National Institute for Health and Care Excellence

FINAL

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

[16] Evidence review: Psychological treatments for people with epilepsies

NICE guideline NG217

Evidence reviews underpinning recommendations 9.2.1 to 9.2.4 and a research recommendation.

April 2022

FINAL

Developed by the National Guideline Centre

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Contents

1 Psychological treatments for people with epilepsy

1.1 What is the effectiveness of psychological treatments on HRQoL for people with epilepsy?

1.1.1 Introduction

People with epilepsy, especially those with drug-resistant epilepsy, often have lower health-related quality of life (HRQOL) compared to those people with other long-term conditions. Factors that can contribute to lower HRQOL include medical aspects such as seizure frequency and severity and side effects from anti-seizure medications (ASMs).) Psychological factors such as depression and anxiety, fear of losing control, concerns about seizure occurrence can also adversely affect the quality of life of a person living with epilepsy.

1.1.2 Cochrane collaboration

An overlap was identified between the Cochrane review 'Psychological treatments for people with epilepsy' and the question within the NICE Epilepsies guideline scope on psychological treatments for people with Epilepsies. NICE and the NGC developers agreed to collaborate with the Cochrane epilepsy group for them to update their review and to incorporate this within the update of the guideline. The NGC technical team and the Epilepsies guideline committee worked with the Cochrane group to finalise the review protocol. The evidence review was conducted in its entirety by the Cochrane team; the full Cochrane review can be found here. A summary of the included studies and evidence is given below.

This evidence review summarises the findings of the Cochrane review on the effectiveness of psychological treatments for people with epilepsy.

1.1.3 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Children, young people and adults with confirmed epilepsy
Interventions	• Skills based interventions that accommodate the opportunity for participants to practice skills • Based on at least one theory of psychotherapy, examples include cognitive behavioural or behaviourally based interventions, and mindfulness-based interventions (such as acceptance and commitment therapy), family systems therapy, motivational interviewing, adherence interventions, and other psychotherapeutic methods • Education only interventions • Defined as interventions that aim to increase knowledge of epilepsy, its comorbidities, and its treatments or the working of the brain (including psychoeducation) • They may accommodate the opportunity for participants to learn about certain skills (such as coping skills), but they do not accommodate guide participants through the practice of these skills.

Comparisons	• Treatment as usual • Wait-list control • Active control (for example, counselling as usual, yoga) • (Comparators will be combined vs the intervention)
Outcomes	Validated HRQoL outcomes
Study design	RCTs

1.1.4 Included studies

Thirty-six completed RCTs matched the inclusion criteria for this review[1-7, 9-25, 28-39, 41]. Based on satisfactory clinical and methodological homogeneity, data was pooled from 11 studies (643 participants) that used the Quality of Life in Epilepsy-31 (QOLIE-31) or other QOLIE inventories (such as QOLIE-89 or QOLIE-31-P) convertible to QOLIE-31.

1.1.5 Summary of studies included in the effectiveness evidence

Table 2: Summary of studies included in the evidence review

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
Skills based psychological interventions								
Au 2003	Cognitive behavioural therapy	Seizure frequency	Stress management, cognitive restructuring, communication skills	Clinical psychologist	Clinic	Group	8 weekly 2-hour sessions	N = 17 adults with at least 2 seizures per month, with subjectively reported psychological distress
Ciechanowski 2010 (PEARLS)		Depressive symptoms	Cognitive restructuring to address negative depressive thinking + behavioural activation	Trained social worker	Home-based + telephone calls	Individual	8 50-min in-home sessions in 5 months + 7 monthly 5- to 10-min telephone calls	N = 80 adults with epilepsy with significant depression
Gandy 2014				Intern psychologist	Clinic	Individual	1 x 1- to 2-hour assessment session + 8 weekly 1-hour sessions	N = 59 adults with epilepsy

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
Gilliam 2019			CBT based on standardized and manual-based Beck guidelines	Nurse educator and trained lay person with epilepsy	Therapist office	Individual	1-hour session per week for 16 weeks	N = 98 adults (age 21 - 75) with epilepsy and current major depressive episode
Hum 2019 (UPLIFT)			see Thompson 2010	Licensed mental health professional and trained layperson with epilepsy	Telephone calls	Group	8 weekly 1-hour sessions	N = 55 adults with epilepsy and depressive symptoms
Martinović 2006			Cognitive restructuring to address negative depressive thinking + behavioural activation	NR	Clinic	Group	8 weekly sessions + 4 monthly sessions	N = 32 adolescents with epilepsy and subthreshold depression
Meyer 2019 (Emyna)			Cognitive restructuring to address negative depressive thinking + behavioural activation	NA	Internet-based	Individual	5 modules with no fixed sequence, each lasting for 60 - 180 min	N 154 adult (> 18) with active epilepsy and a current diagnosis of moderate depression
Orjuela-Rojas 2015				Licensed CBT therapist and psychiatrist	Clinic	Group	12 weekly 90-min sessions	N = 15 adults with epilepsy and major depression

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
Schröder 2014 (Deprexis)				NA	Internet-based	Individual	9 weekly modules (10 - 60 min)	N = 78 adults with self-reported depressive symptoms
Thompson 2010 (UPLIFT)				Master of Public Health student and trained lay person with epilepsy	Internet-based + telephone calls	Group	8 weekly 1-hour sessions	N = 53 adults with epilepsy and depression (but not severe depression)
Dorris 2017	Self-management program	Quality of life	Medical self-management and sleep hygiene, coping strategies and problem-solving techniques based on CBT and mindfulness	Epilepsy nurse and clinical psychologist	Clinic	Group	6 weekly 120-min sessions	N = 69 children and adolescents aged 12 - 17 with epilepsy
Fraser 2015 (PACES)		Self-management	Medical and psychosocial self-management + epilepsy-related communication	Psychologist and trained lay person with epilepsy	Clinic	Group	8 weekly 75-min sessions	N = 83 adults with epilepsy
Leenen 2018 (ZMILE)		Self-management and quality of life	Self-monitoring, risk-evaluation and management; shared decision-making, goal-setting skills	Nurse practitioner	Clinic	Group	5 weekly 2-hour sessions followed by a 2-hour booster session after 3 weeks	N = 87 adults with epilepsy and on AEDs

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
Sajatovic 2016 (TIME)		Depressive symptoms	Personal goal-setting exercises (with focus on coping with mental illness and epilepsy), stress management, and training to communicate with care providers	Nurse educator and trained lay person with epilepsy	Clinic	Group	12 weekly 60- to 90-min sessions	N = 35 adults with epilepsy and comorbid mental illness
Sajatovic 2018		Negative health events	SMART "self-management for people with epilepsy and a history of negative health events"	Nurse educator and trained lay person with epilepsy	Clinic + telephone intervention calls + telephone maintenance	Group + individual	1 face-to-face 60- to 90-min group; 7 Internet-based group; 6 10- to 15-min telephone maintenance	N = 111 adults with at least 1 negative health event within the past 6 months
Yadegary 2015		Quality of life	Medical and psychosocial self-management + seizure communication	NR	Clinic	Group	4 weekly 120-min sessions	N = 60 adults with epilepsy
Dilorio 2011 (WebEase)	Motivational interviewing (MI)	Medication adherence + perceived stress	Medication adherence + stress and sleep management	NA	Internet-based	Individual	3 bi-weekly modules	N = 194 adults with epilepsy
Hosseini 2016		Quality of life	Enhancement of internal motivation for change, by overcoming dualism	Psychologist and trained layperson with epilepsy	Clinic	Group	5 sessions in 20 days	N = 56 adults with epilepsy.

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
Pakpour 2015		Medication adherence	MI techniques	Health psychologist	Clinic	Individual	3 weekly 40- to 60-min sessions	N = 275 adults with epilepsy
Lundgren 2006; Lundgren 2008	Mindfulness therapy (MT)	Quality of life	ACT + seizure management	Clinical psychologist	Clinic	Group + individual	5 individual 90-min sessions + 2 x group 3-hour sessions + 2 x 1-hour boosters at 6 and 12 months	N = 27 (Lundgren 2006) N = 18 adults with epilepsy (Lundgren 2008)
Tang 2015		Quality of life	Epilepsy management + mindfulness techniques + seizure-related acceptance	Clinical psychologist	Clinic	Group	4 x bi-weekly 2 x.5-hour sessions	N = 61 adults with drug-resistant epilepsy
Brown 2019	Behaviour-change counselling	Physical activity and quality of life	Self-regulatory skills to support behaviour change	Trained research assistant	Clinic	Individual	15-min sessions: weekly/bi-weekly/monthly weeks 1 – 4/ 6 – 12/16 – 24	N = Children aged 8 – 14 years with epilepsy
Caller 2016 (HOBSCOTCH)	Cognitive, memory + self-management training	Quality of life	Problem-solving therapy and behaviour modification strategies + seizure management + social skills	Specialized nurse	Home-based + telephone calls	Group + individual	8 weekly 40- to 60-min sessions	N = 66 adolescents and adults with epilepsy and self-reported memory complaints
Helde 2005	Epilepsy education +	Quality of life	Personalized counselling +	Specialized nurse	Clinic + phone calls	Group + individual	1-day group + phone calls	N = 114 adults with epilepsy

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
	nurse-led counselling		disease knowledge + drug adherence				every 3 months for 2 yrs.	
Pramuka 2007	Epilepsy education program	Quality of life	Disease knowledge, advocacy topics, self-management, psychosocial aspects	Psychologist and epilepsy nurse	Clinic	Group	6 weekly 2-hour sessions	N = 55 adults with epilepsy
Ring 2018	Learning Disability Epilepsy Specialist Nurse Competency Framework	Seizure frequency and quality of life	Provide care according to guidelines developed by the UK ESNA and UK Royal College of Nursing	Licensed mental health professional and trained lay person with epilepsy	Home visits, telephone, clinics and visits to the local primary care or ID team base	Individual	On an as-needed basis for 24 weeks	N = 312 adults with epilepsy and intellectual disability
Education only interventions								
Beretta 2014 (EDU-COM)	Patient-tailored medication education	Drug-related problems	Personalized education on drug interaction and tolerability	Treating physician	Clinic	Individual	1-hour session + booster session after 1 month	N = 174 adults with epilepsy and chronic comorbidity
Edward 2019	Epilepsy education program	Seizure frequency	Education program developed based on the self-determination theory (managing epilepsy and medical care, socializing on a budget, healthy lifestyle,	Specialized nurse	Not specified in the publication	Not specified in the publication	1 x 120-min session	N = 35 adults with epilepsy

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
			emotional management)					
Jantzen 2009 (FLIP&FLAP)	Epilepsy education program	Quality of life	Disease knowledge, advocacy topics, self-management, psychosocial aspects	Trained nurses, social workers, medical doctors or psychologists	Clinic	Group	2-day course (14 hours)	N = 192 children and adolescents with epilepsy, including parents
Lua 2013	Epilepsy education program	Quality of life	Disease knowledge, advocacy topics, self-management, psychosocial aspects	NR	SMS-based	Individual	11 weekly modules	N = 144 adults with epilepsy
May 2002 (MOSES)	Epilepsy education program	Quality of life	Disease knowledge, advocacy topics, self-management, psychosocial aspects	Trained nurses, social workers, medical doctors or psychologists	Clinic	Group	2-day course (14 hours)	N = 383 adolescents and adults with epilepsy
Pfäfflin 2016	Counselling	Satisfaction with information and support	Disease knowledge, advocacy topics, self-management, psychosocial aspects	Specialized nurse	Clinic	Individual	Delivery during routine visits	N = 187 adults with epilepsy
Rau 2006 (FAMOSES)	Epilepsy education program	Knowledge + coping	Disease knowledge, advocacy topics, self-management, psychosocial aspects	NR	Clinic	Group	2-day course (14 h)	N = 70 children with epilepsy

Study (intervention acronym)	Main treatment method	Primary treatment goal	Main treatment strategy	Provider	Setting	Delivery	Timing	Participants
Ridsdale 2018 [SMILE (UK)]	Epilepsy education program (May 2002)	Quality of life	see May 2002	Nurse educator and trained lay person with epilepsy	Clinic	Group	2-day course (16 h)	N = 314 adolescents (≥ 16 years) and adults with poorly controlled epilepsy
Turan Gurhopur 2018	Epilepsy education program	Epilepsy-specific knowledge, self-efficacy, quality of life	Modular education program including epilepsy knowledge, seizure management, and social aspects of epilepsy	NR	Clinic	Individual	2 - 3 days with a total of 16 hours	N = 92 including children with epilepsy aged 7 - 18; and parents of children with epilepsy

1.1.1. Effectiveness evidence

Table 3: Clinical evidence summary: psychological treatments versus usual care or supportive care

Outcomes	Comparative effect sizes* (95% CI)		Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Wait-list control, usual care, supportive care or antidepressant drug treatment	Psychological treatments			
QOLIE-31 total score[a]	The range of mean change in the control groups was −1.9 to 15.96 points.	The range of mean change in the intervention groups was 3.27 to 17.2 points. The pooled mean change from baseline in the intervention groups measured at post-intervention[b] was on average 5.23 higher (95% CI 3.02 to 7.44 higher) than the control groups	643 (11 RCTs)	⨁⨁⨁⨀ MODERATE[c]	2 out of 3 studies that could not be included in meta-analysis due to use of QOLIE-89 or QOLIE-31-P reported significantly higher postintervention QOLIE total scores in the treatment over the control groups (Hosseini 2016; Yadegary 2015).
QOLIE-31 emotional well-being subscale[a]	The range of mean change in the control groups was −6.23 to 24.95 points.	The range of mean change in the intervention groups was 0.91 to 20.57 points. The pooled mean change from baseline in the intervention groups measured at post-intervention[b] was on average 4.96 higher (95% CI 0.70 to 9.21 higher) than the control groups	643 (10 RCTs)	⨁⨁⨁⨀ MODERATE[c]	-
QOLIE-31 energy or fatigue subscale[a]	The range of mean change in the control	The range of mean change in the intervention	642 (10 RCTs)	⨁⨁⨁⨀ MODERATE[c]	-

Outcomes	Comparative effect sizes* (95% CI)		Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Wait-list control, usual care, supportive care or antidepressant drug treatment	Psychological treatments			
	groups was −5.3 to 17.69 points.	groups was 0.44 to 18.75 points. The pooled mean change from baseline in the intervention groups measured at post-intervention[b] was on average 5.25 higher (95% CI 1.56 to 8.93 higher) than the control groups			
QOLIE-31 overall QoL subscale[a]	The range of mean change in the control groups was −2.63 to 15 points.	The range of mean change in the intervention groups was 0.13 to 19.64 points. The pooled mean change from baseline in the intervention groups measured at post-intervention[b] was on average 5.95 higher (95% CI 3.05 to 8.85 higher) than the control groups	639 (10 RCTs)	⨁⨁⨁⨀ MODERATE[c]	-
QOLIE-31 seizure worry subscale[a]	The range of mean change in the control groups was −5.18 to 17.26 points.	The range of mean change in the intervention groups was 2.74 to 28.56 points. The pooled mean change from baseline in the intervention groups measured at post-intervention[b] was on average 4.35 higher	632 (10 RCTs)	⨁⨁⨁⨀ MODERATE[c]	-

Outcomes	Comparative effect sizes* (95% CI)		Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Wait-list control, usual care, supportive care or antidepressant drug treatment	Psychological treatments			
		(95% CI 1.35 to 7.35 higher) than the control groups			
QOLIE-31 cognitive functioning subscale[a]	The range of mean change in the control groups was −2.71 to 13.17 points.	The range of mean change in the intervention groups was 2.28 to 16.16 points. The pooled mean change from baseline in the intervention groups measured at post-intervention[b] was on average 4.18 higher (95% CI 1.82 to 6.54 higher) than the control groups	641 (10 RCTs)	⨁⨁⨁⊖ MODERATE[c]	-
QOLIE-31 medication effects subscale[a]	The range of mean change in the control groups was −8.11 to 12.04 points.	The range of mean change in the intervention groups was 0.93 to 6.64 points. The pooled mean change from baseline in the intervention groups measured at post-intervention[b] was on average 3.16 higher (95% CI 0.01 to 6.32 higher) than the control groups	643 (10 RCTs)	⨁⨁⨁⊖ MODERATE[c]	-
QOLIE-31 social function subscale[a]	The range of mean change in the control groups was −4.28 to 13.98 points.	The range of mean change in the intervention groups was 2.3 to 10.49 points. The pooled mean change from baseline in	630 (10 RCTs)	⨁⨁⨁⊖ MODERATE[c]	-

Outcomes	Comparative effect sizes* (95% CI)		Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Wait-list control, usual care, supportive care or antidepressant drug treatment	Psychological treatments			
		the intervention groups measured at post-intervention[b] was on average 3.09 higher (95% CI -0.17 lower to 6.35 higher) than the control groups			
* Comparative effect sizes were calculated from the mean changes between baseline and post-intervention in the intervention and control groups. CI: Confidence interval; QOLIE: Quality of life in epilepsy; RCT: randomized controlled trial					
GRADE Working Group grades of evidence High certainty: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.					

[a]Range 0 - 100 points, higher score means higher quality of life.
[b]The median postintervention measurement point was 3 months (8 weeks to 2 years).
[c]Serious risk of bias, i.e., included studies share serious risk of performance bias and five included studies share serious risk of attrition bias

1.1.6 Economic evidence

1.1.6.1 Included studies

Two health economic studies with relevant comparisons were included in this review: one comparing epilepsy education program to usual care[33] and one comparing a multicomponent self-management intervention to usual care.[40] These are summarised in the health economic evidence profiles below (**Table 4** and **Table 5**) and the health economic evidence tables in Appendix D.

1.1.6.2 Excluded studies

One economic study relating to this review question was identified but was excluded due to methodological limitations[8]. This is listed in Appendix F, with the reasons for exclusion given.

See also the health economic study selection flow chart in Appendix C.

1.1.7 Summary of included economic evidence

Table 4: Health economic evidence profile: epilepsy education program versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost (2vs. 1)	Incremental effects (2 vs. 1)	Cost effectiveness (1 vs. 2)	Uncertainty
Risdale 2018[33] (UK)	Partially applicable [(a)]	Potentially serious limitations[(b)]	• Within-trial analysis (SMILE UK/Risdale 2018[33]) • Cost-utility analysis (QALYs) Population: Adults (≥ 16 years) with epilepsy who were prescribed AEDs, with 2 or more seizures in the previous 12 months and able to provide informed consent, participate in the course and complete questionnaires in English. • Comparators: 1.Usual care 2.Group-based education programme + usual care (SMILE) Follow up: 1 year	Saves £27[(c)]	0.0142 fewer QALYs	£1,901 per QALY gained	Probability SMILE cost effective (£20K threshold): ~40% Results presented as completed cases and ITT The ITT results presented as the base case. The complete case analysis ICER for usual care versus SMILE was £5,548 per QALY.

Abbreviations: ICER= incremental cost-effectiveness ratio; ITT= intention to treat; QALY= quality-adjusted life years; RCT= randomised controlled trial
(a) EQ5D-5L not mapped to 3L as per NICE position statement. Does not include all relevant comparators for this review question.
(b) Within trial analysis based on single RCT, other RCTs on this type of intervention are presented in clinical review and so may not reflect full body of clinical evidence. Short time horizon. Limited sensitivity analyses.

(c) 2014/2015 UK pounds. Cost components incorporated: Epilepsy-specific hospital services and community-based health and social care services, medication and intervention cost.

Table 5: Health economic evidence profile: Self-management versus usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Wijnen 2017[40] (Netherlands)	Partially applicable [(a)]	Potentially serious limitations[(b)]	• Within-RCT analysis (ZMILE/Leenen 2018 [40]) • Cost-utility analysis (QALYs) • Population: Adults (≥18 years) with epilepsy, who lived at home, used AEDs, understood the Dutch language, and were willing and able (based on neurologists' opinion) to use e-Health devices belonging to the MCI. • Comparators: 1.Usual care 2.Multicomponent self-management intervention (MCI) Follow-up: 1 year	£740[(c)]	0.03 QALYs	£24,653 per QALY gained	Probability MCI cost effective (£20/£30K threshold): n/a Sensitivity analyses included: - Using EQ-5D with Dutch tariff - 6-month follow-up - Societal perspective - Using disease-specific QALYs based on the QOLIE-31-P. Note: ITT analysis was used and missing data at follow-up measurements were dealt with using multiple imputation (5 times).

Abbreviations: ICER= incremental cost-effectiveness ratio; ITT= intention to treat; QALY= quality-adjusted life years; RCT= randomised controlled trial
(a) Dutch healthcare perspective. EQ5D-5L not mapped to 3L as per NICE position statement. Does not include all relevant comparators for this review question.
(b) Within-trial analysis based on single RCT, other RCTs on this type of intervention are included in the clinical review and so may not reflect full body of clinical evidence. Short time horizon. Bootstrapping presented from societal perspective only, not available from healthcare perspective.
(c) 2015 Euros converted to UK pounds.[27]. Cost components incorporated: intervention and healthcare costs.

1.1.8 Economic model

This area was not prioritised for a new cost-effectiveness analysis.

1.1.9 Evidence statements

Economic

- One cost-utility analysis found that an epilepsy education program (group-based) plus usual care was not cost-effective compared to usual care for adults with epilepsy (ICER: £1,901 per QALY gained for usual care compared to group self-management plus usual care). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that a multicomponent self-management intervention was not cost-effective compared to usual care in adults with epilepsy (ICER: £24,653 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.

1.1.10 The committee's discussion and interpretation of the evidence

1.1.10.1 The outcomes that matter most

Health-related quality of life was the only outcome data extracted for this review.

1.1.10.2 The quality of the evidence

All the evidence for the outcomes in this review was of moderate quality. The quality was downgraded due to the risk of performance and attrition bias.

The guideline committee agreed there was significant clinical heterogeneity in the clinical evidence in terms of the range and types of psychological therapies delivered, which included both skills-based and educational interventions, who provided the treatments such as psychologist or nurse-led delivery, and the characteristics of people included in the studies. Despite this, no stratification strategies had been devised pre-hoc to allow suitable splitting of data. None of the analyses showed serious statistical heterogeneity, which suggested that clinical differences in treatment and populations did not affect the outcome significantly. However, making recommendations for specific sub-groups of people with respect to particular treatments would be difficult from the pooled evidence, as the overall pooled estimates would have their precision inflated by the pooling. The committee also agreed that the clinical evidence for children and young people was extremely limited.

Based on the clinical evidence presented and in the absence of robust health economic evidence, the committee concluded that it was difficult to make any strong recommendations and agreed to make a health economic research recommendation on the cost-effectiveness of providing tailored psychological treatments for people with epilepsy.

1.1.12.3 Benefits and harms

The guideline committee agreed the evidence suggested benefit for skills-based psychological treatments (CBT, self-management programmes, motivational interviewing, counselling) in people with epilepsy. However, as most of the included trials compared psychological interventions delivered in-person to a waiting list

control or usual care, participants could not be blinded to the interventions. The committee was concerned that the lack of blinding could have given rise to placebo effect in people who knew they were in the treatment arm of the trials, thereby influencing the benefit seen. They were also mindful that the treatment arm of the trials involved regular human contact between the person delivering the intervention and the person with epilepsy, which could contribute to the benefit seen in the evidence, leading to uncertainty about whether any effect is from the intervention or from the human interaction. However, the committee noted the counterargument that social contact is part of the active treatment. The committee acknowledged the difficulty in avoiding such biases in psychological trials and discussed one way of overcoming this would be to have an active control, e.g., education/support delivered in person. It was noted that although two of the eleven studies included in the evidence had an active control, they were pooled with the rest of the trials. The committee was concerned that waiting-list control trials often overestimate the effect seen, which was difficult to investigate because the comparators were all pooled together in the evidence. It was also unclear whether the treatment or comparator arms of the trials received any support outside of the trial interventions. The committee concluded that although psychological interventions showed benefit in people with epilepsy, the extent to which the benefit is a result of the psychological element itself is unclear.

The committee discussed that the interventions were more intensive than would typically be provided in usual practice, noting a median of 8 sessions on a weekly or bi-weekly basis of approximately an hour duration. Follow-up tended to be short across the studies, with the median being 6 months, and the committee agreed the lack of long-term data prevented any conclusion from being drawn on any sustained benefit derived from interventions. The majority of the studies delivered interventions in a group format, although it was noted the studies did not provide information on whether the participants were attending the groups as a means of self-help or if they had been referred by a healthcare professional. The majority of the interventions were delivered face to face, although the committee noted in current practice, telephone or online formats were becoming increasingly used as they were less resource-intensive. The committee observed that the studies reported most interventions were delivered by psychologists; however, the committee noted in current practice, epilepsy nurses often deliver the types of skills-based interventions described within the studies, and health professionals with the required qualifications and skills in CBT and counselling would be able to provide these types of therapies.

The committee agreed there was not enough evidence to assess the benefit of psychological treatments in children. The committee acknowledged the lack of psychological treatments currently made available to people with epilepsy, especially for children. They were aware that some tertiary centres liaise with paediatric hospitals and provide psychological treatments to children and young people with epilepsy; however, this is a limited resource and often, adolescents who require this service are not getting access to treatment because they are falling between children and adult services.

As well as psychological treatments, the committee discussed anti-depressant and other psychotropic medications and noted that there could be a perception that anti-depressant medication may lower the seizure threshold. By consensus, the committee agreed that novel anti-depressants, for example, SSRIs, tend not to result in substantial worsening of seizures. Given how common depression is in people with epilepsy, the committee reiterated that people with epilepsy should be enabled to access l treatments for depression, including but not limited to anti-depressant medication. The committee agreed open dialogue between primary care, neurologists, psychiatrists, psychologists and aligned health care professionals

should be encouraged to ensure e mental health of people with epilepsy can be optimised.

The committee agreed that good epilepsy care should be much more than just control of seizures and needs to attend to the whole person, including a person's comorbidities. Any recommendation should therefore highlight an awareness of common comorbidities, including psychological problems which are often triggered by the diagnosis of epilepsy. The committee acknowledged the negative impact that receiving a diagnosis of epilepsy could have on a person, resulting in feelings of loss of control and the potential for stigmatism. Although the population in the review was heterogeneous, with participants both with and without anxiety or depression, the committee confirmed psychological comorbidities are common in people with a chronic condition such as epilepsy. They also recognised parents or caregivers of children with epilepsy who suffer from psychological comorbidities often need support. The committee emphasised that if assessment identifies psychological disorders, access to appropriate psychological services should be arranged quickly. The guideline committee mentioned the need for both primary and secondary care centres to have access to these services.

1.1.10.3 Cost effectiveness and resource use

Two health economic studies were included in this review (Risdale 2016 and Wijnen 2017).

Risdale 2016 is a cost-utility analysis from a UK NHS perspective comparing an epilepsy education program to usual care. Risdale 2016 found that an epilepsy education program plus usual care was not cost effective compared to usual care for adults with epilepsy. Overall usual care saved £27 and resulted in 0.0142 fewer QALYs compared to the education program resulting in an ICER of £1,901 per QALY gained for usual care.

Wijnen 2017 is a cost-utility analysis from a Dutch healthcare perspective comparing a multicomponent self-management intervention to usual care. Wijnen 2017 found that a multicomponent self-management intervention was not cost-effective compared to usual care in adults with epilepsy. The total cost and QALYs for a multicomponent self-management intervention were £2,658 and 0.88, respectively, and the total costs and QALYs for usual care were £1,919 AND 0.85, respectively. This resulted in an ICER of £24,653 per QALY gained, which is above NICE's £20,000 threshold.

The committee discussed that in both Risdale 2016 and Wijnen 2017 the EQ5D-5L was used, and this was not mapped to the EQ5D- 3L, as in line with the NICE reference case. The committee also noted that both included health economic studies did not include all relevant comparators for this review question (Risdale 2016 only assessed the cost-effectiveness of an epilepsy education program, and Wijnen 2017 assessed the cost-effectiveness of a self-management intervention). In addition, both Risdale 2016 and Wijnen 2017 were within-trial cost-effectiveness analyses based on a single RCT. Other RCTs on both these types of interventions were included in clinical review therefore, the health economic studies may not reflect the full body of clinical evidence. Both studies also had a short time horizon of 1 year, and the committee discussed this time horizon may not be long enough to capture the full effects of the respective interventions.

Overall, based on the clinical and health economics presented, the committee concluded they were unable to make a strong recommendation in favour of psychological treatments for people with epilepsy.

Subsequently, the committee made recommendations to make people aware of the impact epilepsy can have on a person's mental health. The committee also stressed the importance of reviewing a person's neurodevelopment, cognitive function, psychological health, social well-being and learning difficulties as part of their routine management for epilepsy. This recommendation is not expected to result in a substantial resource impact as it is best current practice, and any additional costs associated with extra staff time required for people's routine management for epilepsy will likely be offset in the form of cost savings, whereby identifying psychological problems earlier makes them less costly to treat. The additional recommendations made for this review question are broadly in line with existing NICE guidance and so are not expected to result in a substantial resource impact.

Overall, the committee acknowledged that psychological treatments would likely be of great benefit for people with epilepsy due to the increased prevalence of mental health problems for this population. The committee was disappointed there was insufficient health economic evidence to enable them to make a strong recommendation and so made a research recommendation to assess the cost-effectiveness of providing tailored psychological treatments for people with epilepsy.

1.1.10.4 Other factors the committee took into account

The committee was made aware of the 'depression in adults with a chronic condition' guideline that makes strong evidence-based recommendations about screening and treatment for people with psychological problems. It was agreed that cross-referral to this and the Depression in children and young people guideline would be a way of securing strong recommendations. These guidelines were felt to be particularly relevant in view of their breadth as they encompass assessment and treatment within GP practices or secondary care for all sub-populations of patients.

The committee also discussed other mental health disorders such as anxiety that are often seen in people with epilepsy and agreed cross-referral should be made to other NICE guidance, including: Common mental health problems, Mental health problems in people with learning disabilities, Generalised anxiety disorder and panic disorder in adults, Psychosis and schizophrenia in adults and Psychosis and schizophrenia in children and young people. The committee highlighted, in particular, the guidance provided on identification, early treatment and onward referral as particularly relevant.

1.1.11 Recommendations supported by this evidence review

This evidence review supports recommendations 9.2.1 – 9.2.4 and the research recommendation on providing tailored psychological treatments for people with epilepsy in the NICE guideline.

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Appendices

Appendix A Review protocols

A.1 Review protocol for psychological treatments in people with Epilepsies

ID	Field	Content
1.	Review title	Psychological treatments for people with epilepsy
2.	Review question	What is the effectiveness of psychological treatments on HRQoL for people with epilepsy
3.	Objective	The aim of the review is to examine the effectiveness of psychological interventions. Epilepsy can have a significant impact on quality of life. People living with the condition are at increased risk of psychiatric comorbidities or psychological difficulties. Children have a high prevalence of mental health comorbidities and guidance in this area will be beneficial.
4.	Searches	The following databases will be searched: Cochrane Epilepsy Group Specialized Register Cochrane Central Register of Controlled Trials MEDLINE PsycINFO EBSCO ClinicalTrials.gov WHO International Clinical Trials Registry Platform (ICTRP) Searches will be restricted by: Human studies Randomised or quasi randomised studies Other searches: Reference searching from retrieved studies Contacting colleagues to see if any studies were missed

ID	Field	Content
		The searches may be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion if relevant. The full search strategies for CRS Web, MEDLINE (Ovid), PsychINFO (EBSCOhost), will be published in the final review. The search strategies for ClinicalTrials.gov and ICTRP will also be included unless the searches are updated again before publication. If the searches are updated again before publication, ClinicalTrials.gov and ICTRP will be included in the CRS Web search, so no separate search strategies for ClinicalTrials.gov and ICTRP will be included.
5.	Condition or domain being studied	Epilepsy characterised by involuntary brain activity that manifests as seizures
6.	Population	Inclusion Children, young people and adults with confirmed epilepsy Strata: evidence in people with learning disabilities will be presented separately from evidence in people without learning disabilities Exclusion: New-born babies (under 28 days) with acute symptomatic seizures
7.	Intervention/Exposure/Test	Skills based interventions that accommodate the opportunity for participants to practice skills Based on at least one theory of psychotherapy, examples include cognitive behavioural or behaviourally based interventions, and mindfulness-based interventions (such as acceptance and commitment therapy), family systems therapy, motivational interviewing, adherence interventions, and other psychotherapeutic methods Education only interventions Defined as interventions that aim to increase knowledge of epilepsy, its comorbidities, and its treatments, or the working of the brain (including psychoeducation) They may accommodate the opportunity for participants to learn about certain skills (such as coping skills) but they do not accommodate guide participants through the practice of these skills.
8.	Comparator/Reference standard/Confounding factors	Treatment as usual Wait-list control Active control (for example counselling as usual, yoga)

ID	Field	Content
		Comparators will be combined vs the intervention
9.	Types of study to be included	RCTs Non-randomised studies will not be included Systematic reviews will not be included
10.	Other exclusion criteria	Non-English language studies. Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	
12.	Primary outcomes (critical outcomes)	Validated HRQoL outcomes
13.	Secondary outcomes (important outcomes)	Not applicable
14.	Data extraction (selection and coding)	Reference Manager 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 by 2 review authors independently, resolving disagreements through discussion. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. The electronic Cochrane data collection form will be used that has been adapted to fit the scope of the review.
15.	Risk of bias (quality) assessment	Two review authors will independently assess risk of bias for each randomized trial using Cochrane's recommended domain-based evaluation tool for randomized trials, in which critical assessments are made separately for different domains, including selection bias (random sequence generation, allocation concealment), performance bias (blinding of personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other sources of bias. All outcomes reported in papers for selective outcome reporting will be examined. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion.
16.	Strategy for data synthesis	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness,

ID	Field	Content	
		inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ 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.	
17.	Analysis of sub-groups	Strata: evidence in people with learning disabilities will be presented separately from evidence in people without learning disabilities If possible, heterogeneity in meta-analyses will investigated according to the following subgroups: • Children vs adults • Individuals with treatment-resistant epilepsy vs individuals with treatment-responsive epilepsy • Individuals with primary generalized epilepsy versus individuals with focal epilepsy versus unclassified epilepsy syndromes. • Individuals with sleep-related seizures versus individuals with not sleep-related seizures (seizure-related outcomes only); • • Individuals with seizure warning (aura) vs individuals without seizure warning (seizure-related outcomes only). Women of child-bearing age vs others Face-to-face delivery versus web-based delivery	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic
		☐	Prognostic

ID	Field	Content			
		☐	Qualitative		
		☐	Epidemiologic		
		☐	Service Delivery		
		☐	Other (please specify)		
19.	Language	English			
20.	Country	England			
21.	Anticipated or actual start date	21st February 2019			
22.	Anticipated completion date	End 2019			
23.	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		☐	☐
24.	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			

ID	Field	Content
25.	Review team members	From the Cochrane Epilepsy Group: Rosa Michaelis1, Venus Tang2,3, Janelle L Wagner4, Avani C Modi5, William Curt LaFrance Jr6, Laura H Goldstein7, Tobias Lundgren8, Markus Reuber9 1Department of Neurology, Gemeinschaftskranhaus Herdecke University of Witten/Herdecke, Herdecke, Germany 2Division of Neurosurgery, Department of Surgery, Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong 3Department of Clinical Psychology, Prince of Wales Hospital, Shatin, Hong Kong 4College of Nursing & Department of Paediatrics, Medical University of South Carolina, Charleston, USA 5Division of Behavioural Medicine and Clinical Psychology, University of Cincinnati College of Medicine, Cincinnati, USA 6Departments of Psychiatry and Neurology, Brown University, Providence, Rhode Island, USA 7Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK 8Center for Psychiatry Reseach, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden 9Academic Neurology Unit, University of Sheffield, Royal Hallamshire Hospital, Sheffield, UK National Guideline Centre:
26.	Funding sources/sponsor	This systematic review is being completed by the Cochrane Epilepsy Group which receives funding from Cochrane Epilepsy Group
27.	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.

ID	Field	Content	
28.	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: [NICE guideline webpage].	
29.	Other registration details	Cochrane Collaboration	
30.	Reference/URL for published protocol		
31.	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.	
32.	Keywords	Psychological interventions, epilepsy	
33.	Details of existing review of same topic by same authors	[Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible. NOTE: most NICE reviews will not constitute an update in PROSPERO language. To be an update it needs to be the same review question/search/methodology. If anything has changed it is a new review]	
34.	Current review status	☐	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information	[Provide any other information the review team feel is relevant to the registration of the review.]	
36.	Details of final publication	www.nice.org.uk	

A.2 Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2004, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published after 2004 that were included in the previous guideline(s) will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[26] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with "Minor limitations" then it will be included in the guideline. A health economic evidence table will be completed, and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with "Very serious limitations" then it will usually be excluded from the guideline. If it is excluded, then a health economic evidence table will not be completed, and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.

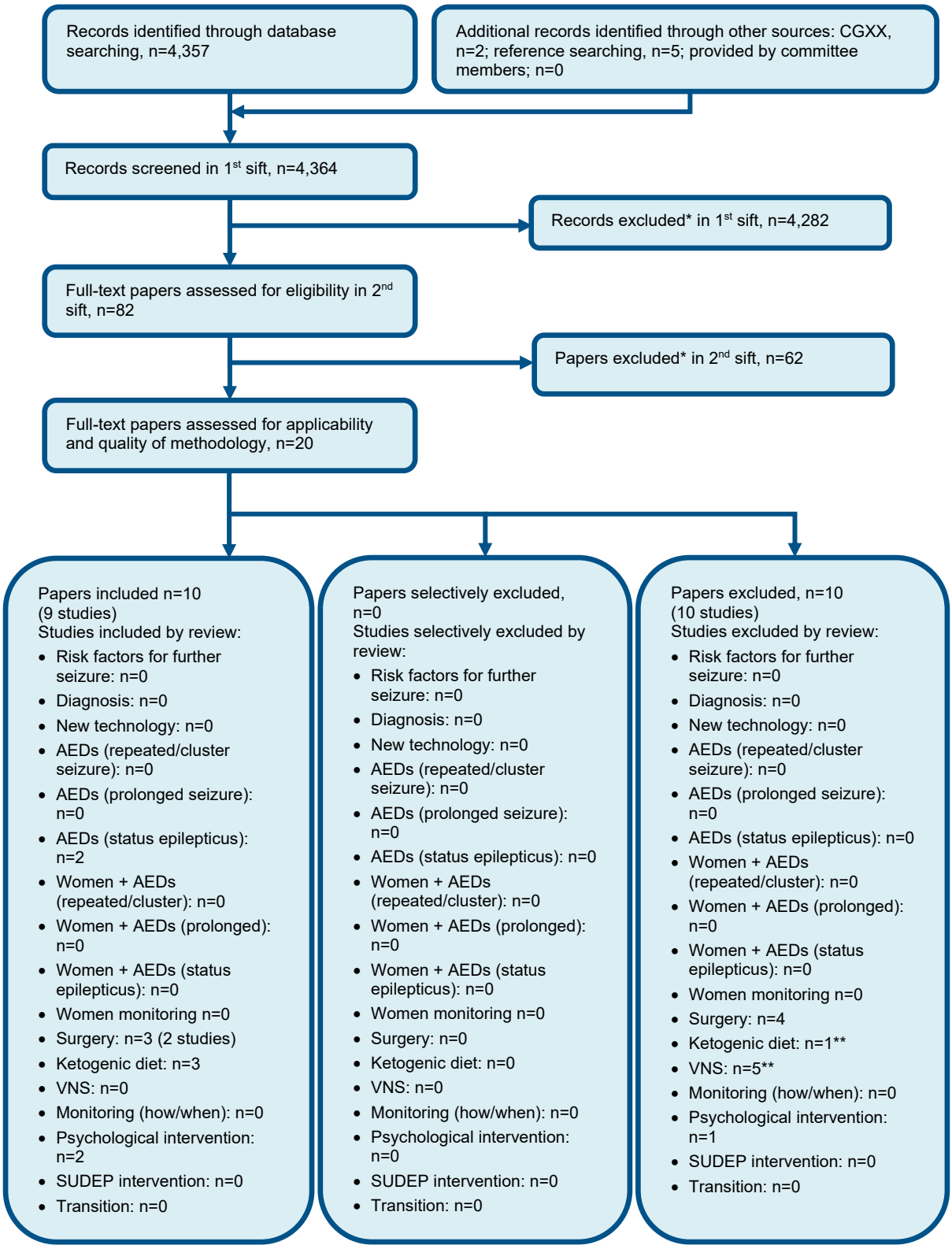
	The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2004 or later (including any such studies included in the previous guideline(s)) but that depend on unit costs and resource data entirely or predominantly from before 2004 will be rated as 'Not applicable'. • Studies published before 2004 (including any such studies included in the previous guideline(s)) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B Literature search strategy

None

Not relevant to Cochrane review.

Appendix C Economic evidence study selection



* Non-relevant population, intervention, comparison, design or setting; non-English language

**Please note that 1 article related to two questions. For this reason, the numbers listed for each review may not total the

Appendix D Economic evidence tables

Study	Risdale 2018[33]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Within-trial analysis (SMILE UK/Risdale 2018[33]) **Approach to analysis:** Analysis of individual level data for EQ-5D and resource use. Missing costs and outcome data were imputed using a single imputation method based on linear extrapolation, adjusted for baseline values. Unit costs applied. **Perspective:** UK NHS **Follow-up:** 1 year **Treatment effect duration:**[(a)] n/a	**Population:** Adults (≥ 16 years) with epilepsy who were prescribed AEDs, with 2 or more seizures in the previous 12 months and able to provide informed consent, participate in the course and complete questionnaires in English. **Cohort settings:** Start age: 41.7 Male: 45.8% **Intervention 1:** Usual care **Intervention 2:** Group-based education programme (SMILE) + usual care	**Total costs (mean per patient):** Intervention 1: unadjusted NR Intervention 2: unadjusted NR Incremental (2−1): saves £27 (95% CI: saves £1,545 to £1,490 more; p=NR) **Currency & cost year:** 2014/2015 UK pounds **Cost components incorporated:** Epilepsy-specific hospital services and community-based health and social care services, medication and intervention cost.	**QALYs (mean per patient):** Intervention 1: unadjusted NR Intervention 2: unadjusted NR Incremental (2−1): 0.0142 fewer (95% CI: 0.0318 fewer to 0.0034 more; p=NR)	**ICER (Intervention 1 versus Intervention 2):** £1,901 per QALY gained (pa) 95% CI:NR Probability Intervention 2 cost effective (£20K threshold): ~40% **Analysis of uncertainty:** Results presented as completed cases and ITT The ITT results presented as the base case. The complete case analysis ICER for usual care versus SMILE was £5,548 per QALY.

Discounting: Costs: n/a; Outcomes: n/a	The SMILE (UK) course is a group-based, interactive education programme. Delivered in 16 hours over 2 days. 6 to 12 participants (including carers or family) per group. Facilitated by 2 trained HCPs. Workbook provided.			
Data sources				
Health outcomes: Baseline and effectiveness data taken from within trial (same paper). Other clinical outcomes reported and presented in a cost-effectiveness analysis include disease specific QoL: QOLIE-31-P, not presented here. QALYs were derived from the transformed EQ-5D-5L utility scores using the area under the curve method. **Quality-of-life weights:** EQ-5D-5L UK tariff. **Cost sources:** Resource use self-reported retrospectively using adapted CSRI questionnaire. Intervention resource use centrally recorded as part of RCT. Unit costs taken from PSSRU and NHS reference costs. Societal costs measured but not included here.				
Comments				
Source of funding: NIHR. Contribution by Sanofi UK for printing of patient workbooks. **Limitations:** EQ5D-5L not mapped to 3L as per NICE position statement. Does not include all relevant comparators for this review question. Within trial analysis based on single RCT, other RCTs on this type of intervention are presented in clinical review and so may not reflect full body of clinical evidence. Short time horizon. Limited sensitivity analyses. **Other:**				
Overall applicability:[c] Partially applicable **Overall quality:[d] Potentially serious limitation**				

Abbreviations: CSRI= Client Service Receipt Inventory; CUA= cost–utility analysis; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); HCP= healthcare professional; ICER= incremental cost-effectiveness ratio; ITT= intention to treat; NIHR= National Institute Health Research; NR= not reported; pa= probabilistic analysis; QALYs= quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

Study	Wijnen2017[40]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Within-trial analysis (ZMILE UK/Wijnen[40]) **Approach to analysis:** Analysis of individual level data for EQ-5D and resource use. ITT analysis presented as base case and missing data at follow-up measurements were dealt with using multiple imputation (5 times). Unit costs applied. **Perspective:** Dutch healthcare perspective **Follow-up:** 1 year **Treatment effect duration:**[(a)] n/a **Discounting:** Costs: n/a; Outcomes: n/a	**Population:** Adults (≥18 years) with epilepsy, who lived at home, used AEDs, understood the Dutch language, and were willing and able (based on neurologists' opinion) to use e-Health devices belonging to the MCI. **Cohort settings:** Start age: 41.7 Male: 45.8% **Intervention 1:** Usual care **Intervention 2:** Multicomponent self-management intervention (MCI, ZMILE) MCI included: 1) group sessions (3-5 patients and family/friends per group, weekly session for 5 weeks, booster	**Total costs (mean per patient):** Intervention 1: £1,919 Intervention 2: £2,658 Incremental (2−1): £740 (95% CI:NR; p=NR) **Currency & cost year:** 2015 Dutch Euros converted to 2015 UK pounds[(b)] **Cost components incorporated:** Intervention costs (included the costs of the MEMS and costs associated with the MCI such as overhead costs, costs for instructors, costs of feedback sessions, and time costs for patients and relatives or friends (if a relative or friend was brought to the group sessions by a patient).) Healthcare sector costs (consultations with healthcare professionals, the use of diagnostic	**QALYs (mean per patient):** Intervention 1: 0.85 Intervention 2: 0.88 Incremental (2−1): 0.03 fewer (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £24,653 per QALY gained (pa) 95% CI:NR Probability Intervention 2 cost effective (£20K threshold): NR **Analysis of uncertainty:** Sensitivity analyses included: - Using EQ-5D with Dutch tariff, healthcare perspective, 12 months: ICER = £23,812 per QALY - Healthcare perspective, UK tariff, 6 months: ICER = £14,535 per QALY - Societal perspective, UK tariff, 12 months: ICER = £14,243 per QALY - Using disease-specific QALYs based on the QOLIE-31-P. ICER= £36,980 per QALY

	session 4 weeks later, each session 2hrs duration led by 2 nurse practitioners) 2) the Medication Event Monitoring System (MEMS; Aardex Ltd., Switzerland); 3) a smartphone application "Eppy" (Epilepsy Foundation, The Netherlands); 4) an Internet accessible patient database	methods, and the frequency of inpatient stay and outpatient treatment).		
Data sources				
Health outcomes: Baseline and effectiveness data taken from within trial (ZMILE/Leenen 2018 [40]). Other clinical outcomes reported including disease specific QoL: QOLIE-31-P, not presented here. Outcomes measured at baseline and during the 12-month study period. QALYs were calculated by means of the "under the curve method," in which the time in a certain health state was multiplied by the utility of this health state. **Quality-of-life weights:** EQ-5D-5L UK tariff, Dutch tariff also reported but not presented here. **Cost sources:** Resource use self-reported via questionnaire at baseline, 3 6, 9 and 12 months using Medical Cost Questionnaire. Unit costs taken from Dutch published reference costs. Societal costs measured but not included here.				
Comments				
Source of funding: Friends of Kempenhaeghe (Vrienden van Kempenhaeghe) foundation and AARDEX Ltd. (Switzerland). **Limitations:** Dutch healthcare perspective. EQ5D-5L not mapped to 3L as per NICE position statement. Does not include all relevant comparators for this review question. Within-trial analysis based on single RCT, other RCTs on this type of intervention are included in the clinical review and so may not reflect full body of clinical evidence. Short time horizon. Bootstrapping presented from societal perspective only, not available from healthcare perspective. **Other:**				
Overall applicability:[(c)] Partially applicable **Overall quality:[(d)] Potentially serious limitation**				

Abbreviations: CUA= cost–utility analysis; da= deterministic analysis; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; ITT= intention to treat; NR= not reported; pa= probabilistic analysis; QALYs= quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2015 purchasing power parities[27]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Appendix E Health economic model

No original health economic analysis was conducted for this question

Appendix F Excluded studies

F.1 Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2004 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 6: Studies excluded from the health economic review

Reference	Reason for exclusion
Dewhurst 2015 [8]	Excluded as rated as very serious limitations due to low methodological quality. The study was a within trial cost effectiveness analysis which had a small sample size of sixty participants. QALYs were assumed to be the same as utilities, the methodology for determining the cost of treatment was not sufficiently justified, and no sensitivity analysis was conducted. Also rated as partially applicable because QALYs were not derived using NICE's preferred methods – QALYs were derived from SF-12 data which was mapped to SF-6D data to obtain QALY values.

Appendix G Research recommendation

Research question

What is the cost-effectiveness of providing tailored psychological treatments for people with epilepsy?

Why this is important

Psychological problems are recognised as an essential comorbidity in epilepsy and can reflect organic factors associated with the disease in addition to difficulties adjusting to and living with the diagnosis. Whilst we have evidence to support the clinical benefit of psychological interventions in this population, evidence for the cost-effectiveness of such treatments is severely lacking. This currently prevents us from making a recommendation with a substantial resource impact.

Rationale for research recommendation

Importance to 'patients' or the population	Psychological difficulties are recognised as an essential comorbidity in epilepsy and are commonly reported by people with the condition. Psychological interventions have been shown to be effective but are not available to many people with epilepsy. If cost-effectiveness can be established and access to these services increases, this will have a significant impact on the severity of comorbidities in this population.
Relevance to NICE guidance	Psychological interventions have been considered in this guideline, and we have found moderate quality evidence to support clinical efficacy in this group. However, we have not found any high-quality data to support the cost-effectiveness of such interventions.
Relevance to the NHS	If cost-effective, the routine provision of psychological treatments for people with epilepsy will have a significant impact on the professional make-up of the treating team for people with epilepsy and the resources they use from the general mental health providers. This will have an impact on strategic planning and service delivery.
National priorities	High. Psychological comorbidities are very common in people with epilepsy and can have a greater impact on the person with epilepsy than the seizures themselves. It is, therefore, essential to have a holistic approach to all people with epilepsy which will offer not only positive impact to the person with epilepsy, but across society more broadly.
Current evidence base	Only two studies conducted to date with very low-quality data. No differentiation in the existing literature between individual and group interventions which have significant cost differentials. No health economic analysis of these interventions with respect to subsequent use of specialist and non-specialist (GP) services.

Equality considerations	The different health-seeking behaviours across genders and cultural factors must be considered in any examination of psychological interventions.

Modified PICO table

Population	Adults with epilepsy reporting anxiety and depression
Intervention	Individual vs group psychological intervention
Comparator	Wait list controls
Outcome	Quality of life, subsequent use of specialist and non-specialist medical services.
Study design	Longitudinal design
Timeframe	5 years
Additional information	None