National Institute for Health and Care Excellence

FINAL

Epilepsies in children, young people and adults: diagnosis and management

[15] Evidence review: Prevalence of psychological disorders in people with epilepsies

NICE guideline NG217

Evidence reviews underpinning recommendations 9.1.1 to 9.1.5 in the NICE guideline

April 2022

FINAL

Developed by the National Guideline Centre

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The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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1 Prevalence of depression, anxiety, learning disability and neurodevelopmental/cognitive difficulties in people with epilepsies

1.1 Review question

What is the prevalence of depression, anxiety, intellectual disability, developmental difficulties and cognitive difficulties in people with epilepsies?

1.1.1 Introduction

Epilepsy is an unusual diagnosis in neurology in that the diagnosis is conferred on the basis of a single symptom, seizures. However, the underlying genetic abnormality or pathology in the brain that results in seizures can also predispose to other disturbances in brain function. Knowledge and awareness of these other disorders are essential for the care of people with epilepsy. Some of the treatments aimed at controlling seizures can have an adverse effect on common co-morbidities.

This chapter examines the prevalence of core mental illnesses (depression, anxiety, psychosis), co-morbid neurodevelopmental disorders (intellectual disability, autistic spectrum disorders, ADHD) and other acquired cognitive difficulties such as dementia in this population.

1.1.2 Summary of the protocol

For full details, see the review protocol in Appendix A

Table 1: PICO characteristics of review question

Population	Inclusion: Children, young people and adults with confirmed epilepsy. Exclusion: New-born babies (under 28 days) with acute symptomatic seizures.
Outcomes/ Comorbidities	In people with Epilepsy, the prevalence of: • Depression • Anxiety • Learning disabilities • Cognitive difficulties • Dementia • psychosis
Study design	Systematic reviews of all studies reporting period prevalence (limited to period prevalence for all conditions except learning disabilities where point prevalence will also be included).

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Prevalence evidence

1.1.4.1 Included studies

A search was conducted for systematic reviews reporting prevalence data of depression, anxiety, learning disabilities, cognitive difficulties, dementia and psychosis in people with epilepsy. Ten studies were included in the review, [7, 27, 39, 42, 43, 51, 52, 69, 95, 96] these are summarised below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3). See also the study selection flow chart in 39Appendix C, study evidence tables in Appendix D, forest plots in Appendix F.

Most of the included systematic reviews were unable to perform meta-analyses due to insufficient reporting of data, therefore, the data predominantly extracted for this evidence review was the range of prevalence percentages from individual studies. Pooled data for prevalence was only reported in two systematic reviews, Scott 2017[95] and Scott 2020[96], where meta-analyses were possible.

The diagnostic method used to measure the comorbidities varied amongst individual studies included in each systematic review; this may explain the wide variation observed in the prevalence statistics.

The risk of bias for the systematic reviews included was assessed using the ROBIS tool, which assesses the risk of bias in systematic reviews by:

1. Assessing the relevance
2. identifying concerns with the review process
3. judging the risk of bias in the review

Please see Appendix E for ROBIS assessment table.

1.1.4.2 Excluded studies

The searches were limited to systematic reviews. Therefore, all individual studies investigating prevalence were excluded.

See the excluded studies list in Appendix G.

1.1.5 Summary of studies included in the prevalence evidence

Table 2: Summary of reviews included in the evidence review

Study	Population	Comorbidity	Comments
Asadi-Pooya 2018[7]	26 studies included for people with epilepsy	Depression	High risk of bias Population age not defined
Cobham 2020[27]	8 studies included 784 children and adolescents with epilepsy	Anxiety	High risk of bias
Fiest 2013[39]	14 studies included Adults with epilepsy	Depression	Low risk of bias
Fonseca 2019[42], Fonseca 2020[43]	33 studies included Children with absence epilepsy	Cognitive difficulties Learning disabilities	Low risk of bias
Jones 2014[51]	Children and adolescents with epilepsy included	Anxiety	Very high risk of bias Narrative literature review, no methodology

Study	Population	Comorbidity	Comments
			or risk of bias assessment for included studies
Jones 2010[52]	13 studies included	Depression Anxiety Psychosis	High risk of bias Population age not defined
Maryam 2013[69]	11 studies included 1095 children (4-19 years) with epilepsy	Depression	High risk of bias
Scott 2017[95]	27 studies included 3221 adults with epilepsy	Depression Anxiety	Low risk of bias
Scott 2020[96]	23 studies Children with epilepsy	Anxiety Depression	Low risk of bis
Subota 2017[105]	2 studies included People with epilepsy	Dementia	Low risk of bias population age not defined

See Appendix D for full evidence tables.

1.1.6 Summary of the evidence

Table 3: Clinical evidence summary: Depression

Prevalence in people with Epilepsy	Systematic review	Type of prevalence Time-frame	Population	Risk of bias rating	comments/ Quality rating in review
6.6%-43.4%	Asadi-Pooya 2018[7]	Period prevalence, unclear time-frame	Unclear	High	2.9%-12.7% depression in general population
13.2%-36.5%	Fiest 2013[39]	Period prevalence of past 30 days -12 months	Adults with active depression	Low	
4.1%-32.5%	Fiest 2013[39]	Period - Lifetime depression prevalence	Adults with lifetime depression	Low	
18%-39.7%	Jones 2010[52]	Period prevalence, unclear time-frame	Unclear	High	
5.2%-39.6%	Maryam 2013[69]	Period prevalence, unclear time-frame	Children	High	Aged 4-19 years old
22.9% pooled prevalence	Subota 2017[105]	Period prevalence, unclear time-frame	Adults	Low	16 years and older Figure 2 for forest plot
13.5% (95% CI 8.8%–20.2%) pooled prevalence	Scott 2020[96]	Period prevalence, unclear time-frame	Children	Low	Up to and including 18 years of age

Table: Clinical evidence summary: Anxiety

Prevalence in people with Epilepsy	Systematic review	Type of prevalence	Population	Risk of bias rating	comments
23.8%-50%	Cobham 2020[27]	Period prevalence, unclear length	Children	High	12.4%-22% anxiety in general population
9%-32%	Jones 2014[51]	Period: lifetime	Children	Very high	Lifetime anxiety

Prevalence in people with Epilepsy	Systematic review	Type of prevalence	Population	Risk of bias rating	comments
8%-21%	Jones 2014[51]	Mixed: current and past 12 months	children	Very high	
10%-25%	Jones 2010[52]	Period prevalence, unclear time-frame	Unclear	High	
20.2%	Scott 2017[95]	Period prevalence, unclear time-frame	Adults	Low	16 years and older Figure 3 for forest plot
18.9% (95% CI 12.0%–28.5%) pooled prevalence	Scott 2020[96]	Period prevalence, unclear time-frame	Children	Low	Up to and including 18 years of age

Table 4: Clinical evidence summary: Learning disabilities

Prevalence in people with Epilepsy	Systematic review	Type of prevalence	Population	Risk of bias rating	comments
Dysgraphia: 26%	Fonseca 2019[42], Fonseca 2020[43]	Unclear, prevalence determined from school reports	Children	Low	Absence epilepsy
school difficulties/requiring special educational support: 23-70%	Fonseca 2019[42], Fonseca 2020[43]	Unclear, prevalence determined from school reports	Children	Low	Absence epilepsy

Table 5: Clinical evidence summary: Cognitive difficulties

Prevalence in people with Epilepsy	Systematic review	Type of prevalence	Population	Risk of bias rating	comments
24%	Fonseca 2019[42], Fonseca 2020[43]	Unclear, prevalence determined from school reports	Children	Low	Absence epilepsy

Table 6: Clinical evidence summary: Dementia

Prevalence in people with epilepsy	Systematic review	Type of prevalence	Population	Risk of bias rating	comments
8.1 to 17.5 per 100 persons	Subota 2017[105]	Period prevalence	Unclear	Low	No age defined

Table 7: Clinical evidence summary: Psychosis

Prevalence results	Systematic review	Type of prevalence	Population	Risk of bias rating	comments
2-7%	Jones 2010[52]	Period prevalence, unclear time-frame	unclear	High	

1.1.7 Economic evidence

The committee agreed that health economic studies would not be relevant to this review question and so were not sought.

1.1.8 The committee's discussion and interpretation of the evidence

1.1.8.1 The outcomes that matter most

This evidence review sought data for the prevalence of depression, anxiety, learning disabilities, cognitive difficulties, dementia and psychosis in people with epilepsy. The committee considered that recognition of prevalence is important in alerting clinicians to common co-morbidities and to planning and delivering care to people with epilepsy.

1.1.8.2 The quality of the evidence

The systematic reviews included in this review matched the protocol requirement (see Appendix A) for their individual studies inclusion criteria; reviews which deviated from this were excluded. In the absence of a standardised quality assessment tool for epidemiological review questions, the ROBIS tool was applied. The ROBIS tool determines the risk of bias in systematic reviews through a three-phase approach. Firstly, considering the relevance of each included systematic review to the research question, secondly, identifying any concerns with the review process and lastly, judging the risk of bias. The rating from these three phases was used to determine an overall risk of bias rating. The risk of bias across the evidence included for this evidence review ranged from low to very high overall risk of bias. High to very high risk of bias ratings were due to the lack of risk of bias assessment within the review and/or insufficient information available on the review methodology to allow the risk of bias assessments.

1.1.8.3 Benefits and harms

The recognition of the common comorbidities in people with epilepsy will benefit patients individually by ensuring they receive appropriate care and should also help inform the appropriate organisation and delivery of services that are made accessible. This evidence review highlighted the increased psychological difficulties experienced by people with epilepsy, with prevalence rates of

depression and anxiety reported at a range of 4.1-43.4% and 8-50% respectively, compared to the general population, which was reported at 2.9-12.7 and 12.4-22%, respectively. Clinically significant levels of dementia and psychosis were also reported in people with epilepsy at 8.1-17.5% and 7%, respectively. A review looking at data from neuropsychological test results and school prevalence reports found children with epilepsy had high prevalence rates for learning disabilities, 26% for dysgraphia and 23-70% for school difficulties and educational support and cognitive difficulties at 24%. Despite the high to very high risk of bias rating of some of the included reviews, the guideline committee acknowledged the importance of these prevalence statistics and the need for better care-plans for people with epilepsy and comorbidities.

The committee was aware of variation in how services are organised and the patient experience of seeing multiple specialists separately for different aspects of their condition. To ensure appropriate care plans are put in place, the guideline committee considered epilepsy specialists and mental health specialists needed to work better together. The committee acknowledged that often mental health specialists do not have enough information about epilepsy to provide adequate support to people with epilepsy when referred to them. Equally, there is a need for neurologists and paediatricians to recognise the clinical presentation of intellectual difficulties in children with epilepsy. The committee also acknowledged the risk associated between dementia and epilepsy and the need for better collaboration between epilepsy and geriatric services. The results of this review highlighted the close link between epilepsy and depression, anxiety, psychosis and dementia. The committee were also aware of the increased risk of suicide amongst people with epilepsy. Although the prevalence of suicide was not investigated in this review, the committee highlighted the importance of healthcare providers to be aware of this risk. A range of issues including mental health difficulties, social deprivation, and alcohol abuse may be factors that contribute to an increased risk of suicide, and the committee acknowledged the cause is multifactorial and a complex area. However, they agreed early recognition and intervention can mitigate risk. The committee expressed a need for shared working across all specialities involved as a joint multidisciplinary team. The committee noted that this close working relationship should also address the disconnect felt

by people with epilepsy and their families/carers when having care split across separate clinicians. Furthermore, since ASM and anti-psychotic medication have adverse effects when taken together, joint-multidisciplinary working can help manage and review treatment plans.

1.1.9 Cost effectiveness and resource use

Cost effectiveness evidence was not sought as this is a question about prevalence.

The committee discussed the clinical evidence noting the prevalence of mental health co-morbidities, learning disabilities and dementia is increased in people with epilepsy. The committee acknowledged that current best practice for people with epilepsy with mental health co-morbidities is to provide coordinated care using a multidisciplinary team approach and to ensure effective communication and liaison between health care professionals across the relevant services involved in the care of the person with epilepsy. The committee noted that current best practice is observed in around 25% of NHS settings. Therefore, although the recommendations made by the committee reflect current best practice, they do not reflect current practice for the majority of people.

The committee noted that although there will be a change in practice for the majority of health care providers, a multidisciplinary team approach for delivering care will likely be cost-saving in the long run. A multidisciplinary team approach with effective communication and liaison between health care professionals will also allow for better care to be delivered to people with epilepsy who have mental health co-morbidities. The approach enables people to access services simultaneously or consecutively with more effective sharing of information. Sharing of information allows for better-tailored health care plans, and being able to access services simultaneously or consecutively results in cost savings in the form of fewer appointments and less administration time. For example, if a person presenting to a routine epilepsy appointment can then automatically be referred to a mental health service if required, the person in question does not have to access the mental health service through a primary care referral. The mental health service will also be aware of the type of assessment or care required. This will either omit the need for an initial assessment or decrease the face-to-face time required for initial assessment depending on what

is most suitable for the person's health care needs. The committee also noted it may allow for initial appointments to be conducted via telephone, which would also result in cost savings.

The committee also acknowledged that this approach would likely improve the person's quality-of-life as quicker referral times and more coherent health care are likely to make people feel more valued and listened to. The committee noted that an epilepsy diagnosis could be very challenging to live with. Some people receiving care feel as though their voice is not heard and find it demoralising when they have to explain the same problem to different health care professionals a number of times before they receive the appropriate care. This positive impact on patient's quality of life would likely be seen for all epilepsy patients but would be greatest for people who may feel more vulnerable initially (for example, people with anxiety, learning disabilities or dementia).

Although the recommendations made will change practice for a large proportion of people, the costs associated with this change will likely only be short-term whilst healthcare providers adapt to the changes required in communication across services. The additional costs observed will be seen in the form of additional staff time spent liaising with different services, but the committee noted this would be negligible if appropriate systems are put in place. For example, a consultant may have to spend an additional couple of minutes after an appointment with a patient communicating with other teams or organising a referral, but less administration in within the healthcare system will be observed overall compared to if a person had to access a service through a primary care referral.

The committee did note that the recommendations may result in additional appointments within the healthcare service as some people who would not have accessed services on their own may now be referred for an appointment. However, the committee noted this would likely only be a small number of patients. Also, for this group of people their care would have been sub-optimal which would have likely had a negative impact on their quality of life and potentially result in additional costs when accessing services at a later date.

Overall, the recommendations made may result in an initial increase in costs for the NHS but will be cost-saving in the long-run and result in better health outcomes for patients.

1.1.10 Other factors the committee took into account

The committee agreed the comorbidities of learning disabilities and dementia found within the review should be highlighted within the guideline by making a cross referral to existing NICE guidance

Mental health problems in people with learning disabilities: prevention, assessment and management (https://www.nice.org.uk/guidance/ng54)

Learning disabilities and behaviour that challenges: service design and delivery (https://www.nice.org.uk/guidance/ng93)

Dementia: assessment, management and support for people living with dementia and their carers (https://www.nice.org.uk/guidance/ng97)

See also evidence review 16 on Psychological treatments in people with epilepsy for cross-reference to NICE mental health guidance:

Depression in adults with a chronic health problem, Depression in children and young people, Common mental health problems, Generalised anxiety disorder and panic disorder, Psychosis and schizophrenia in adults, and Psychosis and schizophrenia in children and young people.

1.1.11 Recommendations supported by this evidence review

This evidence review supports recommendations 9.1.1 – 9.1.5 in the NICE guideline.

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Appendices

Appendix A Review protocols

A.1 Review protocol for prevalence of depression, anxiety, learning disability and behavioural/cognitive difficulties in people with epilepsies

ID	Field	Content
1.	Review title	Prevalence of depression, anxiety, learning disability and behavioural/cognitive difficulties in people with epilepsies.
2.	Review question	What is the prevalence of depression, anxiety, intellectual disability, developmental difficulties and cognitive difficulties in people with epilepsies?
3.	Objective	To determine the prevalence of depression, anxiety, intellectual disability, developmental difficulties, and cognitive difficulties in people with epilepsies
4.	Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • PsycInfo Searches will be restricted by: • English language studies • Human studies Other searches:

		• Inclusion lists of systematic reviews The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	
6.	Population	Inclusion: Children, young people and adults with confirmed epilepsy Exclusion: New-born babies (under 28 days) with acute symptomatic seizures.
7.	Types of study to be included	Systematic reviews of all studies reporting period prevalence (limited to period prevalence for all conditions except learning disabilities where point prevalence will also be included)
8.	Other exclusion criteria	Point prevalence reviews will be excluded as they risk an underestimation of the true prevalence (except for lifetime conditions i.e., learning disabilities) Non-English language studies. Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
9.	Context	Psychological difficulties are common comorbidities in patients with epilepsy, with a significant negative impact on quality of life. Many children and young people with epilepsy between the ages of 4 and 15 have one or more additional neurological disorders. Learning disabilities, for example, are more prevalent in individuals with epilepsy than in the general population. Cognitive impairment, including, but not limited to, memory difficulties, are observed in people with epilepsy. Such impairments can range from poor concentration and minor forgetfulness to those that have a significant impact on a person's ability to function independently. There are also emerging data relating to bidirectional links between epilepsy and dementia. All of these potential comorbidities are often under-recognised and may be improperly managed in people with epilepsies.
10.	Primary outcomes (critical outcomes)/ comorbidities	In people with Epilepsy, the prevalence of: • Depression • Anxiety • Learning disabilities • Cognitive difficulties

		• Dementia • Psychosis
11.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
12.	Risk of bias (quality) assessment	ROBIS tool for assessing risk in systematic reviews. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
13.	Strategy for data synthesis	Extracting prevalence as reported by systematic reviews.
14.	Analysis of sub-groups	Stratification: • Adults (>16 years) and children (≤16 years)

		Subgroup: none	
15.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☒	Epidemiologic (Prevalence)
		☐	Service Delivery
		☐	Other (please specify)
16.	Language	English	
17.	Country	England	
18.	Anticipated or actual start date		
22.	Anticipated completion date		
19.	Stage of review at time of this submission	Review stage	Started / Completed
		Preliminary searches	☐ / ☐
		Piloting of the study selection process	☐ / ☐
		Formal screening of search results against eligibility criteria	☐ / ☐
		Data extraction	☐ / ☐
		Risk of bias (quality) assessment	☐ / ☐

		Data analysis	☐	☐
20.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail NGCEpilepsies@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
21.	Review team members	National Guideline Centre:		
2.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.		
23.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		
24.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10112/documents		
25.	Other registration details			
26.	Reference/URL for published protocol			
27.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:		

		• notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
28.	Keywords		
29.	Details of existing review of same topic by same authors		
30.	Current review status	☐	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
31.	Additional information		
32.	Details of final publication	www.nice.org.uk	

Appendix B Literature search strategies

This literature search strategy was used for the following review:

- What is the prevalence of depression, anxiety, intellectual disability, developmental difficulties and cognitive difficulties in people with epilepsies?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[79]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 18 February 2021	Systematic review studies Exclusions
Embase (OVID)	1974 – 18 February 2021	Systematic review studies Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews to 2021 Issue 2 of 12 CENTRAL to 2021 Issue 2 of 12	None
PsycINFO (ProQuest)	Inception – 18 February 2021	Systematic review studies

Medline (Ovid) search terms

1.	exp epilepsy/
2.	seizures/
3.	exp status epilepticus/
4.	seizures, febrile/
5.	(dravet syndrome or epilep* or convuls* or continuous spike wave or slow sleep or landau kleffner syndrome or lennox gastaut syndrome or infant* spasm* or seizure* or west syndrome).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/

14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Meta-Analysis/
28.	exp Meta-Analysis as Topic/
29.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
30.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
31.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
32.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
33.	(search* adj4 literature).ab.
34.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
35.	cochrane.jw.
36.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
37.	or/27-36
38.	cognitive dysfunction/
39.	((cognit* or neurocognit*) adj (dysfunction* or impair* or defec* or declin* or disorder* or deteriorat* or deficit* or difficult* or disabilit* or disabl*)).ti,ab.
40.	depression/ or depressive disorder/
41.	anxiety/
42.	(anxiet* or anxious or depression or low mood or tearfulness or nervousness or sadness or depress* or melanchol*).ti,ab.
43.	exp Mental Disorders/
44.	((concentrat* or memory) adj2 (disorder* or difficult* or poor or lack* or impair* or disabilit* or disable*)).ti,ab.
45.	((attention or behavior* or behaviour* or intellectual* or language or neurodevelopment* or neurological* or perception or psych* or learning) adj3 (deficit* or difficult* or disabilit* or disabl* or disorder* or impair* or declin* or deteriorat*)).ti,ab.
46.	(mental* adj3 (illness or ill or disorder* or factor* or impairment*)).ti,ab.
47.	((psychiatric or psychological*) adj3 (illness or ill or factor*)).ti,ab.
48.	Learning Disabilities/
49.	dementia/ or alzheimer disease/
50.	(alzheimer* or dement*).ti,ab.
51.	Psychotic Disorders/
52.	(psychotic* or psychoses or psychosis).ti,ab.
53.	or/38-52
54.	26 and 37 and 53

Embase (Ovid) search terms

1.	exp *epilepsy/
2.	*landau kleffner syndrome/
3.	exp *seizure/
4.	"seizure, epilepsy and convulsion"/
5.	(dravet syndrome or epilep* or continuous spike wave or slow sleep or landau kleffner syndrome or lennox gastaut syndrome or infant* spasm* or seizure* or west syndrome).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/15-21
23.	6 not 22
24.	limit 23 to English language
25.	systematic review/
26.	meta-analysis/
27.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
28.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
29.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
30.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
31.	(search* adj4 literature).ab.
32.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
33.	cochrane.jw.
34.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
35.	or/25-34
36.	*cognitive defect/
37.	((cognit* or neurocognit*) adj (dysfunction* or impair* or defec* or declin* or disorder* or deteriorat* or deficit* or difficult* or disabilit* or disabl*)).ti,ab.
38.	depression/
39.	*anxiety/
40.	(anxiet* or anxious or depression or low mood or tearfulness or nervousness or sadness or depress* or melanchol*).ti,ab.
41.	exp mental disease/

42.	((concentrat* or memory) adj2 (disorder* or difficult* or poor or lack* or impair* or disabilit* or disable*)).ti,ab.
43.	((attention or behavior* or behaviour* or intellectual* or language or neurodevelopment* or neurological* or perception or psych* or learning) adj3 (deficit* or difficult* or disabilit* or disabl* or disorder* or impair* or declin* or deteriorat*)).ti,ab.
44.	(mental* adj3 (illness or ill or disorder* or factor* or impairment*)).ti,ab.
45.	((psychiatric or psychological*) adj3 (illness or ill or factor*)).ti,ab.
46.	learning disorder/
47.	dementia/
48.	(alzheimer* or dement*).ti,ab.
49.	psychosis/
50.	(psychotic* or psychoses or psychosis).ti,ab.
51.	or/36-50
52.	24 and 35 and 51

Cochrane Library (Wiley) search terms

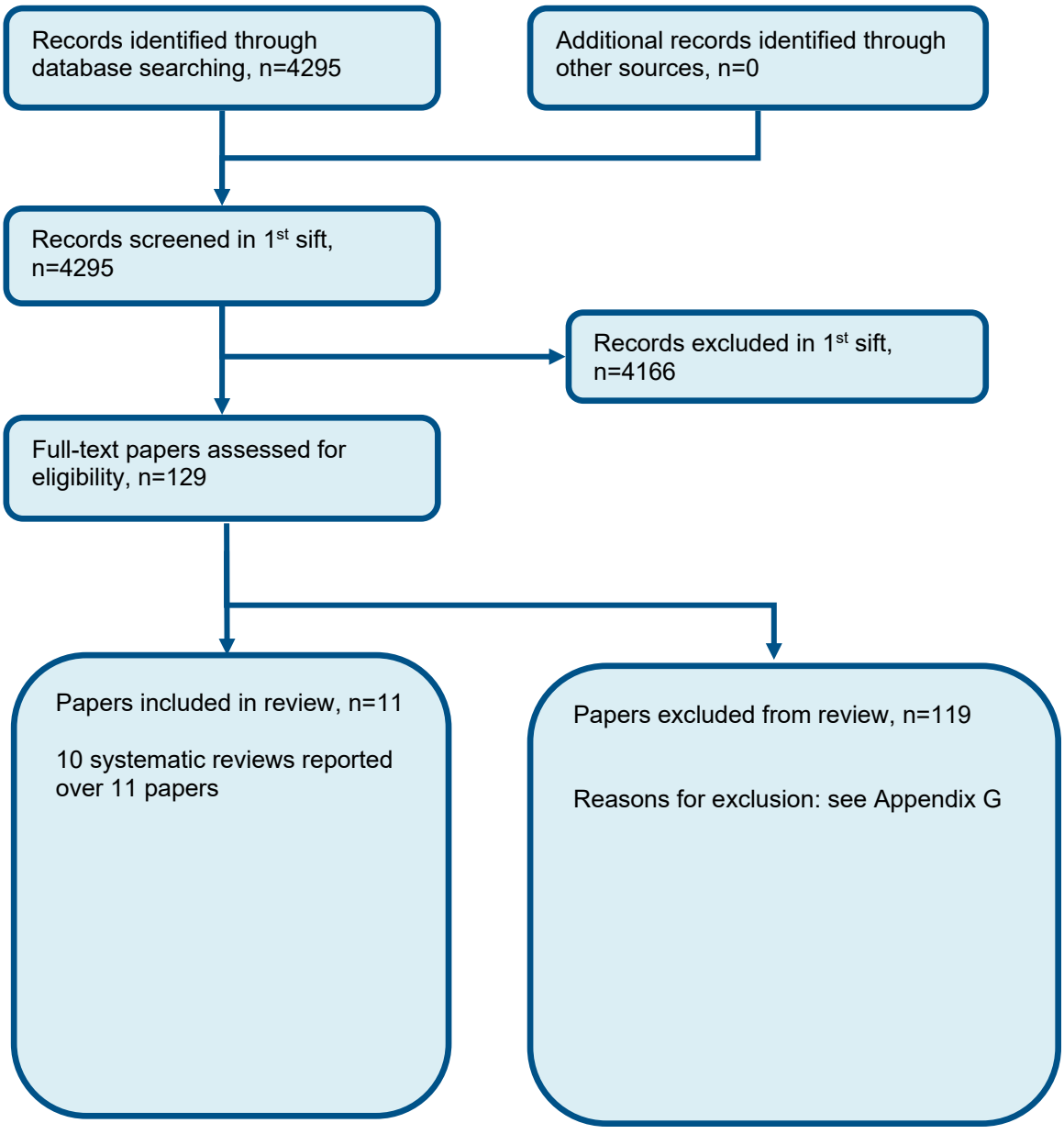
#1.	MeSH descriptor: [Epilepsy] explode all trees
#2.	MeSH descriptor: [Seizures] this term only
#3.	MeSH descriptor: [Status Epilepticus] explode all trees
#4.	MeSH descriptor: [Seizures, Febrile] this term only
#5.	(dravet syndrome or epilep* or convuls* or continuous spike wave or slow sleep or landau kleffner syndrome or lennox gastaut syndrome or infant* spasm* or seizure* or west syndrome):ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Cognitive Dysfunction] explode all trees
#8.	((cognit* or neurocognit*) near/1 (dysfunction* or impair* or defec* or declin* or disorder* or deteriorat* or deficit* or difficult* or disabilit* or disabl*)):ti,ab
#9.	MeSH descriptor: [Depression] explode all trees
#10.	MeSH descriptor: [Anxiety] explode all trees
#11.	(anxiet* or anxious or depression or low mood or tearfulness or nervousness or sadness or depress* or melanchol*):ti,ab
#12.	MeSH descriptor: [Mental Disorders] explode all trees
#13.	((concentrat* or memory) near/2 (disorder* or difficult* or poor or lack* or impair* or disabilit* or disable*)):ti,ab
#14.	((attention or behavior* or behaviour* or intellectual* or language or neurodevelopment* or neurological* or perception or psych* or learning) near/3 (deficit* or difficult* or disabilit* or disabl* or disorder* or impair* or declin* or deteriorat*)):ti,ab
#15.	(mental* near/3 (illness or ill or disorder* or factor* or impairment*)):ti,ab
#16.	((psychiatric or psychological*) near/3 (illness or ill or factor*)):ti,ab
#17.	MeSH descriptor: [Learning Disabilities] explode all trees
#18.	MeSH descriptor: [Dementia] explode all trees
#19.	MeSH descriptor: [Alzheimer Disease] explode all trees
#20.	(alzheimer* or dement*):ti,ab
#21.	MeSH descriptor: [Psychotic Disorders] explode all trees
#22.	(psychotic* or psychoses or psychosis):ti,ab
#23.	(or #7-#22)
#24.	#6 and #23

PsycINFO (ProQuest) search terms

1.	((MJMAINSUBJECT.EXACT.EXPLODE("Epilepsy") OR MAINSUBJECT.EXACT("Seizures") OR MAINSUBJECT.EXACT("Status Epilepticus") OR TI,AB(dravet syndrome OR epilep* OR continuous spike wave OR slow sleep OR landau kleffner syndrome OR lennox gastaut syndrome OR infant* spasm* OR seizure* OR west syndrome)) AND ((MAINSUBJECT.EXACT("Cognitive Impairment") OR MAINSUBJECT.EXACT("Major Depression") OR MAINSUBJECT.EXACT("Anxiety") OR MAINSUBJECT.EXACT("Mental Disorders") OR MAINSUBJECT.EXACT("Dementia") OR MAINSUBJECT.EXACT("Alzheimer's Disease") AND MAINSUBJECT.EXACT("Psychosis")) OR TI,AB((cognit* OR neurocognit*) adj (dysfunction* OR impair* OR defec* OR declin* OR disorder* OR deteriorat* OR deficit* OR difficult* OR disabilit* OR disabl*)) OR TI,AB(anxiet* OR anxious OR depression OR low mood OR tearfulness OR nervousness OR sadness OR depress* OR melanchol*) OR TI,AB((concentrat* OR memory) NEAR/2 (disorder* OR difficult* OR poor OR lack* OR impair* OR disabilit* OR disable*)) OR TI,AB((concentrat* OR memory) NEAR/2 (disorder* OR difficult* OR poor OR lack* OR impair* OR disabilit* OR disable*)) OR TI,AB((attention OR behavior* OR behaviour* OR intellectual* OR language OR neurodevelopment* OR neurological* OR perception OR psych* OR learning) NEAR/3 (deficit* OR difficult* OR disabilit* OR disabl* OR disorder* OR impair* OR declin* OR deteriorat*)) OR TI,AB(mental* NEAR/3 (illness OR ill OR disorder* OR factor* OR impairment*)) OR TI,AB((psychiatric OR psychological*) NEAR/3 (illness OR ill OR factor*)) OR TI,AB(alzheimer* or dement*) OR TI,AB(psychotic* OR psychoses OR psychosis))) AND (((SU.EXACT("Literature Review") OR RTYPE(review) OR ti(review) OR me(literature review)) AND (ti,ab(systematic OR evidence OR methodol* OR quantitative*))) OR (SU.EXACT("Meta Analysis") OR ti,ab(meta-analys* OR metanalys* OR metaanalys* OR meta analys*) OR ti,ab((systematic OR evidence* OR methodol* OR quantitative*) NEAR/3 (review* OR overview*)) OR ti,ab((pool* OR combined OR combining) NEAR/2 (data OR trials OR studies OR results)) OR RTYPE(systematic OR meta*) OR ME(meta analysis OR systematic review)))

Appendix C Evidence study selection

Figure 1: Flow chart of clinical study selection for the review of prevalence of psychological disorders



Appendix D Clinical evidence

Reference	**Asadi-Pooya 2018[7]**
Study type and analysis	Systematic review of studies looking at depression prevalence in people with epilepsy.
Number of participants and characteristics	26 studies were included in the review. Studies included were published between 1947 and 2017. Studies which focussed on special groups e.g., elderly and veterans were excluded. Specialists were invited from several countries to give prevalence data of depression for their respective countries.
Country	Counties across Asia
Outcomes/ Comorbidities	Prevalence of depression in people with Epilepsy
Results	• Japan: 18.6% of people with epilepsy had depression, measured using the Japanese version of the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) was used to diagnose depression. The prevalence of major depression in the general population was reported at 2.9%, diagnostic information for this statistic was not given. • South Korea: 21.5-27.8% of people with epilepsy had major depressive disorder compared to 3.3-5.6% life-time prevalence of major depressive disorder in the general population. The Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E) was used to diagnose depression, with a cut-off score of 11 suggesting major depressive disorder. • China: 16.5-43.4% of people with epilepsy had depression compared to 3.6% life-time prevalence of major depressive disorder in the general population. The Chinese version of the Neurological Disorders Depression Inventory for Epilepsy (C-NDDI-E) was used to diagnose depression, cut-off score of 12 suggesting major depressive disorder. • Taiwan: national health insurance research database showed people newly diagnosed with Epilepsy had higher occurrence of depression that people without epilepsy, HR 7.16 (95% CO 4.87-10.5), diagnostic information for this statistic was not given. Using the hospital anxiety and depression scale (HADS) in one clinic-based study of 260 PWE, 8.5% had scores suggestive of moderate to severe depression and 14.2% of mild depression. Psychiatric comorbidities were present in 24.6% of children with epilepsy, diagnostic information for this statistic was not given.

Reference	**Asadi-Pooya 2018[7]**
	• Iran: In one cross-sectional hospital-based study of 74 adult PWE 26 (35%) patients had symptoms of depression identified with the Beck Depression Inventory (BDI). 12.7% period prevalence of major depressive-disorder in the general population over 12 months was measured using the validated Persian translation of the Composite International Diagnostic Interview (CIDI; version 2.1). Overall range for depression in people with Epilepsy from the 26 studies included was 6.6-43.4%
Comments	No age group specified when searching papers, all data mixed for children and adults.
ROBIS rating	Overall rating: High risk of bias, this was due to the lack of risk of bias assessments carried out in the review for included studies.

Reference	**Cobham 2020[27]**
Study type and analysis	Systematic review of studies looking at anxiety prevalence in children with chronic medical conditions, i.e., epilepsy.
Number of participants and characteristics	8 studies included, 784 participants, focussing on anxiety in children and adolescents with Epilepsy. Studies included were published between 1990 and 2018.
Country	Studies included were carried out in Nigeria, USA, Norway, Italy.
Outcomes/ Comorbidities	Anxiety
Results	The prevalence rates for any anxiety disorder in children with epilepsy was 23.8 to 50%, compared to 12.4 to 22% in healthy controls. The scales used to diagnose anxiety were Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) combining parent and child interviews, Diagnostic Interview Schedule for Children (DISC-IV), Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS).
Comments	Study reported prevalence of other chronic conditions, only epilepsy data extracted.

Reference	**Cobham 2020[27]**
ROBIS rating	Overall rating: High risk of bias, this was due to the lack of risk of bias assessments carried out in the review for included studies.

Reference	**Fiest 2013[39]**
Study type and analysis	Systematic review of studies looking at depression prevalence in people with epilepsy.
Number of participants and characteristics	14 studies were included, 4 reported lifetime depression, 6 reported depression over the past 12 months and 4 reported depression over the past 30 days. The age of people included ranged from 37.2 to 52.4 years. Studies included were published between 1996 and 2011 and limited to cohort and cross-sectional design.
Country	Canada, USA, Europe, Asia, UK, Brazil
Outcomes/ Comorbidities	Depression
Results	Prevalence of active depression in adults with Epilepsy was taken from 9 studies (studies looking at past 30 days and 12 months) ranging from 13.2 to 36.5%. Lifetime depression in adults with Epilepsy was reported by 4 studies with a prevalence of 4.1 to 32.5%. Diagnosis of anxiety: World Mental Health Composite International Diagnostic Interview (WMH CIDI), outpatient visits, GP diagnosis, Schedule for Affective Disorders and Schizophrenia (SADS), Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), self-reported of diagnosis by health professional, Composite International Diagnostic Interview - Short Form (CIDI-SF), Kessler 6 mental health scale, Centre for Epidemiology Studies–Depression Scale (CES-D) score of 15 or above, Hospital Anxiety and Depression Scale (HADS) 7 or above, HADS 8 or above.
Comments	Adults included in the review, but the search was not restricted to adults. Odds ratios were reported however this evidence review is focussing on prevalence and not association, therefore odds ratio data were not extracted.
ROBIS rating	Low risk of bias.

Reference	**Fonseca 2019[42], Fonseca 2020[43]**
Study type and analysis	Systematic review looking at prevalence of cognitive deficits in children with absence epilepsy.
Number of participants and characteristics	33 studies were included Absence epilepsy: defined as 3–4Hz spike-wave complexes or a syndromic classification of childhood absence epilepsy and juvenile absence epilepsy
Country	Not stated
Outcomes/ Comorbidities	Cognitive difficulties, learning disabilities
Results	Results from single studies found the following cognitive deficits in children with absence epilepsy; 24% cognitive difficulties and 26% dysgraphia. Data taken from school reports. Four studies looking investigating either school difficulties/requiring special educational support found a prevalence of 23-70% in children with absence epilepsy. Diagnosis: neuropsychological test results.
Comments	No pooled data was provided in this review.
ROBIS rating	Low risk of bias

Reference	**Jones 2014[51]**
Study type and analysis	Narrative review of studies looking at anxiety prevalence in children and adolescents with epilepsy.
Number of participants and characteristics	No information given regarding studies included, characteristics of populations reviewed.
Country	Not stated

Reference	**Jones 2014[51]**
Outcomes/ Comorbidities	Anxiety
Results	The prevalence of lifetime anxiety ranged from 9-32% in children and adolescents with epilepsy compared to current/past 12-month prevalence of rates of 8-21%. Diagnostic scales: Anxiety and Depression in Adolescents; A Self-Test, Anxiety and Depression in Children; A Test for Parents, Beck Anxiety Inventory for Youth (BYI_II), Multidimensional Anxiety Scale for Children (MASC 2). Revised Children's Manifest Anxiety Scale-Second Edition (RCMAS-2), Self-Report for Childhood Anxiety Related Emotional Disorders (SCARED), Spence Children's Anxiety Scale (SCAS), Self-Trait Anxiety Inventory for Children (STAIC).
Comments	This was a narrative summary of studies reporting anxiety prevalence's in children and adolescence. There were no details on methodology given in the review. In the absence of this information, this review will be downgraded in the ROBIS assessment.
ROBIS rating	Very high risk of bias due to the lack of methodology data and no risk of bias assessment.

Reference	**Jones 2010[52]**
Study type and analysis	Systematic review of select studies to investigate prevalence of psychiatric disorders in epilepsy
Number of participants and characteristics	13 studies included in this review looking at prevalence of psychiatric disorders in people with epilepsy.
Country	Not stated
Outcomes/ Comorbidities	Depression Anxiety psychosis

Reference	**Jones 2010[52]**
Results	Depression prevalence: 18-39.7%, diagnosis: community-based self-report mail survey, Diagnostic and Statistical Manual of Mental Disorders (DSM) defined Anxiety disorders prevalence: 10-25%, diagnosis: DSM defined. Psychosis prevalence: 2-7%, diagnosis: DSM defined.
Comments	This review also reported the prevalence of mood disorders at 24-75% and personality disorders at 1-2% in people with epilepsy. Populations were not defined based on adults or children.
ROBIS rating	High risk of bias due to lack of information on protocol details and study selection.

Reference	**Maryam 2013[69]**
Study type and analysis	Systematic review focussing on depression in children and adolescents with epilepsy.
Number of participants and characteristics	11 cross-sectional studies included total of 1095 children and adolescents ages 4-19 years old. Searches carried out for studies published in the past 15 years.
Country	USA, UK, Nigeria, Turkey, Brazil
Outcomes/ Comorbidities	Depression
Results	Prevalence of depression in children and adolescents with epilepsy ranged from 5.2-39.6%. Diagnosis: Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD) criteria.
Comments	One study found higher depression scores from parents (39.5%) compared to self-assessment from the children (23.1%). No risk of bias assessment reported.
ROBIS rating	High risk of bias due to the lack of risk of bias assessments.

Reference	**Scott 2017[95]**
Study type and analysis	Systematic review of studies looking at the prevalence of anxiety and depression in people with Epilepsy. Meta-analysis of the prevalence data was carried out to deduce pooled prevalence values.
Number of participants and characteristics	27 studies and total of 3221 adults, aged 16 years and older, with epilepsy were included. Databases were searched for relevant studies up until July 2016.
Country	Not stated
Outcomes/ Comorbidities	Depression anxiety
Results	Overall pooled prevalence of depression disorders in people with epilepsy was 22.9%. (Figure 2) Overall pooled prevalence of anxiety disorders in people with epilepsy was 20.2%. (Figure 3) Diagnosis: Diagnostic and Statistical Manual of Mental Disorders (DSM IV), International Classification of Diseases Tenth Revision (ICS 10),
Comments	
ROBIS rating	Low risk of bias

Reference	**Scott 2020[96]**
Study type and analysis	Systematic review of studies looking at the prevalence of anxiety and depression in youths with Epilepsy. Meta-analysis of the prevalence data was carried out to deduce pooled prevalence values.
Number of participants and characteristics	Databases were searched for relevant studies up until October 2018. 23 studies were included with children aged up to and including 18 years with a confirmed diagnosis of epilepsy.

Reference	**Scott 2020[96]**
Country	USA, Africa, Europe
Outcomes/ Comorbidities	Anxiety Depression
Results	The overall pooled prevalence of anxiety disorders in children with epilepsy was 18.9% (95% CI 12.0%–28.5%), and for depression the pooled prevalence was 13.5% (95% CI 8.8%–20.2%). Diagnosis: Diagnostic and Statistical Manual of Mental Disorders (DSM III), Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS), Diagnostic Interview Schedule for Children (DISC-IV)
Comments	
ROBIS rating	Low risk of bias

Reference	**Subota 2017[105]**
Study type and analysis	Systematic review of studies looking at the prevalence of dementia in people with epilepsy.
Number of participants and characteristics	Of the 8 studies included in this review, only 2 studies were in people with epilepsy who later developed dementia that prevalence data for dementia
Country	Sweden, USA
Outcomes/ Comorbidities	Dementia
Results	The period prevalence of dementia ranged from 8.1 to 17.5 per 100 persons among persons with epilepsy. Diagnosis: National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA), International Classification of Diseases Ninth Revision (ICD-9)

Reference	**Subota 2017[105]**
Comments	Populations were not defined based on adults or children. Meta-analysis could not be carried out due to insufficient data.
ROBIS rating	Low risk of bias

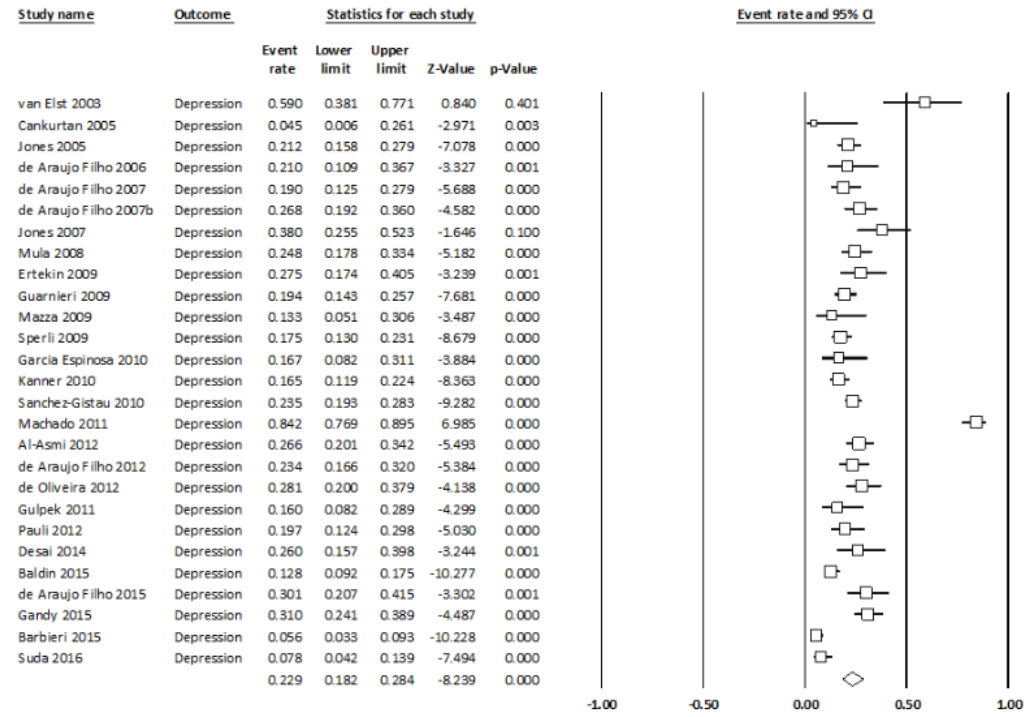
Appendix E ROBIS assessment

	Phase 2				Phase 3
Study	1. STUDY ELIGIBILITY CRITERIA	2. IDENTIFICATION AND SELECTION OF STUDIES	3. DATA COLLECTION AND STUDY APPRAISAL	4. SYNTHESIS AND FINDINGS	RISK OF BIAS IN THE REVIEW
Asadi-Pooya 2018	Low	Low	High	Low	**High[1]**
Cobham 2020	Low	Low	High	Low	**High[1]**
Fiest 2013	Low	Low	Low	Low	**Low**
Fonseca 2019, 2020	Low	Low	Low	Low	**Low**
Jones 2014	High	High	High	Low	**Very high[1,2]**
Jones 2010	High	High	Low	low	**High[2]**
Maryam 2012	Low	Low	High	Low	**High[1]**
Scott 2017	Low	Low	Low	Low	**Low**
Scott 2019	Low	Low	Low	Low	**Low**
Subota 2017	Low	Low	Low	Low	**Low**

[1]*There was no details on risk of bias assessment in this review.*
[2]*There was insufficient information on the review methodology*

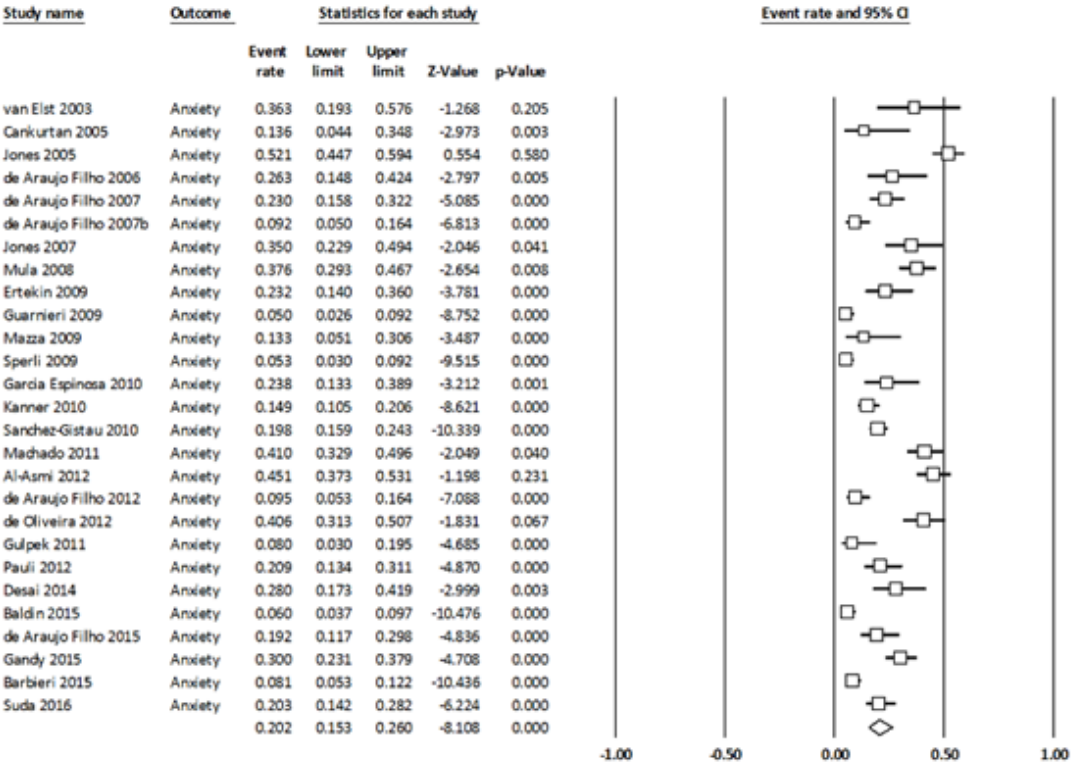
Appendix F Forest plots

Figure 2: Prevalence of depression in adults with Epilepsy



Scott 2017[95]

Figure 3: Prevalence of anxiety in adults with Epilepsy



Scott 2017[95]

Appendix G Excluded studies

G.1 Clinical studies

Table 9: Studies excluded from the clinical review

Reference	Exclusion reason
Sajatovi, 2019[93]	Systematic review investigating Self-management strategies of epilepsy
Abraham, 2019[1]	Systematic review investigating suicide rates
Allebone, 2018[2]	Systematic review did not investigate prevalence of psychosis
Amiet, 2008[3]	association study for autism, learning disability and epilepsy focussing on an autistic population
Anderson, 2010[4]	Systematic review focussed on drug monitoring and safety
Arana, 2010[5]	Systematic review investigating suicide rates
Arico, 2020[6]	Systematic review did not investigate prevalence
Bagary, 2017[8]	Conference abstract
Banach, 2010[9]	looking at effects of prenatal AEDs on children's intellectual development
Baranowski, 2018[10]	Systematic review investigating quality of life in epilepsy
Beavis, 2007[11]	Systematic review did not investigate prevalence
Bell, 2008[12]	Systematic review investigating drowning
Bell, 2009[13]	Systematic review investigating suicide rates
Bell, 2009[14]	Systematic review investigating suicide rates
Benamer, 2009[15]	systematic review focussed on the prevalence of epilepsy
Besag, 2015[16]	Systematic review on epileptic surgery
Beyenburg, 2005[17]	Systematic review did not investigate prevalence
Blickwedel, 2019[18]	Systematic review did not investigate prevalence
Boot, 2012[19]	Systematic review did not investigate prevalence
Bowley, 2000[20]	Incorrect population
Brandt, 2016[21]	Systematic review did not investigate prevalence
Breuer, 2016[22]	Systematic review did not investigate prevalence
Britton, 2010[23]	Systematic review did not investigate prevalence
Brodie, 2016[24]	Conference abstract
Butler, 2008[25]	Systematic review did not investigate prevalence
Cavanna, 2010[26]	Systematic review did not investigate prevalence
Cobham, 2020[27]	
Collaborators, 2019[46]	systematic review looking at the prevalence of epilepsy
Cubała, 2018[28]	Conference abstract
Cyr, 2021[29]	Systematic review did not investigate prevalence
de Winter, 2011[30]	Systematic review did not investigate prevalence
Deb, 2020[31]	Systematic review did not investigate prevalence
Doran, 2016[32]	Systematic review did not investigate prevalence
Doran, 2015[33]	Conference abstract

Reference	Exclusion reason
Elliott, 2014[34]	Systematic review with incorrect population
Ferrer, 2013[35]	Conference abstract
Ferrer, 2014[36]	Systematic review did not investigate prevalence
Fiest, 2012[37]	Conference abstract
Fiest, 2012[38]	Conference abstract
Fiest, 2013[39]	
Finzel, 2009[40]	conference abstract
Fitzgerald, 2009[41]	Incorrect population
Fonseca Wald, 2019[42]	
Gandy, 2012[45]	risk prediction review
Gandy, 2013[44]	Systematic review did not investigate prevalence
Gill, 2017[47]	Systematic review did not investigate prevalence
Hall, 2009[48]	No prevalence data
Johnson, 2018[49]	review on panic attacks
Johnson, 2016[50]	No prevalence data
Kanner, 2003[53]	No prevalence data
Kanner, 2002[54]	No prevalence data
Kattimani, 2011[55]	No relevant data
Kavros, 2008[56]	No prevalence data
Kim, 2018[57]	point prevalence data only
Kolc, 2019[58]	Systematic review did not investigate prevalence
Kolevzon, 2019[59]	Incorrect population
Kutlubaev, 2018[60]	Systematic review did not investigate prevalence
Kwok, 2007[61]	Incorrect population
Lagogianni, 2020[62]	review focussing on fatigue
Lai, 1997[63]	Not focussing on prevalence
Lax-Pericall, 2019[64]	Looking at gender as a risk factor for psychiatric disorders in epilepsy
Loughman, 2016[65]	Not focussing on prevalence
Loughman, 2014[66]	Not focussing on prevalence
Lukmanji, 2019[67]	Not relevant information, review focussing on autism
M, 2015[68]	point prevalence data only
Maryam, 2013[69]	
Menlove, 2015[70]	No prevalence data
Michelucci, 1989[71]	Incorrect population
Monteagudo-Gimeno, 2020[72]	Not focussing on prevalence
Monti, 2015[73]	Not focussing on prevalence
Muhigwa, 2020[74]	Not focussing on prevalence of psychological disorders
Mula, 2010[75]	Not focussing on prevalence

Reference	Exclusion reason
Mula, 2011[76]	Reviewing suicide rates
Mula, 2020[77]	The only relevant data is a summary of Fiest 2013 which is already included
Mula, 2010[78]	Not focussing on prevalence
Neumann, 2016[80]	Not in English
Otero, 2009[81]	Not focussed on prevalence
Parnas, 1982[82]	Not focussed on prevalence
Patten, 2018[83]	Not focussed on prevalence
Pinquart, 2011[85]	Review not focussing on prevalence
Pinquart, 2011[84]	Not focussed on Epilepsy and prevalence
Quintas, 2012[86]	Not focussed on prevalence
Ramanujam, 2017[87]	Systematic review aspect of study was not focussed on prevalence
Reilly, 2013[88]	No relevant data
Reilly, 2011[89]	Looking at academic performance in children with and without learning difficulties in an epilepsy population
Ricciardi, 2015[90]	Not focussed on prevalence
Richard, 2017[91]	Not focussed on prevalence
Rodenburg, 2005[92]	Not focussed on prevalence
Sanya, 2010[94]	Not focussed on prevalence
Secinti, 2017[97]	Not focussed on prevalence
Seethalakshmi, 2007[98]	Not focussed on prevalence
Sen, 2018[99]	Not focussed on prevalence
Srinivas, 2017[100]	Not focussed on prevalence of conditions in protocol
Stevelink, 2019[101]	Not focussed on prevalence of conditions in protocol
Stewart, 2016[102]	Not focussed on prevalence
Stewart, 2019[103]	Not focussed on prevalence
Strasser, 2018[104]	No relevant data
Tao, 2016[106]	Not focussed on prevalence
Taylor, 2011[107]	Not focussed on prevalence, HRQoL and costing
Theodore, 2006[108]	Not focussed on prevalence of conditions in protocol
Thomson, 2014[109]	Not focussed on prevalence, HRQoL
Tramoni-Negre, 2017[110]	Not focussed on prevalence
Trimble, 2003[111]	Not focussed on prevalence
Trinka, 2019[112]	Looking at prevalence of epilepsy
Tuchman, 2011[113]	Not focussed on prevalence
van Ool, 2016[114]	Not focussed on prevalence
Vannest, 2015[115]	Not focussed on prevalence
Vazquez, 2003[116]	Not focussed on prevalence
Verche, 2018[117]	Not focussed on prevalence

Reference	Exclusion reason
Verrotti, 2015[118]	Not focussed on prevalence
Vonberg, 2016[119]	Conference abstract
Wade, 1986[120]	looking at the prevalence of long-term diseases
Walsh, 2017[121]	Not focussed on prevalence
Walsh, 2018[122]	Not focussed on prevalence
Werhahn, 2009[123]	Not focussed on prevalence
Wickens, 2017[124]	Not focussed on prevalence
Wiglusz, 2012[125]	Not focussed on prevalence
Williams, 2016[126]	No relevant data
Yang, 2020[127]	Not focussed on prevalence
Yoong, 2015[128]	Not focussed on prevalence
Yrondi, 2017[129]	Not in English
Zapata Barco, 2020[130]	Not in English