate sample size for an ESM study in YPwE that allows more sophistically statistical analysis procedures, it would be advisable, from the outset, to recruit from multiple NHS sites and for potential participants to be approached by HCPs, who can act as gatekeepers, and to spend time explaining the study and developing collaborative relationships with relevant HCPs.

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Appendix G. Statistical Analyses Exploring whether Compliance Rates are Associated with Demographic and Clinical Characteristics.

Pearson correlation outcomes

Variable	Compliance rate: r (p value)
Anxiety score	-0.6 (p=80)
Depression score	-0.18 (p=0.49)
Age	0.2 (p=0.43)
Age of epilepsy diagnosis	-0.11 (p=0.69)
Epilepsy duration	0.15 (p=0.57

T-test & ANOVA outcomes

	Compliance rate: mean	*t* or F (p value)
Gender		
Male	-31.5	f = 0.2 (p = 0.82)
Female	33.62	
Prefer not to say	37	
Ethnicity		
White British	33.59	*t* = 0.55 (p=0.59)
White & Black African	29	
Type of epilepsy		
Generalised	32	F = 0.61 (p=0.56)
Focal	33.43	
Unknown	39	
Seizure severity		
Mild	31.6	F = 1 (p = 0.39)
Moderate	31.75	
Unknown	37.6	
AED protocol	-0.11 (p=0.69)	
Monotherapy	32.82	*t* = -0.38 (p=0.71)
Polytherapy	34.14	
Additional medical conditions		
Yes	33	*t* = 0.09 (p=0.93)
No	33,43	
Clinically depressed or anxious		
Yes	33.83	t = 0.37 (p = 0.36)
No	32.33	

Appendix H. Calculation of *T*-scores for RCADS

To calculate cut-off scores, total scores for the anxiety and depression subscales for the RCADS are converted to *T*-scores, which account for gender and grade of each young person. *T*-scores <65 are classed as below the clinical threshold for anxiety and depression. T-scores of 65-70 are classed as borderline clinical threshold for anxiety or depression, T-scores of >70 are classed as above the clinical threshold for anxiety or depression. As participant age can fall within two grade categories, all participants were categorised in the lower grade (e.g., as a 12 year old, could be in either grade 7 or 8, they were classed as grade 7).

Appendix I. Sensitivity Analysis

Table 1. Multilevel multiple regression for the dependent variables (momentary worry, momentary rumination) with independent variables entered simultaneously and the inclusion of baseline worry and rumination, respectively.

Momentary worry	**β**	**95% CI**	**p**
Intercept	.37	-1.10 - 1.83	ns
Baseline worry	.01	-.07 - .09	ns
Momentary positive beliefs about worry	.07	-.04 -.18	ns
Momentary positive metacognitive beliefs about rumination	.16	.04 - .28	<.01
Momentary negative metacognitive beliefs about worry and rumination	.17	.12 - .21	<.001
Model summary Assessments: 589 ICC = .49 Marginal R^2 / Conditional R^2 = .17 / .57			
Momentary rumination	**B**	**95% CI**	**p**
Intercept	.41	-.88 – 1.7	ns
Baseline rumination	-.01	-.11 - .09	ns
Momentary positive metacognitive beliefs about worry	0	-.10 - .11	ns
Momentary positive metacognitive beliefs about rumination	.17	.06 - .28	<.01
Momentary negative metacognitive beliefs about worry and rumination	.20	.15 - .24	<.001
Model summary Assessments: 589 ICC = .51 Marginal R^2 / Conditional R^2 = .21 / .61			

Note. ns=non-significant; β=unstandardised beta coefficient

Table 2. Multilevel multiple regression for the dependent variables (momentary anxiety, momentary depression) with independent variables entered simultaneously and the inclusion of baseline anxiety and depression, respectively.

Momentary anxiety	**β**	**95% CI**	**P**
Intercept	.21	-.45 - .88	ns
Baseline anxiety	.01	-.03 - .06	ns
Momentary rumination	.45	.40 - .51	<.001
Momentary positive metacognitive beliefs about rumination	.06	-.02 - .13	ns
Momentary negative metacognitive beliefs about worry and rumination	-.01	-.04 - .02	ns
Model summary Assessments: 589 ICC = .46 Marginal R^2 / Conditional R^2 = .36 / .65			
Momentary depression	**β**	**95% CI**	**p**
Intercept	.30	-.71 – 1.31	ns
Baseline depression	.03	-.04 - .10	ns
Momentary rumination	.31	.25 - .37	<.001
Momentary positive metacognitive beliefs about rumination	.04	-.01 - .12	ns
Momentary negative metacognitive beliefs about worry and rumination	-0	-.04 - .03	ns
Model summary Assessments: 589 ICC = .66 Marginal R^2 / Conditional R^2 = .13 / .71			

Note. ns=non-significant; β=unstandardised beta coefficient