National Institute for Health and Care Excellence

FINAL

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

[5] Evidence review: New technologies

NICE guideline NG217

Evidence review underpinning research recommendations in the NICE guideline

April 2022

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Developed by the National Guideline Centre

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1.1 Review question

What is the clinical and cost effectiveness of digital health technologies (for example, night monitors, wearable devices and Apps) in people with epilepsy?

1.1.1 Introduction

Epilepsy is a paroxysmal disorder, and seizures can lead to loss or impairment of consciousness. Seizures may start with minimal warning and recall be impaired after the event. This puts people with epilepsy at risk of injury and death (including SUDEP), and it makes recall and recording of seizures problematic. Digital health technologies range from electronic seizure diaries, wearable and immediate seizure detection (watches), surveillance devices such as night monitors, and self-empowerment and decision support apps. Technology is now available to support epilepsy care by identifying impending or ongoing seizures, alerting carers, and accurately recording the frequency and duration of seizures. Digital technologies may have the potential to facilitate self-management and contribute to clinical decision support, thereby contributing to improved outcomes and possibly reducing emergencies and death. This review aims to assess the clinical and cost-effectiveness of digital health technologies.

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	Children, young adults and adults with epilepsy
Interventions	DHTs designed for epilepsy within the following functional classifications: • Self-Management: DHTs that aim to improve self-management, including adherence to medication. Example: phone applications. • Alert: DHTs that detect seizure activity and alert the person or carer to take action. Example: wearables. • Track and Monitor: DHTs that enable tracking and monitoring of the condition, often involving data transmission to HCPs (transmission may or may not be automated/remote). Example: remote EEG. • Clinical Decision Support: data collection, calculation and artificial intelligence approaches to inform clinical decision making. Example: Clinical Decision Support Systems.
Comparison(s)	• Interventions (above) compared with each other • Usual care (including advice or information giving) / no intervention • Sham devices Each of the above comparator categories will be kept separate in the analysis.
Outcomes	• mortality including SUDEP at 12 months • medicines adherence at 12 months • healthcare resource impact (including changes in medication use, consultations and hospitalisations) at 12 months • frequency of seizure-associated risks (such as falls and fractures) at 12 months • quality of life (measured with a validated scale) at 12 months

	• seizure frequency (50% or greater reduction in seizure frequency) at 12 months • adverse events (total adverse events, anxiety (measured using a validated scale), and false alarms (each reported separately) Outcomes reported at time points of < 3 months will not be extracted (other than for adverse events). If outcomes are reported at multiple time points, the closest time point to 12 months will be extracted.
Study design	• Randomised controlled trials (RCTs) • Systematic reviews of RCTs

1.1.3 Clinical evidence

1.1.3.1 Included studies

Two RCTs were included in this review.[23, 31] One compared anti-seizure medication (ASM) adherence among groups randomised either to a mobile phone medication reminder application or to usual care.[23] Follow-up was three months. The other compared the reduction in seizure frequency among groups randomised either to a smartphone app designed to assist self-management or to usual care.[31] Follow-up was six months. The two included studies are summarised in Table 2 below.

See also the study selection flow chart in Appendix C:, study evidence tables in Appendix D:, forest plots in Appendix E: and GRADE tables in Appendix F:.

1.1.3.2 Excluded studies

See the excluded studies list in Appendix J:.

1.1.4 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Mirpuri (2021)[23] RCT	Mobile phone app (n=48) versus usual care (n=48) Follow-up: 12 weeks.	Persons with epilepsy, age 18 or over, without physical dependencies, independent in taking medications, in possession of smartphone, at least one year into epilepsy treatment, and able to return for follow-up interview at the hospital. Mean age (SD) in years: mobile app group: 27.35 (6.71); usual care group 30.73 (10.22) Conducted in India.	Number adherent to antiseizure medication regime at 12 weeks, assessed using Morisky, Green Levine Adherence Scale (MGLS) and seizure diary.	Proportion adherent at baseline was 16.7% in the mobile application group and 29.2% in the control group. Groups also differed at baseline for marital status and education. Randomisation used sealed, opaque (but not numbered) envelopes.
Si (2020)[31] RCT	Smartphone app (n=190) versus usual care (n=190) Follow-up: 6 months.	Persons aged over 18 and under 60 years, with epilepsy of more than one year duration, more than three seizures during the 6 months preceding recruitment, residing in the study area, and proficient in the use of smartphones. Conducted in China.	Seizure freedom (100% reduction in seizure frequency) at 6 months. Reduction in seizure frequency ≥75% and <100% at 6 months. Reduction in seizure frequency ≥50% and <75% at 6 months.	Of 380 randomised participants, 327 (86.1%) completed the follow-up assessment (app group, 176; control group, 151). However, for seizure frequency outcomes, data were provided for the full randomised numbers (190 in each group) by ITT analysis.

1.1.5 Summary of the effectiveness evidence

Table 3: Clinical evidence summary: Mobile phone app versus usual care for ASM adherence

Outcomes	**No of Participants (studies)** Follow up	**Quality of the evidence** (GRADE)	**Relative effect (95% CI)**	**Anticipated absolute effects**	
				Risk with Control	**Risk difference with Mobile phone app versus usual care** (95% CI)
ASM adherence at 3 months MGLS adherence scale	96 (1 study) 3 months	VERY LOW[1,2] due to risk of bias, imprecision	RR 1.74 (1.17 to 2.59)	Study population	
				396 per 1000	293 more per 1000 (from 67 more to 629 more)

[1] No description of sequence generation. Groups differed at baseline for the outcome (adherence), marital status and education.
[2] Downgraded by 1 increment as the confidence interval crossed one MID.

Table 4: Clinical evidence summary: Smartphone app versus usual care for reduction in seizure frequency at 6 months

Outcomes	**No of Participants (studies)** Follow up	**Quality of the evidence** (GRADE)	**Relative effect (95% CI)**	**Anticipated absolute effects**	
				Risk with Control	**Risk difference with Smartphone app versus usual care** (95% CI)
Reduced seizure frequency (50 to 74%) self-report	380 (1 study) 6 months	VERY LOW[1,2] due to risk of bias	RR 0.35 (0.22 to 0.55)	Study population	
				316 per 1000	205 fewer per 1000 (from 142 fewer to 246 fewer)
Reduced seizure frequency 75 to 99% self-report	380 (1 study) 6 months	VERY LOW[1,2] due to risk of bias	RR 2.75 (1.26 to 6.02)	Study population	
				42 per 1000	74 more per 1000 (from 11 more to 211 more)
Reduced seizure frequency of 100% (seizure freedom) self-report	380 (1 study) 6 months	VERY LOW[1,2] due to risk of bias	RR 2.45 (1.56 to 3.86)	Study population	
				116 per 1000	168 more per 1000 (from 65 more to 331 more)

[1] Block randomisation with known block size, introducing predictability. No blinding for assessment of a subjective outcome.
[2]App was limited to Chinese language and built on a Chinese social media platform.

See Appendix F: for full GRADE tables

1.1.6 Economic evidence

1.1.6.1 Included studies

No health economic studies were included.

1.1.6.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G:

1.1.7 Health economic modelling

This area was discussed as a potential priority; however, no clinical data has been identified to enable this.

1.1.8 Unit costs

A variety of products are available, which also lead to variability in costs. Some can be free such as certain apps. Some are wearable devices such as smartwatches or apps that can be added to smartwatches which also have a subscription where professionals could be contacted in emergencies.

The unit costs presented below are from the Epilepsy action website and are for devices that are not provided by the NHS; therefore, the cost of these devices are incurred by people who chose to purchase these devices themselves. Only the lowest and highest cost products are reported here for an illustration of the range of costs of the different types of products.

Table 4: Costs of technology devices for managing epilepsy

Product	Description	Review category	Cost
App			
EpSMon	EpSMon is a self- monitoring app designed for adults who experience seizures. It uses evidence on risk factors for SUDEP and includes the major risk factors known to be associated with fatality in epilepsy. It supports people to assess themselves every three months. It informs people if they report a risk and to seek help to review whether action may be needed. It highlights when the person reports a risk factor or a worsening of a risk factor that may be life-threatening but is something that could be changed.	Self-management	Free
Wearable devices (a)			
Pulseguard	Designed to detect any seizure that causes a change in heart rate. Sends an alert to pager.	Alert	£360 upfront cost, then £30 a month rental charge on 18-month contract.
Epi-care standard	Detects tonic-clonic seizures based on movement. Sends an alert to pager or can be connected to careline.	Alert	£1,399 for pager option; £1,519 for careline option

Product	Description	Review category	Cost
			including one year's service.
Bed monitors			
Medpage MP5-UT	Detects most seizure types where movement occurs. Sends alert to pager.	Alert	£170
Guardian	Seizures detected depending on options chosen may detect tonic-clonic, focal, tonic, atonic, myoclonic. Depending on options chosen can monitor movement, bed vacation, sound, vomiting and incontinence. Extra sensors can be purchased. Sends an alert to pager or can be connected to a telecare service.	Alert	£680

Source/Note: Wearable devices and bed monitor costs are from Epilepsy action: https://www.epilepsy.org.uk/info/daily-life/safety-aids-equipment/alarms-monitors

(a) Seizure alert subscription services can also be purchased to alert a caregiver or connect to a careline that can alert professionals. These start at around £9.99 a month.

1.1.9 Committee's interpretation and discussion of the evidence

1.1.9.1 The outcomes that matter most

The outcomes included in this review were mortality including SUDEP, medicine adherence, healthcare resource impact, frequency of seizure associated risks, quality of life, all measured at 12 months, seizure frequency (50% or greater reduction in seizure frequency) at 12 months and adverse events reported at any time point.

Medicine adherence and reduction in seizure frequency were the only outcomes reported in the included studies, both of which were self-reported.

1.1.9.2 The quality of the evidence

Two randomised controlled trials were included in this review: a trial evaluating the effectiveness of a mobile phone app for improving medication adherence, and a trial evaluating the effectiveness of a mobile phone app for reducing seizure frequency. The quality of the trial evaluating the effectiveness of a mobile phone app for improving medication adherence was rated very low (due to risk of bias and imprecision). The risk of bias was derived from a lack of clarity on how the random sequence was generated, potentially flawed randomisation (indicated by baseline group differences in adherence, marital and educational status) and from self-reporting of adherence by patients. The evidence was also severely limited by the brief follow-up of only three months. The quality of the trial evaluating the effectiveness of a mobile phone app for reducing seizure frequency was rated very low. The risk of bias was derived from potential predictability of the random allocation sequence (through use of block randomisation with a small, known, fixed block size). The six-month follow-up of this trial was also severely limiting. External validity was reduced by the design of the app, which was limited to Chinese language and built on a Chinese social media platform, the evidence was therefore downgraded for indirectness.

1.1.9.3 Benefits and harms

Randomised controlled trial (RCT) evidence favoured use of a mobile phone app with a medication reminder function over usual care, in terms of antiseizure medication adherence at three months follow-up. App users were nearly twice as likely as those on usual care to adhere at 3 months. The committee agreed however that the quality of evidence was very low. The short follow-up of three months was highlighted as a particular shortcoming, given

the importance of continuous adherence over a much longer time frame in epilepsy. RCT evidence favoured the use of a smartphone app designed to improve self-management over usual care, in terms of achieving seizure freedom at six months follow-up. The same study found a higher proportion of app users (versus those receiving usual care) experienced a reduction in seizure frequency of between 75 and 99%. The proportion experiencing reduced seizure frequency between 50 and 74% was lower among app users than among those receiving usual care. However, this was because more people in the app group reported higher frequencies of seizure reduction at ≥75% and seizure freedom than those in the usual care group which in turn skewed the measure of seizure reduction below 75%, displaying supposed benefit for usual care. The committee agreed that the quality of evidence for seizure frequency outcomes was low. Again, there was concern that the short follow-up (six months) was a major limitation. No evidence was gleaned about adverse effects.

The committee discussed the availability of free applications, programmes and systems, but they noted that many of the widely used technologies are subscription based and expensive. It was also noted that mobile phones and wearable devices can now monitor changes in heart rate (an indicator of a possible impending seizure), so there may be scope for future development of notification systems as alert tools. However, it was also pointed out that the use of applications and other self-management devices could sometimes provide false readings to users. The committee agreed that digital technologies might lead to excessive anxiety and overuse of health care services, and that recommending them could discriminate against people who do not have access to digital technologies, or who are not competent in their use.

1.1.9.4 Cost effectiveness and resource use

No economic evidence was identified for this review question.

The committee discussed the clinical evidence presented and concluded they were unable to make a recommendation for digital health technologies due to evidence presented being graded as low to very low quality. The committee acknowledged that in the future, the area of digital technologies could be very beneficial to people with epilepsies and so made a research recommendation to assess the clinical and cost effectiveness of digital health technologies in people with epilepsy.

As no recommendation was made for the use of digital health technologies there will be no resource impact associated with this review question.

The committee were presented with unit costs associated with some of the technologies available. However, these unit costs were sourced from the Epilepsy Action website and are not currently provided on the NHS.

In general, new technologies for managing epilepsy come in a variety of forms, ranging from free apps to expensive night-time monitors or smartwatches that can have ongoing subscription costs for alerting friends/family/medical professionals. The purposes of the devices can also vary, with some being used to detect seizures and alert other people, and other devices to aid self-management, relying on the user to enter information on seizure patterns or to remind people to take medication. The effectiveness and cost effectiveness of the new technologies depend on their ability to alter management. This could be through inadvertent mechanisms of action such as improved medication adherence, or by recording seizure patterns and discussing this information with clinicians, which could lead to more tailored management. There may however also be unintended resource consequences of the technologies. Inputting information into an app could result in the app directing the person to their GP, leading to more health seeking behaviour without necessarily any improvements in the management of the person’s epilepsy.

1.1.9.5 Other factors the committee took into account

The importance of adherence to antiseizure medications was recognised, particularly in reducing the risk of sudden, unexplained death in epilepsy (SUDEP), and that it is important to help people with epilepsy improve their adherence whenever possible.

Some committee members were in favour of making a consensus recommendation to alert people with epilepsy to the availability of digital health technologies that might improve adherence to antiseizure medications. In support of this view, the point was made that medication reminder apps are in common use, that some people with epilepsy – particularly those with memory problems – find they help adherence, and that it is already considered usual practice to encourage a person having difficulty with adherence to explore available apps. It was recognised that different people respond best to different apps, that their personal choice should be respected, and that they should be trusted to make their own judgement. It was suggested that clinicians could highlight epilepsy charity organisations, e.g., Epilepsy Action, that provide lists of digital technologies without bias towards a particular product.

It was noted that the evidence available – albeit of very low quality – did support the use of a mobile phone app to improve adherence, the importance of which was agreed by all. Developing the discussion of evidence further, the point was made that many aspects of medical care can be justified because they are intuitively helpful and make simple sense, and that the suggestion that patients having difficulty with adherence might wish to explore available apps falls into that category. The point was also made that improvement of adherence is the only means available of controlling epilepsy, apart from surgery.

Other committee members, however, were not in favour of making a consensus recommendation. One of the concerns was the very low quality of evidence. The point was made that poor adherence is a complex problem, that might relate to many issues, such as adverse effects from antiseizure medications, drug interactions, affordability of medications and many other factors. Any effective intervention will be correspondingly complex, and it was felt that without sufficiently robust evidence, there is no basis upon which to discuss with patients the technologies that might be available. Another concern was a potential risk of adverse effects. Use of medication reminder apps could result in excessive anxiety and overuse of health care services. Their recommendation could discriminate against people who do not have access to digital technologies, or who are not competent in using them. The potential opportunity cost was also raised, of channelling resources into the use of digital health technology (based on poor evidence) when those resources might be more gainfully deployed in alternative strategies to improve quality of life. It was also thought that clinicians must be aware of the profit motive that might underpin the promotion of digital technologies by their developers. In response to the suggestion that people with epilepsy could be signposted to charities that provide lists of available technologies, the point was offered that this might be moving ahead of the evidence.

All committee members agreed that the use of digital health technologies holds great potential, and that a research recommendation should be made. It was finally agreed that in the absence of robust evidence, no consensus recommendation could be made. It was felt however, that the divergence of opinion on this issue was valuable and should be fully reflected in this committee discussion report.

1.1.10 Recommendations supported by this evidence review

This evidence review supports research recommendations on digital health technologies.

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Appendices

Appendix A: Review Protocols

Table 5: Review protocol: New digital technologies

ID	Field	Content
0.	PROSPERO registration number	
1.	Review title	Effectiveness of digital health technologies in people with epilepsy
2.	Review question	What is the clinical and cost-effectiveness of digital health technologies (for example, night monitors, wearable devices and Apps) in people with epilepsy?
3.	Objective	Digital health technologies (DHTs) are apps, programmes and software used in the health and care system. They may be standalone or combined with devices. The objective of this review is to consider how DHTs may aid in the management of epilepsy. The aim is to identify which technologies are effective at improving epilepsy outcomes. DHTs may improve outcomes by detecting a seizure before it occurs, or by alerting a carer to the occurrence of a seizure, thereby enabling the person or carer to take action. Improvement in outcomes may also occur by improving self-management (such as enhancing drug adherence) or by providing data or analytical tools to healthcare professionals to enable more tailored management. Relevant DHTs designed for epilepsy may include: • Digital night monitoring devices (for example, bed/mattress alarms that are integrated with digital systems) • Wearable devices (for example, fall alarms, tracking devices, vital sign monitors, movement monitors, mobile EEG) • Apps (for example, self-management apps) • Clinical Decision Support Systems

ID	Field	Content
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • English language studies • Human studies 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	Epilepsies in children, young people and adults
6.	Population	Inclusion: Children, young adults and adults with epilepsy Exclusion: New-born babies (under 28 days) with acute symptomatic seizures.
7.	Intervention/Exposure/Test	DHTs designed for epilepsy within the following functional classifications: • Self-Management: DHTs that aim to improve self-management, including adherence to medication. Example: phone applications. • Alert: DHTs that detect seizure activity and alert the person or carer to take action. Example: wearables. • Track and Monitor: DHTs that enable tracking and monitoring of the condition, often involving data transmission to HCPs (transmission may or may not be automated/remote). Example: remote EEG. • Clinical Decision Support: data collection, calculation and artificial intelligence approaches to inform clinical decision making. Example: Clinical Decision Support Systems. The analysis will combine data within each of the above functional classifications. The following types of DHTs will be excluded:

ID	Field	Content
		• DHTs with potential system benefits but no direct user benefits (for example, electronic prescribing, electronic health records). • DHTs that aim to educate or provide information to patients and carers, but do not facilitate active self-management and are unlikely to have measurable user outcomes (for example, apps providing information about epilepsy and its treatment). Such interventions may be covered by a separate review of information and support needs. • DHTs that provide psychological therapies, such as digital therapy platforms (including biofeedback and brain training). Such interventions will be covered by a separate review of psychological therapies
8.	Comparator/Reference standard/Confounding factors	• Interventions (above) compared with each other • Usual care (including advice or information giving) / no intervention • Sham devices Each of the above comparator categories will be kept separate in the analysis.
9.	Types of study to be included	• Randomised controlled trials (RCTs) • Systematic reviews of RCTs
10.	Other exclusion criteria	Exclusions: • Non-English language studies • Conference abstracts
11.	Context	
12.	Primary outcomes	• mortality including SUDEP at 12 months • medicines adherence at 12 months • healthcare resource impact (including changes in medication use, consultations and hospitalisations) at 12 months • frequency of seizure-associated risks (such as falls and fractures) at 12 months • quality of life (measured with a validated scale) at 12 months • seizure frequency (50% or greater reduction in seizure frequency) at 12 months • adverse events (total adverse events, anxiety (measured using a validated scale), and false alarms (each reported separately))

ID	Field	Content
		Outcomes reported at time points of < 3 months will not be extracted (other than for adverse events). If outcomes are reported at multiple time points, the closest time point to 12 months will be extracted.
14.	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. EviBASE will be used for data extraction.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) 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 the involvement of a third review author where necessary.
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, 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/ Where meta-analysis is not possible, data will be presented, and quality assessed individually per outcome.

ID	Field	Content			
		Statistically, heterogeneity will be assessed by visually examining the forest plots and by calculating the I^2 inconsistency statistic (with an I^2 value of more than 50% indicating significant heterogeneity and an I^2 value of more than 75% indicating very significant heterogeneity).			
17.	Analysis of sub-groups	In the event of heterogeneity, subgroup analysis will be undertaken based on the risk of bias of the included studies and the following possible modifiers of treatment effect: • age (children, young people, adults, older people) • seizure type (generalised tonic-clonic versus other) • learning disabilities (people with learning disabilities and people without learning disabilities) • ethnicity (BAME versus not BAME) • socioeconomic background			
18.	Type and method of review	✓	Intervention		
			Diagnostic		
			Prognostic		
			Qualitative		
			Epidemiologic		
			Service Delivery		
			Other (please specify)		
19.	Language	English			
20.	Country	England			
21.	Anticipated or actual start date	TBC- after NICE sign-off			
22.	Anticipated completion date	TBC			
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			

ID	Field	Content
		National Guideline Centre 5b Named contact e-mail Epilepsies@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre
25.	Review team members	From the National Guideline Centre: Gill Ritchie, Guideline lead Jacqui Real, Senior systematic reviewer Angela Cooper, Senior systematic reviewer Rafina Yarde, Systematic reviewer Margaret Constanti, Health economist Joseph Runicles, Information specialist Tamara Diaz, Project manager
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
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.
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	
30.	Reference/URL for published protocol	

ID	Field	Content	
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	Epilepsy, new technologies, digital health technologies, apps, wearables, wearable devices, remote monitoring, clinical decision support	
33.	Details of existing review of same topic by same authors		
34.	Current review status	☐	Ongoing
		☒	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35..	Additional information		
36.	Details of final publication	www.nice.org.uk	

Table 6: 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).[25] **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 strategies

This literature search strategy was used for the following review:

- What is the clinical and cost effectiveness of digital health technologies (for example, night monitors, wearable devices and Apps) in people with epilepsy?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[25]

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 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 13 May 2021	Randomised controlled trials Systematic review studies Exclusions
Embase (OVID)	1974 – 13 May 2021	Randomised controlled trials Systematic review studies Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews to 2021 Issue 5 of 12 CENTRAL to 2021 Issue 5 of 12	None

Medline (Ovid) search terms

1.	exp epilepsy/
2.	seizures/
3.	exp status epilepticus/
4.	seizures, febrile/
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/
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.	randomized controlled trial.pt.
28.	controlled clinical trial.pt.
29.	randomi#ed.ti,ab.
30.	placebo.ab.
31.	randomly.ti,ab.
32.	Clinical Trials as topic.sh.
33.	trial.ti.
34.	or/27-33
35.	Meta-Analysis/
36.	exp Meta-Analysis as Topic/
37.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(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.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	exp mobile applications/
47.	exp monitoring, ambulatory/
48.	exp smartphone/
49.	telemedicine/
50.	digital health technolog*.ti,ab.
51.	((digital or wearable or track* or fall* or vital sign* or movement or moving or bed or mattress or night*) adj3 (device* or alert* or detect* or alarm* or sensor* or technolog*)).ti,ab.
52.	(monitor* adj3 (device* or alarm* or sensor* or technolog* or digital or wearable or track* or fall* or vital sign* or movement or moving or bed or mattress or nocturnal or night*)).ti,ab.
53.	(Mobile electroencephalogr* or mobile EEG or ambulatory monitor*).ti,ab.
54.	((handheld or hand held or portable) adj3 (sensor* or alarm* or app or apps or application*)).ti,ab.

55.	((mobile or phone or tech* or monitor* or alert* or detect*) adj2 ("app" or "apps" or application)).ti,ab.
56.	(smart phone* or smartphone*).ti,ab.
57.	((application or "app" or "apps" or mobile* or phone*) adj3 (self management or self care)).ti,ab.
58.	(smartwatch or smart watch or "embrace* and alert app" or "Epilert" or "neuronaute" or "esap" or "neuromedic" or "mycarecentric epilspy" or "periictal cardiorespiratory detection devices" or Nexfin or "EpSMon" or "young epilepsy app" or "Epiwatch research kit" or "nightwatch" or "Neutun" or "Seizalarm" or "texting 4 control" or "emfit" or "epi-care" or "varia").ti,ab.
59.	(telemedicine or tele-medicine or tele-care or telecare or tele-nurs* or telenurs* or ehealth or e-health or mhealth or m-health or mobile health).ti,ab.
60.	Decision Support Systems, Clinical/
61.	((data collection or data calculation or artificial intelligence) and decision making).ti,ab.
62.	(decision* adj2 (support* or system*)).ti,ab.
63.	or/46-62
64.	26 and 63 and (34 or 45)

Embase (Ovid) search terms

1.	exp epilepsy/
2.	seizure/
3.	epileptic state/
4.	febrile 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/14-21
23.	6 not 22
24.	Limit 23 to English language
25.	random*.ti,ab.
26.	factorial*.ti,ab.
27.	(crossover* or cross over*).ti,ab.
28.	((doubl* or singl*) adj blind*).ti,ab.

29.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
30.	crossover procedure/
31.	single blind procedure/
32.	randomized controlled trial/
33.	double blind procedure/
34.	or/25-33
35.	systematic review/
36.	meta-analysis/
37.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(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.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	exp mobile application/
47.	exp ambulatory monitoring/
48.	smartphone/ or mobile phone/
49.	telemedicine/
50.	digital health technolog*.ti,ab.
51.	((digital or wearable or track* or fall* or vital sign* or movement or moving or bed or mattress or night*) adj3 (device* or alert* or detect* or alarm* or sensor* or technolog*)).ti,ab.
52.	(monitor* adj3 (device* or alarm* or sensor* or technolog* or digital or wearable or track* or fall* or vital sign* or movement or moving or bed or mattress or nocturnal or night*)).ti,ab.
53.	(Mobile electroencephalogr* or mobile EEG or ambulatory monitor*).ti,ab.
54.	((handheld or hand held or portable) adj3 (sensor* or alarm* or app or apps or application*)).ti,ab.
55.	((mobile or phone or tech* or monitor* or alert* or detect*) adj2 ("app" or "apps" or application)).ti,ab.
56.	(smart phone* or smartphone*).ti,ab.
57.	((application or "app" or "apps" or mobile* or phone*) adj3 (self management or self care)).ti,ab.
58.	(smartwatch or smart watch or "embrace* and alert app" or "Epilert" or "neuronaute" or "esap" or "neuromedic" or "mycarecentric epilspy" or "periictal cardiorespiratory detection devices" or Nexfin or "EpSMon" or "young epilepsy app" or "Epiwatch research kit" or "nightwatch" or "Neutun" or "Seizalarm" or "texting 4 control" or "emfit" or "epi-care" or "varia").ti,ab.
59.	(telemedicine or tele-medicine or tele-care or telecare or tele-nurs* or telenurs* or ehealth or e-health or mhealth or m-health or mobile health).ti,ab.
60.	clinical decision support system/
61.	((data collection or data calculation or artificial intelligence) and decision making).ti,ab.
62.	(decision* adj2 (support* or system*)).ti,ab.
63.	or/46-62

64.	24 and 63 and (34 or 45)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Epilepsy] explode all trees
#2.	MeSH descriptor: [Seizures] explode all trees
#3.	MeSH descriptor: [Status Epilepticus] explode all trees
#4.	MeSH descriptor: [Seizures, Febrile] explode all trees
#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.	MeSH descriptor: [Mobile Applications] explode all trees
#8.	MeSH descriptor: [Monitoring, Ambulatory] explode all trees
#9.	MeSH descriptor: [Smartphone] explode all trees
#10.	MeSH descriptor: [Telemedicine] explode all trees
#11.	digital health technolog*:ti,ab
#12.	((digital or wearable or track* or fall* or vital sign* or movement or moving or bed or mattress or night*) near/3 (device* or alert* or detect* or alarm* or sensor* or technolog*)):ti,ab
#13.	(monitor* near/3 (device* or alarm* or sensor* or technolog* or digital or wearable or track* or fall* or vital sign* or movement or moving or bed or mattress or nocturnal or night*)):ti,ab
#14.	(Mobile electroencephalogr* or mobile EEG or ambulatory monitor*):ti,ab
#15.	((handheld or hand held or portable) near/3 (sensor* or alarm* or app or apps or application*)):ti,ab
#16.	((mobile or phone or tech* or monitor* or alert* or detect*) near/2 ("app" or "apps" or application)):ti,ab
#17.	(smart phone* or smartphone*):ti,ab
#18.	((application or "app" or "apps" or mobile* or phone*) near/3 (self management or self care)):ti,ab
#19.	(smartwatch or smart watch or "embrace* and alert app" or "Epilert" or "neuronaute" or "esap" or "neuromedic" or "mycarecentric epilspy" or "periictal cardiorespiratory detection devices" or Nexfin or "EpSMon" or "young epilepsy app" or "Epiwatch research kit" or "nightwatch" or "Neutun" or "Seizalarm" or "texting 4 control" or "emfit" or "epi-care" or "varia"):ti,ab
#20.	(telemedicine or tele-medicine or tele-care or telecare or tele-nurs* or telenurs* or ehealth or e-health or mhealth or m-health or mobile health):ti,ab
#21.	MeSH descriptor: [Decision Support Systems, Clinical] explode all trees
#22.	((data collection or data calculation or artificial intelligence) and decision making):ti,ab
#23.	(decision* near/2 (support* or system*)):ti,ab
#24.	(or #7-#23)
#25.	#6 and #24

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to an Epilepsies population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics and quality of life studies.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	Health Economics 1 January 2014 – 13 May 2021 Quality of Life 1946 – 13 May 2021	Health economics studies Quality of life studies Exclusions
Embase	Health Economics 1 January 2014 – 13 May 2021 Quality of Life 1974 – 13 May 2021	Health economics studies Quality of life studies Exclusions
Centre for Research and Dissemination (CRD)	HTA - Inception – 13 May 2021 NHSEED - Inception to 31 March 2015	None

Medline (Ovid) search terms

1.	exp epilepsy/
2.	seizures/
3.	exp status epilepticus/
4.	seizures, febrile/
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/
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.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/

30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	quality-adjusted life years/
45.	sickness impact profile/
46.	(quality adj2 (wellbeing or well being)).ti,ab.
47.	sickness impact profile.ti,ab.
48.	disability adjusted life.ti,ab.
49.	(qal* or qtime* or qwb* or daly*).ti,ab.
50.	(euroqol* or eq5d* or eq 5*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/44-61
63.	26 and (43 or 62)

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.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	quality adjusted life year/
40.	sickness impact profile/
41.	(quality adj2 (wellbeing or well being)).ti,ab.
42.	sickness impact profile.ti,ab.
43.	disability adjusted life.ti,ab.
44.	(qal* or qtime* or qwb* or daly*).ti,ab.
45.	(euroqol* or eq5d* or eq 5*).ti,ab.
46.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
47.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
48.	(hui or hui1 or hui2 or hui3).ti,ab.
49.	(health* year* equivalent* or hye or hyes).ti,ab.
50.	discrete choice*.ti,ab.
51.	rosser.ti,ab.
52.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
53.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
54.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.

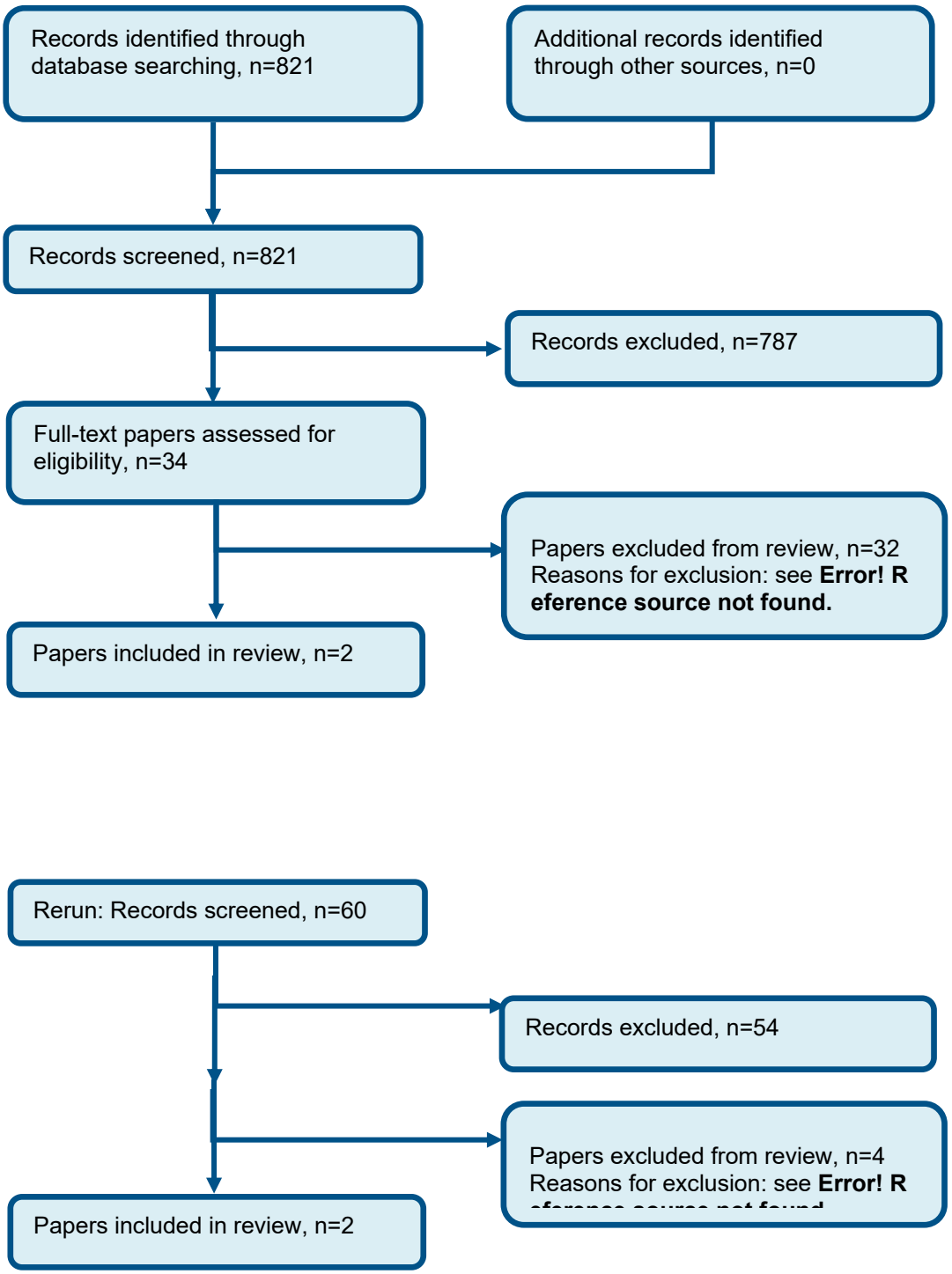
55.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
56.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
57.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
58.	or/39-57
59.	24 and (38 or 58)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Epilepsy EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Seizures EXPLODE ALL TREES
#3.	MeSH DESCRIPTOR Status Epilepticus EXPLODE ALL TREES
#4.	MeSH DESCRIPTOR Seizures, Febrile EXPLODE ALL TREES
#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))
#6.	#1 OR #2 OR #3 OR #4 OR #5

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of New digital technologies



Appendix D: Clinical evidence tables

Study	**Mirpuri 2021 trial: Mirpuri 2021[23]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=96)
Countries and setting	Conducted in India; Setting: Tertiary care outpatient department
Line of therapy	Not applicable
Duration of study	3 months
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 18 or over, without physical dependencies, independent in taking medications, in possession of smartphone, at least one year into epilepsy treatment, and able to return for follow-up interview at the hospital
Exclusion criteria	Not stated
Age, gender and ethnicity	Age - Mean (SD): Intervention group: 27.35 (6.71); control group 30.73 (10.22). Gender (M:F): Intervention group: 33.3% male/66.7% female; control group: 47.9% male/52.1% female. Ethnicity: not stated

Further population details	1. Age (children, young people, adults, older people): 2. Ethnicity (BAME versus not BAME): 3. Learning disabilities (people with learning disabilities and people without learning disabilities): 4. Socioeconomic background:
Indirectness of population	No indirectness
Interventions	(n=48) Intervention 1: Self-management - Phone applications. Mobile phone application with medication reminder system. Duration 3 months. Concurrent medication/care: 10-minute counselling session on use of the app by a senior researcher at initial encounter. Indirectness: No indirectness Further details: 1. Seizure type (generalised tonic-clonic versus other): (n=48) Intervention 2: Self-management. Standard care. Duration 3 months. Concurrent medication/care: Advised on treatment as per the usual outpatient prescription. Indirectness: No indirectness Further details: 1. Seizure type (generalised tonic-clonic versus other):
Funding	Academic or government funding (Commercial application developed by Timble Technologies pvt ltd)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PHONE APPLICATIONS versus SELF MANAGEMENT Protocol outcome 1: Medicines adherence at 12 months - Actual outcome: Proportion adherent at 3 months; Group 1: 33/48, Group 2: 19/48; Comments: Only the post-intervention raw data will be analysed for this outcome, rather than a comparison of the change in proportion adherent in each group from baseline to 3 months (which is provided in the study). As the proportion adherent in each group at baseline differed, this will be noted in the quality assessment as potentially indicative of selection bias. Risk of bias: All domain - Very high, Selection - Very high, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - Proportion in each group with comorbidities was identical. No missing data described for this outcome.; Indirectness of outcome: No indirectness; Baseline details: Proportion adherent at baseline was 16.7% in the mobile application group and 29.2% in the control group. Groups also differed at baseline for marital status and education.; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life at 12 months; Mortality including SUDEP at 12 months; Healthcare resource impact (including changes in medication use, consultations and hospitalisations) at 12 months; Frequency of

	seizure associated risks (such as falls and fractures) at 12 months; Seizure frequency (50% or greater reduction in seizure frequency) at 12 months at 12 months; Adverse events (total adverse events, anxiety (measured using a validated scale), and false alarms (each reported separately)) at N/A

Study	**Si 2020 trial: Si 2020[31]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=380)
Countries and setting	Conducted in China; Setting: Epilepsy Centre of the Sichuan Provincial People's Hospital
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Adult patients (more than 18 but less than 60 years of age) with epilepsy of more than one year's duration who had more than three seizures during the 6 months preceding recruitment; participants also needed to reside in the study area, be proficient in the use of smartphones, and have provided written consent to participate in the study.

Exclusion criteria	Severe intellectual and developmental impairment, neurologic disease, psychosis, or other severe medical conditions (e.g., tumours, fractures); illiteracy or mental incompetence; and current participation in another research project.
Recruitment/selection of patients	Eligible patients from Sichuan Provincial People's Hospital epilepsy registry database were recruited consecutively and randomised using permuted blocks.
Age, gender and ethnicity	Age - Mean (SD): App group: 32.3 (11.0); control group: 32.2 (11.6). Gender (M:F): 206 men and 174 women. Ethnicity: Not stated
Further population details	1. Age (children, young people, adults, older people): 2. Ethnicity (BAME versus not BAME): 3. Learning disabilities (people with learning disabilities and people without learning disabilities): 4. Socioeconomic background:
Indirectness of population	No indirectness
Interventions	(n=190) Intervention 1: Track and monitor - Tracking and monitoring device. Smartphone epilepsy management app built on the WeChat platform, one of the leading Chinese multipurpose messaging and social media apps. the core functions of the app were a medication calendar, online educational forums and blogs, a facility for prompt online reporting of seizures and online consultations (messaging or video call), and online questionnaires. Duration 6 months. Concurrent medication/care: Before the intervention commenced, the participants in the app group were trained by a staff member in how to use the app; the participants in the control group received only a routine clinic consultation. Participants in the control group were asked to report their seizure frequency each month by phone call, email, or in person at the clinic. The seizure frequency of participants in the app group was recorded by online self-report in the app and confirmed by the same methods as for the control group. Indirectness: No indirectness Further details: 1. Seizure type (generalised tonic-clonic versus other): (n=190) Intervention 2: Self-management. Usual care. Duration 6 months. Concurrent medication/care: Participants were asked to report their seizure frequency each month by phone call, email, or in person at the clinic. Indirectness: No indirectness

	Further details: 1. Seizure type (generalised tonic-clonic versus other):
Funding	Academic or government funding (Supported by the National Natural Science Foundation of China (NSFC, 81701269).)

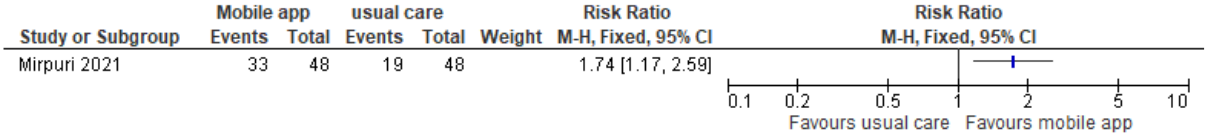
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRACKING AND MONITORING DEVICE versus SELF MANAGEMENT
Protocol outcome 1: Seizure frequency (50% or greater reduction in seizure frequency) at 12 months at 12 months
- Actual outcome: Reduction in seizure frequency of ≥50%, <75% (patient self-report) at 6 months; Group 1: 21/190, Group 2: 60/190
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Very high, Comments - Of 380 randomised participants, 327 (86.1%) completed the follow-up assessment (app group, 176; control group, 151). However, for seizure frequency outcomes, data are provided for the full randomised numbers (190 in each group) by ITT analysis. ; Indirectness of outcome: No indirectness ; Baseline details: Groups were comparable for sex, age, education level, unemployed, residency (urban area), currently married, seizure onset age, disease duration (years), seizure type, baseline seizure frequency (per 6 months), monotherapy and Chinese Epilepsy Self-Management Scale score; Blinding details: The study schedule (intervention allocation) was not revealed to the research staff who collected and analysed the data; participants were asked to not reveal their allocation to the interviewer who undertook their follow-up assessments; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Reduction in seizure frequency of ≥75%, <100% (patient self-report) at 6 months; Group 1: 22/190, Group 2: 8/190
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Very high, Comments - Of 380 randomised participants, 327 (86.1%) completed the follow-up assessment (app group, 176; control group, 151). However, for seizure frequency outcomes, data are provided for the full randomised numbers (190 in each group) by ITT analysis. ; Indirectness of outcome: No indirectness ; Baseline details: Groups were comparable for sex, age, education level, unemployed, residency (urban area), currently married, seizure onset age, disease duration (years), seizure type, baseline seizure frequency (per 6 months), monotherapy and Chinese Epilepsy Self-Management Scale score; Blinding details: The study schedule (intervention allocation) was not revealed to the research staff who collected and analysed the data; participants were asked to not reveal their allocation to the interviewer who undertook their follow-up assessments; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Reduction in seizure frequency of 100% (patient self-report) at 6 months; Group 1: 54/190, Group 2: 22/190
Risk of bias: All domain - Very high, Selection - High, Blinding - Very high, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Very high, Comments - Of 380 randomised participants, 327 (86.1%) completed the follow-up assessment (app group, 176; control group, 151). However, for seizure frequency outcomes, data are provided for the full randomised numbers (190 in each group) by ITT analysis. ; Indirectness of outcome: No indirectness ; Baseline details: Groups were comparable for sex, age, education level, unemployed, residency (urban area), currently married, seizure onset age, disease duration (years), seizure type, baseline seizure frequency (per 6 months), monotherapy and Chinese Epilepsy Self-Management Scale score; Blinding details: The study schedule (intervention allocation) was not revealed to the research staff who collected and analysed the data;

participants were asked to not reveal their allocation to the interviewer who undertook their follow-up assessments; Group 1 Number missing: 0; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life at 12 months; Mortality including SUDEP at 12 months; Medicines adherence at 12 months; Healthcare resource impact (including changes in medication use, consultations and hospitalisations) at 12 months; Frequency of seizure associated risks (such as falls and fractures) at 12 months; Adverse events (total adverse events, anxiety (measured using a validated scale), and false alarms (each reported separately)) at N/A

Appendix E: Forest plots

Mobile phone application versus usual care for ASM adherence at 3 months

Figure 2: Anti-seizure medication adherence at 3 months



Smartphone application versus usual care for reduction in seizure frequency at 6 months

Figure 3: Reduction in seizure frequency at 6 months: >50% and <75%

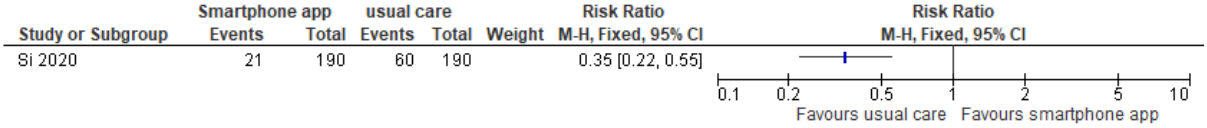


Figure 4: Reduction in seizure frequency at 6 months: >75% and <100%

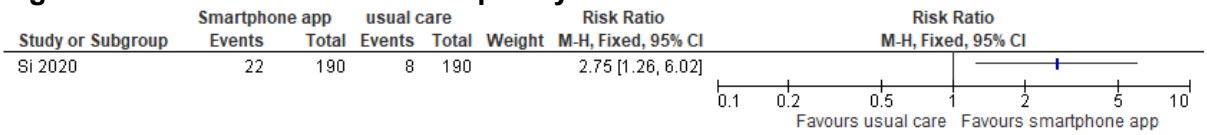
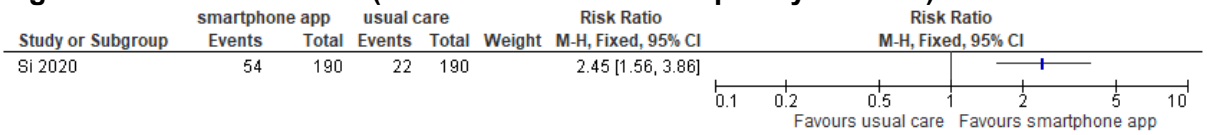


Figure 5: Seizure freedom (reduction in seizure frequency of 100%) at 6 months



Appendix F: GRADE tables

Table 6: Clinical evidence profile: mobile phone application versus usual care for ASM adherence at 3 months

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mobile phone app	Usual care	Relative (95% CI)	Absolute		
ASM adherence at 3 months (follow-up 3 months; assessed with: MGLS adherence scale)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	33/48 (68.8%)	19/48 (39.6%)	RR 1.74 (1.17 to 2.59)	293 more per 1000 (from 67 more to 629 more)	⊕OOO VERY LOW	CRITICAL

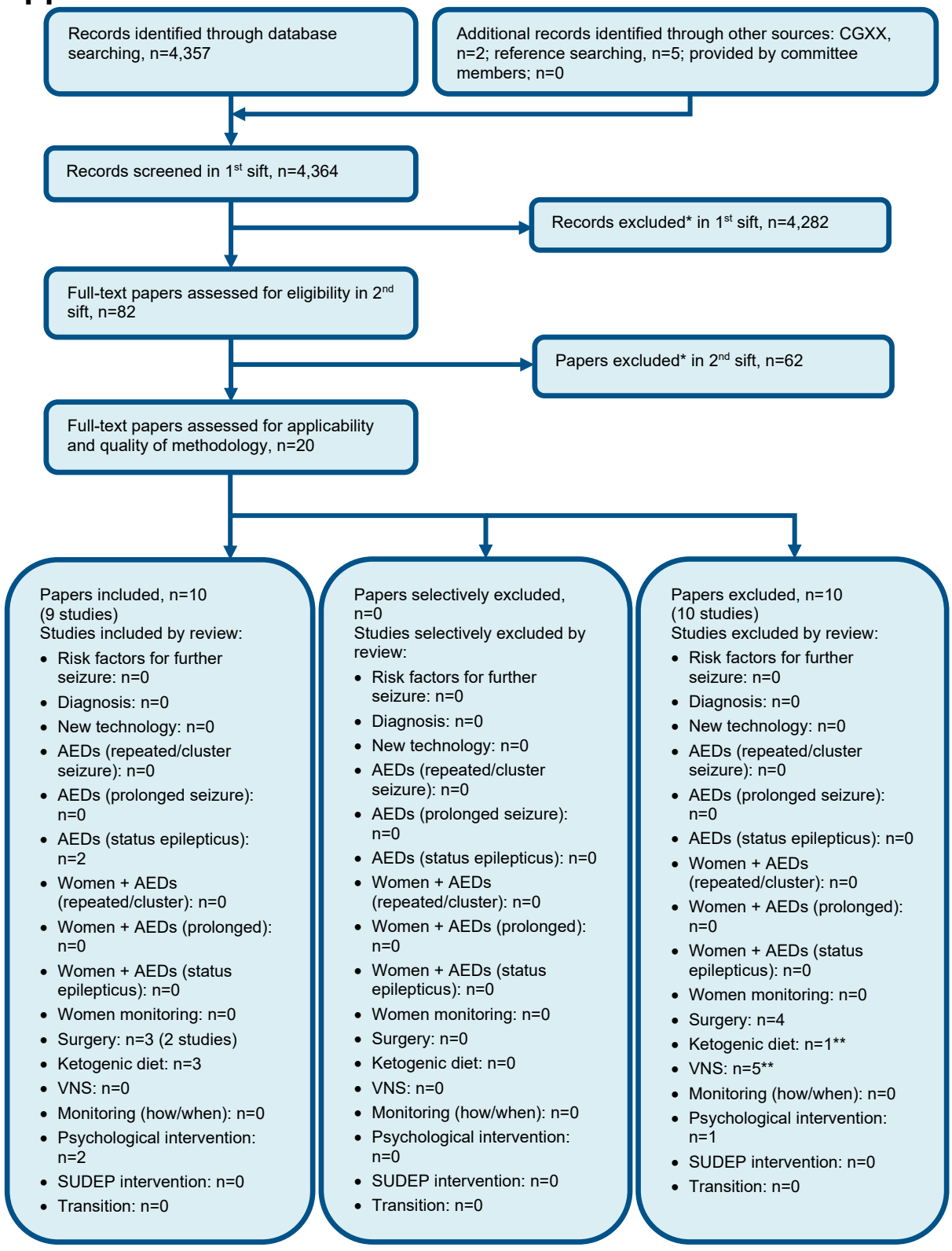
[1] No description of sequence generation. Groups differed at baseline for the outcome (adherence), marital status and education.
[2] Downgraded by 1 increment as the confidence interval crossed one MID.

Table 7: Clinical evidence profile: Smartphone app versus usual care for reduction in seizure frequency at 6 months

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Smartphone app	Usual care	Relative (95% CI)	Absolute		
Reduced seizure frequency (50 to 74%) (follow-up 6 months; assessed with: self-report)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	21/190 (11.1%)	60/190 (31.6%)	RR 0.35 (0.22 to 0.55)	205 fewer per 1000 (from 142 fewer to 246 fewer)	⊕⊕OO LOW	IMPORTANT
Reduced seizure frequency 75 to 99% (follow-up 6 months; assessed with: self-report)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	22/190 (11.6%)	8/190 (4.2%)	RR 2.75 (1.26 to 6.02)	74 more per 1000 (from 11 more to 211 more)	⊕⊕OO LOW	IMPORTANT
Reduced seizure frequency of 100% (seizure freedom) (follow-up 6 months; assessed with: self-report)												
1	randomised trials	very serious[1]	no serious inconsistency	serious indirectness[2]	no serious imprecision	none	54/190 (28.4%)	22/190 (11.6%)	RR 2.45 (1.56 to 3.86)	168 more per 1000 (from 65 more to 331 more)	⊕⊕OO LOW	IMPORTANT
								11.6%		168 more per 1000 (from 65 more to 332 more)		

[1] Block randomisation with known block size, introducing predictability. No blinding for assessment of a subjective outcome.
[2] App was limited to Chinese language and built on a Chinese social media platform.

Appendix G: Health economic evidence 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 number of full text articles assessed for applicability and quality of methodology.

Appendix H: Health economic evidence tables

None

Appendix I: Health economic model

No original economic modelling was undertaken.

Appendix J: Excluded studies

J.1 Excluded clinical studies

Table 9: Studies excluded from the clinical review

Study	Exclusion reason
Arends 2018[1]	Incorrect study design, cohort study
Beniczky 2021[2]	Automated seizure detection using wearable devices: A clinical practice guideline Systematic review
Borusiak 2016[3]	No outcomes as per protocol
Bruno 2020[4]	study design (survey) self-report with no multivariate analysis.
Conradsen 2012[5]	Incorrect study design, cohort study
Curcio 2015[6]	Incorrect study design; crossover RCT
Diiorio 2009[7]	Incorrect interventions
Ernst 2016[8]	Incorrect study design, NRS, comparing women with epilepsy to healthy controls
Escoffery 2018[9]	Incorrect comparisons
Johansson 2018[10]	Systematic review, studies individually assessed for inclusion, cohort studies
Johansson 2019[11]	Incorrect study design, prospective cohort
Kiral-kornek 2018[12]	Incorrect study design, incorrect comparisons
Kramer 2011[13]	Incorrect study design, prospective cohort
Lazaro 2020[14]	Armband device prototype pilot study
Leenen 2014[15]	Protocol
Liporace 1998[16]	Incorrect study design, cohort
Lua 2012[17]	Incorrect study design, sample of patients randomly selected from each hospital to receive text messages
Lua 2013[18]	Incorrect interventions - printed epilepsy education information vs printed epilepsy education information plus texts with educational information
Luedke 2019[19]	Systematic review, studies individually assessed for inclusion, incorrect interventions

Lutz 2005[20]	Incorrect study design; NRS
Maguire 2020[21]	Systematic review which included studies already included or excluded from this review
Mcgonigal 2002[22]	Incorrect interventions, no relevant outcomes;
Modi 2016[24]	Less than minimum duration; 1 month follow up
Patterson 2015[26]	Incorrect study design, validation study
Pediaditis 2012[27]	Incorrect intervention
Ranganathan 2015[28]	Incorrect study design, literature review
Ryvlin 2018[29]	Incorrect study design, literature review
Sajatovic 2018[30]	SMART intervention vs waitlist control
Tatum 2016[32]	Incorrect study design; NRS, prospective and retrospective
Van andel 2015[33]	Incorrect study design, Cohort
Van ness 2019[34]	Incorrect study design, commentary on abstracts
Zhao 2018[35]	Incorrect study design, literature review

J.2 Excluded 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 10: Studies excluded from the health economic review

Reference	Reason for exclusion
None.	

Appendix K: Research recommendations

Research question

What is the clinical and cost-effectiveness of digital health technologies (for example, night monitors, wearable devices and Apps) in people with epilepsy?

Why this is important

Seizures can start with minimal warning. This puts people with epilepsy at risk of injury and death (including SUDEP). Digital health technologies include electronic seizure diaries, wearable and immediate seizure detection (watches), surveillance devices such as night monitors, and self-empowerment and decision support apps. Costs vary, and devices are rarely prescribed/funded by the NHS.

This is an important and emerging area for research because of the increase in the availability and range of technologies. It is not known whether their use improves outcomes for children, young people and adults with epilepsy. Amongst available digital health technologies, manufacturers make claims about potential or actual benefits, but it is not known if they are effective, cost-effective or user-friendly. Importantly, the impacts of unintended consequences such as delayed care, unnecessary health care utilisation, false alarms, and anxiety are uncertain.

Rationale for research recommendation

Importance to 'patients' or the population	Little is known about the effectiveness of available digital health technologies in reducing the risk of death and injury in children, young people and adults who have seizures. Families seek advice, and in the absence of evidence, this is hard to provide. Many products are marketed and continue to be developed. There is an impact on the quality of life of parents/carers who for example, watch their sleeping children/charges and get very little sleep themselves or who try to track the whereabouts and wellbeing of people who have seizures without reducing their independence. Digital health technology has the potential to make an important contribution to epilepsy care by identifying impending or ongoing seizures, alerting carers, and accurately recording the frequency and duration of seizures. Some companies report solutions to record stress levels, mood change and sleep quality. Digital health technologies could facilitate self-management and contribute to clinical decision support, thereby contributing to improved outcomes and possibly reduce emergencies and death.
Relevance to NICE guidance	It is not known whether the use of available digital health technologies improves outcomes for children, young people and adults with epilepsy. Developers and manufacturers make claims about potential or actual benefits, but it is not known if they are effective, cost-effective or user-friendly. Importantly, the impacts of unintended consequences such as delayed care, unnecessary health care utilisation, false alarms, and anxiety are uncertain. Future guidelines should offer recommendations related to when particular technologies can offer benefit, or caution about their limitations.

Relevance to the NHS	The outcome would help clarify what technology could be procured for NHS patient use. It would assist in the development of risk management strategies for individuals in their care plan and support patient safety and seizure management. There could be an impact on remote delivery of NHS services and improved data quality where for example, digital technologies communicate with electronic patient records.
National priorities	High Digital health technologies may have particular benefits for people with learning disabilities where early mortality is more common, and LeDeR reports seizures as a frequent cause. There is the potential to support young people leaving home into independent life, including university or supported living arrangements in accordance with the NHS Long Term Plan.
Current evidence base	There is very little long-term data on the use of digital technologies, including monitoring technologies, in managing epilepsies. The committee agreed no practice recommendation could be made but felt strongly that a research recommendation was required.
Equality considerations	Some of the available technologies are wearable, and consideration should be given to their suitability across all age groups and when people have other disabilities e.g., learning disabilities. Health inequality could arise due to some technology being very expensive. Some devices are fragile and may not be suitable for those who may unintentionally damage them. Monitoring may not be acceptable to people wanting privacy.

Modified PICO table

Population	Children, young adults and adults with epilepsy who have active seizures
Intervention	Digital health technologies (DHTs) designed for epilepsy within the following functional classifications: • Alert: DHTs that detect seizure activity and alert the person or carer to take action. Example: wearables. • Track and Monitor: DHTs that enable tracking and monitoring of the condition, often involving data transmission to HCPs (transmission may or may not be automated/remote). Example: remote EEG. • Self-Management: DHTs that aim to improve self-management, including adherence to medication. Example: phone applications. Clinical Decision Support: data collection, calculation and artificial intelligence approaches to inform clinical decision making. Example: Clinical Decision Support Systems.
Comparator	Interventions (above) compared with each other • Usual care (including advice or information giving) / no intervention • Sham devices

Outcome	**Critical** • Mortality, including SUDEP, at 12 months • medicines adherence at 12 months • healthcare resource impact (including changes in medication use, consultations and hospitalisations) at 12 months • frequency of seizure-associated risks (such as falls and fractures) at 12 months • quality of life (measured with a validated scale) at 12 months **Important** • seizure frequency (50% or greater reduction in seizure frequency) at 12 months • adverse events (total adverse events, anxiety (measured using a validated scale), and false alarms (each reported separately)) Outcomes reported at time points of < 3 months will not be extracted (other than for adverse events). If outcomes are reported at multiple time points, the closest time point to 12 months will be extracted.
Study design	Randomised Controlled Trial
Timeframe	12 months
Additional information	None